COVERA™

Vascular Covered Stent

Instructions for Use

BARD | PERIPHERAL VASCULAR

B05872 Rev.3/05-18

DEVICE DESCRIPTION

IMPLANT

The Covera™ Vascular Covered Stent is a flexible, self-expanding endoprosthesis comprised of expanded polytetrafluoroethylene (ePTFE) encapsulating a nitinol (nickel-titanium) stent framework. The inner lumen of the covered stent (blood contacting surface) is carbon impregnated.

The Covera™ Vascular Covered Stent is available in a variety of diameters and lengths and in straight (Figure 1) and flared (Figure 2) configurations. The distal (outflow) end of the flared configuration device is approximately 3 mm larger in diameter than the body and begins approximately 15 mm from the distal end of the device.

Figure 1: Straight Configuration

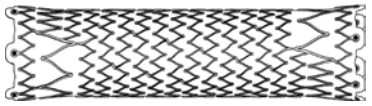


Figure 2: Flared Configuration

Straight device configurations are intended for use in anatomies where the diameter of the outflow vessel is equal to or smaller than the diameter of the inflow vessel. Flared device configurations are intended for use in anatomies where the diameter of the outflow vessel segment is larger than the inflow segment.

COVERED STENT SIZE SELECTION

Special care must be taken to ensure that an appropriately sized device is selected. In the case of a diameter difference between the inflow and the outflow end, always use the graft diameter as the reference vessel diameter.

Table 1: Covered Stent Diameter Selection

Covered Stent Diameter	Recommended Oversizing	Graft Diameter
6 mm	0.5 mm–1.5 mm	4.5 mm–5.5 mm
7 mm	0.5 mm–1.5 mm	5.5 mm–6.5 mm
8 mm	1 mm–2 mm	6 mm–7 mm
9 mm	1 mm–2 mm	7 mm–8 mm
10 mm	1 mm–2 mm	8 mm–9 mm

Note: Covered stent length change ranges from -2% to 3% depending upon covered stent diameter selection. Change in length is a mathematical calculation between the undeployed mounted covered stent inside the delivery system and the expanded labeled-diameter condition. A negative value describes covered stent shortening whereas a positive value describes covered stent elongation.

Covered Stent Length

Ensure the selected covered stent length covers the entire lesion and both ends of the implant extend at least 5 mm into the non-diseased segment of the vessel.

X-RAY MARKERS

Radiopaque ePTFE encapsulated tantalum markers are evenly distributed around the circumference of the proximal and distal ends of the covered stent.

DELIVERY SYSTEM

The delivery system is illustrated in Figure 3. The inner catheter (not visible to the operator) contains the guidewire lumen. An atraumatic tip (A) is affixed to the distal end of the inner catheter which terminates at the female Luer connector (B) at the proximal end of the handle. A proximal white stability sheath (C) is connected to the distal end of the handle and remains stationary throughout the deployment process.

The distal catheter assembly (30 cm in length) consists of two segments. The transparent covered stent delivery sheath (D), housing the compressed covered stent (implant) and a darker brown, smaller diameter extension catheter (E). During covered stent deployment, the entire distal catheter assembly retracts towards the handle while the dark catheter segment is drawn inside the white stability sheath until the covered stent is fully deployed.

Retraction of the distal catheter and deployment of the covered stent is initiated by rotating the large wheel (G) on the handle. The large deployment wheel is used for the initiation of deployment and a slower deployment rate whereas the small deployment wheel (H) may be used for faster deployment after initiation.

Figure 3: Itemized Drawing of the Covera™ Vascular Covered Stent Delivery System

A red safety lock (F) on the handle prevents premature release of the covered stent. Prior to covered stent deployment, the safety lock must be retracted from the locked position into the unlocked position (Figure 4).

.Figure 4: Handle Top View

1 = Red Safety Lock (F)
2 = Large Deployment Wheel for initial and slow deployment (G)
3 = Small Deployment Wheel for faster deployment (H)

Legend for Figures 3 & 4

Reference	Corresponding Information
A	Delivery System Tip
B	Female Luer Port
C	Proximal Stability Sheath (white, stationary)
D	Distal Catheter Sheath Segment (transparent, retracts during deployment) housing the Compressed Covered Stent
E	Distal Catheter Sheath Segment (dark brown, retracts during deployment)
F	Red Safety Lock
G	Large Deployment Wheel (initial and slow deployment)
H	Small Deployment Wheel (fast deployment)

The Covera™ Vascular Covered Stent device is an over-the-wire delivery system. The delivery system is compatible with 0.035 inch guidewires and 8F or 9F introducer sheaths. The delivery system is available in working lengths of 80 cm and 120 cm.

INDICATION FOR USE

The Covera™ Vascular Covered Stent is indicated for use in the treatment of stenoses at the venous anastomosis of ePTFE or other synthetic arterio-venous (AV) access grafts.

CONTRAINDICATIONS

There are no known contraindications for the Covera™ Vascular Covered Stent.

WARNINGS

- This device should be used only by physicians who are familiar with the complications, side effects, and hazards commonly associated with dialysis access shunt revisions and endovascular procedures.
- **DO NOT** expose the covered stent to temperatures higher than 500 °F (260 °C). ePTFE decomposes at elevated temperatures, producing highly toxic decomposition byproducts.
- **DO NOT** use the device if packaging / pouch is damaged.
- The Covera™ Vascular Covered Stent device is supplied **STERILE** and is intended for **SINGLE USE ONLY. DO NOT RESTERILIZE AND/OR REUSE** this device.
- **DO NOT** use in patients with uncorrectable coagulation disorders.
- DO NOT use in patients with bacteremia or septicaemia and/or evidence of graft infection.
- **DO NOT** use in patients that cannot be adequately premedicated and have a known allergy or sensitivity to contrast media.
- **DO NOT** use in patients with known hypersensitivity to nickel-titanium or tantalum.
- **DO NOT** use in patients whose AV Access grafts have been implanted less than 30 days.
- **DO NOT** use the device in patients where full expansion of an appropriately sized PTA balloon catheter could not be achieved during pre-dilation with an angioplasty balloon.
- Placing a covered stent across a vessel side branch may impede blood flow and hinder or prevent future procedures.
- **DO NOT** place a flared covered stent with the flared end in a straight vessel segment since this may lead to flow turbulences. The flared end is not intended to provide additional device fixation.

PRECAUTIONS

- Prior to covered stent implantation refer to the sizing table (Table 1) and read the Instructions for Use. Careful attention should be paid to ensure the device is appropriately sized to the actual graft diameter, taking into account any change to the stated graft diameter that may have resulted from previous interventions. The appropriate length device(s) should be selected so that the stent graft extends beyond the stenosis into at least 5 mm of the non-diseased graft towards the arterial inflow and into the non-diseased vein approximately 5 mm beyond the stenosis.
- The delivery system is not intended for any use other than covered stent deployment.
- The covered stent (implant) cannot be repositioned after total or partial deployment.
- Once partially or fully deployed, the covered stent cannot be retracted or remounted onto the delivery system. Device removal after deployment can only be done with a surgical approach.
- If unusual resistance is met during covered stent system introduction, the system should be removed and another covered stent system should be used.
- **DO NOT** introduce, manipulate or remove the delivery system without an appropriately sized guidewire in place and without fluoroscopic guidance.
- **DO NOT kink or** use a kinked delivery system.
- During covered stent release **DO NOT** hold the 30 cm long distal catheter assembly segment as it must be free to move and slide into the white stability sheath.
- Careful attention by the operator is warranted to mitigate the potential for distal migration of the covered stent during deployment.
- Post dilation of the covered stent must be performed using an appropriately sized PTA balloon catheter to avoid damage to the covered stent. The covered stent cannot be post dilated beyond its labelled diameter. The flared distal end does not require post dilation.
- The effect of placing the device across an aneurysm or a pseudo-aneurysm has not been evaluated.
- The effect of using the device in central veins has not been evaluated.
- The effect of placing the device across a previously placed bare metal stent has not been evaluated.
- The effect of placing the device across the antecubital fossa has not been evaluated.
- The effect of using the device in pediatrics has not been evaluated.
- Vessel angulation was not measured as part of the clinical study, as such limitations in covered stent angulation are unknown.
- **DO NOT** cannulate the covered stent. Notify the patient that the covered stent should not be directly cannulated for hemodialysis and that applying pressure to the implant area should be avoided.
- The device has not been tested for use in an overlapped condition with a bare metal stent or covered stent.
- Higher deployment force may be encountered with longer length covered stents.
- The device has not been tested for tracking and deployment around an AV loop graft.
- Serious complications, such as migration to the heart or lungs, may occur post-discharge when covered stents have not been appropriately sized.
- Stent graft dislodgement may occur during removal of the delivery system; therefore, careful attention should be paid during this portion of the procedure to prevent such occurrences.

MAGNETIC RESONANCE IMAGING (MRI) COMPATIBILITY

Non-clinical testing has demonstrated that the Covera™ Vascular Covered Stent is MR Conditional for placement in the vessels of the arm for all clinically relevant lengths. Based upon the preclinical testing, patients with the Covera™ Vascular Covered Stent can be scanned safely, immediately after placement of this implant, under the following conditions:

- Static magnetic field of 1.5 Tesla or 3.0 Tesla.
- Spatial gradient field of 3000 Gauss/cm or less.
- Maximum whole-body-averaged specific absorption rate (SAR) of 1 W/kg for 15 minutes of scanning.

3.0 Tesla Temperature Rise

In an analysis based on non-clinical testing according to ASTM F2182-11a and computer modeling of a patient, the 6 x 100 mm Covera™ Vascular Covered Stent was determined to produce a potential worst-case temperature rise of 2.9 °C at a whole body SAR of 1 W/kg for 15 minutes of MR scanning in a 3.0 Tesla whole body MR system. Cooling due to blood flow inside the covered stent and perfusion in the vascular bed surrounding the covered stent was included in the assessment of in-vivo temperature rise.

1.5 Tesla Temperature Rise

In an analysis based on non-clinical testing according to ASTM F2182-11a and computer modeling of a patient, the 6 x 100 mm Covera™ Vascular Covered Stent was determined to produce a potential worst-case temperature rise of 2.7 °C at the a whole body SAR of 1 W/kg for 15 minutes of MR scanning in a 1.5 Tesla whole body MR system. Cooling due to blood flow inside the covered stent and perfusion in the vascular bed surrounding the covered stent was included in the assessment of in-vivo temperature rise.

Image Artifact

MR image quality may be compromised if the area of interest is in the exact same area or relatively close to the position of the covered stent. Artifact tests were performed according to ASTM F2119-07. Maximum artifact extended 5.5 mm beyond the covered stent for the spin echo sequence and 5.5 mm for the gradient echo sequence. The lumen was obscured.

Additional Information

Good clinical MR practice should be followed, including placement of padding between the bore wall and the patient and avoiding contact between the hands and the body.

The Covera™ Vascular Covered Stent has not been evaluated in MRI systems with field strengths other than 1.5 or 3.0 Tesla. The heating effect in the MRI environment for fractured covered stents is not known. The presence of other implants or the health state of the patient may require reduction of the MRI limits listed above.

POTENTIAL COMPLICATIONS AND ADVERSE EVENTS

Complications and Adverse Events associated with the use of the Covera™ Vascular Covered Stent may include the usual complications associated with endovascular stent and covered stent placement and dialysis shunt revisions.

Potential complications may include, but are not limited to:

Thrombotic occlusion, restenosis requiring reintervention, pseudoaneurysm, vessel rupture, dissection, extravasation, perforation, pain, infection, hemorrhage, hematoma, arm or hand edema, steal syndrome, congestive heart failure, cerebrovascular accident, allergic reaction, rash, reaction to contrast, fever, sepsis, prolonged bleeding, ventricular fibrillation, face or neck edema, bleeding at access site, numbness, venous spasm, hemoptysis and death.

Covered stent specific events that could be associated with clinical complications include:

Misplacement, migration, embolism, fracture, kinking and insufficient covered stent expansion.

Delivery System specific events that could be associated with clinical complications include:

Bond joint failures, detachment of parts, incompatibility with accessory devices, premature deployment, inaccurate deployment, failure to

deploy, high deployment forces, delivery system kinking, poor visibility under fluoroscopy, inability to track to target location and blood leakage from delivery system.

HOW SUPPLIED

The Covera™ Vascular Covered Stent is supplied sterile (by ethylene oxide gas). For single use only.

STORAGE

Store in a cool, dry place. Keep away from sunlight. **DO NOT** use the device after the "Use By" date specified on the label.

DISPOSAL INSTRUCTIONS

After use, this product may be a potential biohazard. Handle and dispose of in accordance with accepted medical practice and applicable local, state and federal laws and regulations.

CLINICAL USE INFORMATION

- Read all instructions for use thoroughly.
- Antibiotic therapy may be prescribed at the physician's discretion.
- The Covera™ Vascular Covered Stent should be used only by physicians who are familiar with the complications, side effects, and hazards commonly associated with dialysis access shunt revisions and endovascular procedures.

MATERIALS REQUIRED FOR THE Covera™ VASCULAR COVERED STENT PROCEDURE

- Heparinized saline
- Sterile Luer lock syringes
- Contrast medium
- 0.035 inch guidewire of appropriate length to allow safe delivery of the covered stent and removal of the delivery system
- Introducer sheath with appropriate inner diameter
- Diagnostic catheters and accessories
- Balloon angioplasty catheter for pre and/or post dilation
- Inflation device

INSTRUCTIONS FOR USE

Preparation

1. After removal from the packaging, verify that the safety lock is in the locked position.
2. Using standard endovascular access techniques and fluoroscopy, access the target vessel from a site that permits the straightest possible path to the target lesion and advance an 0.035 inch guidewire across the target lesion.
3. Pre-dilate the stenosis with a PTA balloon catheter of appropriate length and diameter for the lesion to be treated.
4. Select the appropriate covered stent diameter based on the sizing table (Table 1).
5. Examine the packaging and delivery system to determine whether there is any damage or whether the sterile barrier has been compromised. Do not use the device if any of these conditions are observed.
6. Flush the delivery system through the Luer port at the proximal end of the handle with sterile saline until the saline exits the tip of the system (Figure 5).

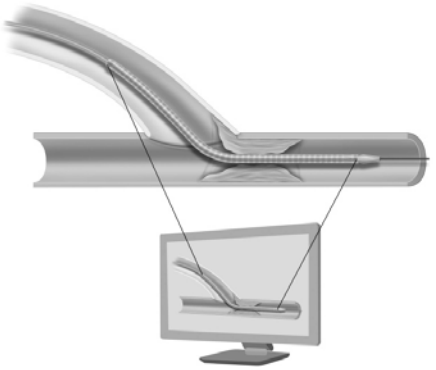
Figure 5

NOTE: Do not retract the red safety lock until the covered stent is positioned across the lesion and ready to be deployed.

Delivery System Introduction

7. Under radiographic guidance, advance the delivery system over the guidewire past the target lesion and then pull back slightly on the entire system to attain correct positioning of the radiopaque markers. Use the radiopaque covered stent ends to center the covered stent across the lesion (Figure 6).

Figure 6

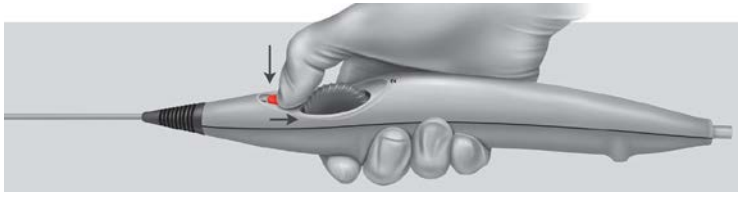


NOTE:
Ensure the selected covered stent length covers the entire lesion and both ends of the implant extend at least 5 mm into the non-diseased segment of the vessel.

Covered Stent Deployment

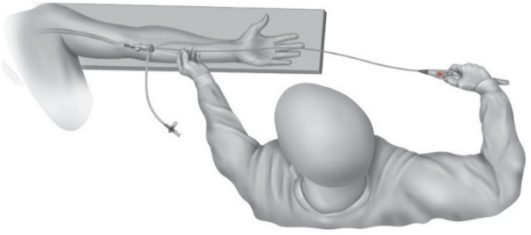
8. Prior to covered stent deployment, unlock the red safety lock (Figure 7) by pressing down and pulling it back towards the end of the grip from the locked position into the unlocked position. Ensure that the red safety lock is completely retracted and that the symbol for the unlocked position is fully visible.

Figure 7



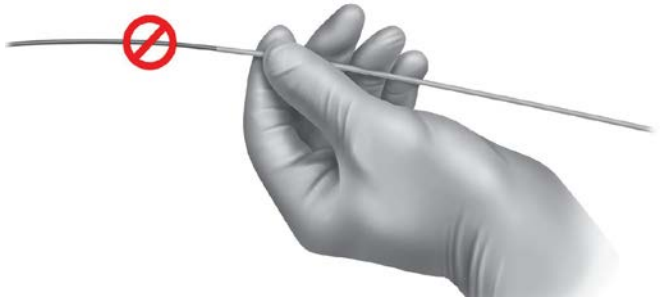
9. With your free hand, maintain a stationary hold on the white stability sheath during covered stent deployment and adjust for placement accuracy if necessary (Figure 8). Hold the white stability sheath as close as possible to the introducer without touching the dark brown moving catheter of the distal catheter assembly. Maintain the remainder of the white stability sheath (segment between left and right hand on illustration) relaxed and avoid tension.

Figure 8



IMPORTANT:
Do not touch the distal catheter assembly (i.e. the dark brown catheter segment) during covered stent deployment since this may interfere with covered stent deployment and may lead to misplacement (Figure 9).

Figure 9

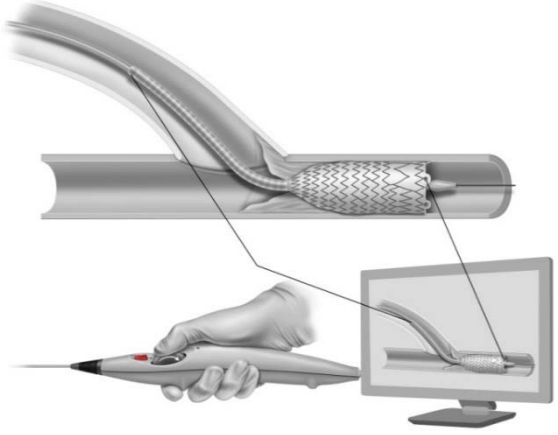


10. Slowly and carefully activate the covered stent release mechanism by rotating the large wheel on the top of the handle backwards.

NOTE: For accurate placement, subtle repositioning may be performed during initial wheel activation while the covered stent is still compressed in the catheter.

After deployment of approximately 15 mm, wait several seconds to allow the distal end of the covered stent to fully expand. Ensure the covered stent has wall apposition before completing deployment (Figure 10).

Figure 10



11. Complete the covered stent deployment with either the large wheel (slow release) or switch to the small wheel for faster release.

    NOTE: Higher friction forces may occur with longer length covered stents.

12. Carefully remove the delivery system under fluoroscopy while maintaining guidewire access.

13. Post dilate the covered stent with an angioplasty balloon sized appropriately as to ensure complete wall apposition to the reference vessel. Avoid balloon dilation in the healthy, non-stenosed segment of the vein.

    NOTE: It is recommended to advance the PTA balloon catheter through the deployed covered stent under fluoroscopy to ensure that the covered stent remains well positioned.

14. Using standard procedures, verify location and patency of the covered stent.

PATIENT IMPLANT INFORMATION CARD

A Patient Implant Information Card is provided within the product packaging.

The patient, implant and hospital information should be recorded on the card. Ensure a peel-away sticker from the product label is placed on the card before it is given to the patient. The sticker contains important information about the implant.

The patient should carry the implant information card with them and present it to any medical personnel involved in their care.

SUMMARY OF CLINICAL STUDY

The COVERA™ Vascular Covered Stent was evaluated in the prospective, multi-center, non-randomized, single-arm, AVeVA study for the treatment of stenotic lesions at the graft-vein anastomosis of hemodialysis patients dialyzing with an AV graft. Safety and effectiveness measures of subjects receiving the COVERA™ Vascular Covered Stent are presented with information derived from clinical literature as well as other prospective pivotal and post-market studies to provide clinical context for the results.

A total of 181 patients were screened for eligibility of which 110 were treated with the COVERA™ Vascular Covered Stent at 14 U.S. investigational sites. The primary reason for exclusion from the study was failure to meet the target lesion angiographic specific criteria. The endpoint analyses were conducted on subjects who had reached pre-specified follow-up time points: 30 days for primary safety and 6 months for effectiveness. Subjects will be followed through 24 months.

Study Endpoints

The primary safety endpoint was a measure based on safety through 30 days post index procedure. Safety is defined as freedom from any adverse events (AEs) (Clinical Events Committee (CEC) adjudicated), localized or systemic, that reasonably suggests the involvement of the AV access circuit (not including stenosis or thrombosis) that require or result in any of the following alone or in combination: Additional interventions (including surgery); in-patient hospitalization or prolongation of an existing hospitalization; or death. The primary safety endpoint was evaluated against a PG of 88%.

The effectiveness endpoints of the study included measures based on Target Lesion Primary Patency (TLPP), Access Circuit Primary Patency (ACPP) and Post-intervention Secondary Patency (Secondary Patency) through 6 months post index procedure. These endpoints are presented with data from previous studies of the same indication to provide clinical context. TLPP was defined as the interval following the index intervention until the next clinically driven reintervention at or adjacent to (approximately 5 mm proximal or distal to, by visual estimation) the original treatment site or until the extremity was abandoned for permanent access. Primary patency ended when any of the following occurred: a) clinically driven reintervention in the treatment area; b) thrombotic occlusion within the treatment area; c) surgical intervention that excludes the original treatment area from the AV access circuit; and/or d) abandonment of the AV access graft due to inability to treat the original treatment area. ACPP was defined as the interval following the index intervention until the next access thrombosis or clinically driven repeated intervention. ACPP ended with a clinically driven reintervention anywhere within the access circuit; from the arterial inflow to the SVC-right atrial junction. Vessel rupture caused by PTA was not a TLPP or ACPP failure unless achieving hemostasis also caused thrombosis or required any treatment other than the study device. Secondary Patency was defined as the interval after the index intervention until the access is abandoned. Multiple repetitive treatments could be included in secondary patency.

Additional endpoints include: (1) TLPP through 30 days, 90 days, 12 months, 18 months and 24 months; (2) ACPP through 30 days, 90 days, 6 months, 12 months, 18 months and 24 months; (3) Rate of device and procedure related AEs involving the AV access circuit through 90 days, 6 months, 12 months, 18 months and 24 months; (4) Total Number of AV Access Circuit Reinterventions through 30 days, 90 days, 6 months, 12 months, 18 months and 24 months; (5) Total Number of Target Lesion Reinterventions through 30 days, 90 days, 6 months, 12 months, 18 months and 24 months; (6) Index of Patency Function (IPF) evaluated at 30

days, 90 days, 6 months, 12 months, 18 months and 24 months; (7) Index of Patency Function – Target Lesion (IPF-T) evaluated at 30 days, 90 days, 6 months, 12 months, 18 months and 24 months; (8) Secondary Patency evaluated through 30 days, 90 days, 12 months, 18 months and 24 months; (9) Acute Technical Success; and (10) Acute Procedure Success (Anatomic and Clinical Success). Information presented below includes data through 6-month follow-up as well as site reported data through 12-month follow-up.

Information was also collected regarding vessel injury, deaths, and device malfunctions.

For sample size determinations, safety at 30 days assumed a rate of 98% for subjects treated with the study device and the PG was set at 88% with attrition rate assumptions of 5%. A sample size of 109 subjects provided 104 evaluable subjects. The sample size was adequate to provide descriptive statistics related to the effectiveness and secondary endpoints as well.

Patients Studied

Eligible patients presented with a hemodynamically significant stenosis (≥ 50% by visual estimate) accompanied by a hemodynamic functional or clinical abnormality at the AV-access, graft-vein anastomosis. To be included in the study, the target lesion was required to be ≤ 9 cm in length and have a reference vessel diameter (of the adjacent, non-stenotic vessel) between 5.0 and 9.0 mm. The AV access graft had to be located in an arm, must have been implanted for ≥ 30 days, and must have undergone at least one successful dialysis session prior to the index procedure. Thrombosed and non-thrombosed grafts were included in the study.

Patients were excluded from the study if they had additional stenotic lesions (≥ 50%) in the venous outflow (> 3 cm from the edge of the target lesion) that were not successfully treated (defined as < 30% residual stenosis) prior to treating the target lesion, if they had an aneurysm or pseudoaneurysm present within the target lesion, or if they had a target lesion located such that treatment would require the Covera™ Vascular Covered Stent be deployed across the elbow joint or within a stent or stent graft.

Methods

All patients underwent a clinical evaluation at screening (prior to index procedure); treated subjects underwent a clinical evaluation prior to hospital discharge. A telephone screen to the subject and the dialysis center was performed at 30 days, 90 days, and 6 months, to collect data on the AV access circuit status, AEs, reinterventions performed, and changes in applicable medications. Site investigators and dialysis centers followed their institutional procedures for hemodialysis access surveillance. Investigational sites were responsible for collecting follow-up information from subjects, dialysis centers, and any outside institutions that conducted secondary interventions on study subjects. Additionally, the majority of secondary interventions were conducted at the investigational sites. An independent CEC reviewed all AEs and performed adjudications of these events in accordance with their charter.

Results

SUBJECT DEMOGRAPHICS AND BASELINE CHARACTERISTICS

Subject demographics and baseline characteristics are consistent with those in the pivotal and post market (RENOVA) studies of the FLAIR® device. When comparing to the previous studies, specific areas of similarity include: age, sex, graft location in the left, upper arm, as well as comparable mean target lesion length and target lesion percent stenosis. The most common stent graft diameter across all studies was an 8 mm, and the most common stent graft length utilized was in the range of 40 – 60 mm. A notable difference between the studies is that only the AVeVA study included thrombosed patients. Specific demographics and baseline characteristics for the subjects enrolled in the AVeVA study are provided in Table 2 through Table 7.

Table 2: Subject Demographics

Age Categories	**n (%)**
< 65 years	52 (47.3)
≥ 65 and < 75 years	31 (28.2)
≥ 75 years	27 (24.5)
Sex	**n (%)**
Male	50 (45.5)
Female	60 (54.5)
Ethnicity	**n (%)**
Hispanic or Latino	24 (21.8)
Not Hispanic or Latino	86 (78.2)
Race	**n (%)**
American Indians/Alaska Native	1 (0.9)
Asian	4 (3.6)
Black or African American	44 (40.0)
White	60 (54.5)
Other	1 (0.9)
BMI Categories	**n (%)**
< 30	68 (61.8)
≥ 30	42 (38.2)

Note that N=110 subjects.

Table 3: Medical History

Risk Factors	**n (%)**
Subjects With at Least One Risk Factor	*110 (100.0)*
Diabetes - Total	72 (65.5)
Diabetes (Type 1)	4 (3.6)
Diabetes (Type 2)	68 (61.8)
Dyslipidemia	62 (56.4)
Hypertension	108 (98.2)
Cigarette Smoking - Total	43 (39.1)

Cigarette Smoking - Current	9 (8.2)
Cigarette Smoking - Former	34 (30.9)
Cardiovascular Disease	**n (%)**
Subjects With at Least One Type of Cardiovascular Disease	*80 (72.7)*
Congestive Heart Failure	32 (29.1)
Stroke	21 (19.1)
Coronary Artery Disease (CAD)	40 (36.4)
Myocardial Infarction (MI)	9 (8.2)
Transient Ischemic Attack (TIA)	11 (10.0)
Valvular Heart Disease	5 (4.5)
Aortic Disease	1 (0.9)
Deep Vein Thrombosis (DVT)	7 (6.4)
Peripheral Arterial/Vascular Disease (PAD) (PVD)	14 (12.7)
Atrial Fibrillation (A-Fib)	14 (12.7)
Other	33 (30.0)
Other Disease	**n (%)**
Subjects With at Least One Other Disease	*105 (95.5)*
Bleeding Disorder	4 (3.6)
Cancer	20 (18.2)
Steal Syndrome	1 (0.9)
Other	103 (93.6)

Note that N=110 subjects

Table 4: Description of Access Circuit

Target Limb	**n (%)**
Left Arm	88 (80.0)
Right Arm	22 (20.0)
Graft Location	**n (%)**
Forearm	2 (1.8)
Upper Arm	108 (98.2)
Arterial Anastomosis	**n (%)**
Axillary	14 (12.7)
Brachial	94 (85.5)
Radial	1 (0.9)
Ulnar	1 (0.9)
Venous Anastomosis	**n (%)**
Axillary	54 (49.1)
Basilic	44 (40.0)
Brachial	9 (8.2)
Cephalic	2 (1.8)

Median Cubital	1 (0.9)
Graft Configuration	**n (%)**
Loop	33 (30.0)
Straight	77 (70.0)
Graft Material	**n (%)**
Bovine	10 (9.1)
ePTFE	85 (77.3)
Other	4 (3.6)
Unknown [1]	11 (10.0)
Graft Tapered?	**n (%)**
Yes	32 (29.1)
No	78 (70.9)
Graft Diameter (mm)	**N=107 [2]**
Mean (SD)	6.6 (0.77)
Min - Max	4.0 - 9.0
Thrombus Present at Index Procedure?	**n (%)**
Yes	28 (25.5)
No	82 (74.5)
Non-Target Lesions Present at Index Procedure?	**n (%)**
Yes	44 (40.0)
No	66 (60.0)

Note that N=110 subjects unless otherwise noted.
[1] For subjects whose graft material was indicated to be unknown it was verified to be nonautologous.
[2] For three (3) subjects the diameter of the graft at the time of implantation was unknown.

Table 5: Previous Index AV Access Circuit Interventions

	n/N (%)
Number of subjects who underwent any interventions of the index AV Access Circuit within 30 days	16/110 (14.5)
Number of Previous Interventions within 30 days prior	**n**
Total Number of Previous Interventions	22
Number of Subjects with Previous Interventions	16
Intervention	**n/n (%)**
Standard PTA	10/22 (45.5)
Thrombolysis/Thrombectomy	12/22 (54.5)
Involved Target Lesion	**n/n (%)**
Yes	16/22 (72.7)
No	6/22 (27.3)
Location	**n/n (%)**
Anastomotic	11/22 (50.0)
Basilic Vein Outflow	3/22 (13.6)

Intra-Graft	4/22 (18.2)
Subclavian Vein	1/22 (4.5)
Other	3/22 (13.6)

Note that some subjects had multiple interventions.

Table 6: Target Lesion Characteristics

Lesion Characteristics	n (%)
de Novo	31 (28.2)
Re-stenotic	79 (71.8)

Note that N=110 target lesions.

	N	Mean (SD)	Min-Max
Number of Lesions within Target Lesion Area	110	1.0 (0.16)	1 - 2
Target Lesion Length (mm)	110	24.1 (15.27)	2 - 70
Target Lesion Stenosis (%)	110	71.5 (14.82)	50.0 - 100.0

Table 7: Summary of Study Device* Details

Stent Graft Configuration	n (%)
Flared	92 (83.6)
Straight	18 (16.4)
Stent Graft Diameter	**n (%)**
7 mm	10 (9.1)
8 mm	62 (56.4)
9 mm	33 (30.0)
10 mm	5 (4.5)
Stent Graft Length	**n (%)**
40 mm	54 (49.1)
60 mm	47 (42.7)
80 mm	9 (8.2)

* Only one Covera™ Vascular Covered Stent could be implanted in each patient per the study protocol.

Subject Accountability

Investigators treated 110 subjects at 14 sites. One-hundred and eight (108) of the 110 treated subjects completed their 30-day follow-up contact. Of the two (2) subjects that did not complete their 30-day follow-up contact, one (1) subject was withdrawn due to the investigator's decision and one (1) subject died.

One-hundred and two (102) of the 110 treated subjects completed their 6-month follow-up contact. Of the six (6) additional subjects that did not complete their 6-month follow-up contact, one (1) subject was lost to follow-up and five (5) additional subjects died.

Deaths were not considered to be related to the study device or the index procedure. The denominators used in safety and effectiveness analyses are different, and are described in respective sections.

Summary of Safety

The performance goal for the composite primary safety endpoint was met. The proportion of subjects free from primary safety events was 96.4% which met the PG of 88% (p-value=0.0021).

Table 8: Freedom from any Safety Event through 30 days (All Treated Subjects)

Primary Safety Endpoint	Proportion n/N (%) [3]	90% CI (%) [2]	P-value [1]
Proportion Free from Primary Safety Events	106/110 (96.4)	(91.9, 98.7)	0.0021
Had Failure:			
Death	0		
Required Additional Intervention	4/110 (3.6)		
In-Patient Hospitalization or Prolongation	1/110 (0.9)		

[1] The p-value is compared to the PG (88%) and computed using the exact binomial test.
[2] 90% confidence interval is calculated using the exact binomial method.
[3] Two subjects missed the 30-day follow-up but were included in the denominator because they were followed for at least 23 days.
Note: The safety events are based on CEC adjudicated outcomes.

Four (4) subjects experienced safety events which counted as failures of the primary safety endpoint. One (1) subject experienced two (2) vessel ruptures in their AV access circuit during two (2) separate reinterventions performed after the index procedure. Another subject was reported to have an open wound infection proximal to the AV graft and as a precautionary measure their graft (and as such the previously implanted study device at the anastomosis) was explanted and discarded. A venous spasm in the axillary vein was noted in another subject, which ultimately resulted in the placement of a bare metal stent for adequate resolution. The remaining subject reported pain in their access arm during the index procedure and the subject preferred that the arm not be used for cannulation, which led to the placement of an alternate access.

A list of Safety Events observed in the Clinical Study through 6 months can be found in Table 9, and a list of CEC adjudicated device and/or procedure related AEs can be found in Table 10. AEs are defined as those that reasonably suggest the involvement of the AV access circuit (not including stenosis or thrombosis).

Table 9: Safety Events through 6 months (All Treated Subjects)

AEs by Type	Follow-Up Time Point		
	30 Days n (%)	90 Days n (%)	6 Months n (%)
Subjects With At Least One AE	**11 (10.0)**	**19 (17.3)**	**26 (23.6)**
Arteriovenous Fistula*	0	1 (0.9)	1 (0.9)
Arteriovenous Graft Site Hemorrhage	0	1 (0.9)	2 (1.8)
Arteriovenous Graft Site Infection	1 (0.9)	1 (0.9)	3 (2.7)
Local Swelling	0	1 (0.9)	1 (0.9)
Paraesthesia	0	1 (0.9)	1 (0.9)
Steal Syndrome	1 (0.9)	3 (2.7)	3 (2.7)
Vascular Graft Complication**	4 (3.6)	8 (7.3)	17 (15.5)
Vascular Rupture	1 (0.9)	1 (0.9)	1 (0.9)
Vasospasm	5 (4.5)	(12)	5 (4.5)

Note that n=subjects with at least one event.
Note that events were coded using MedDRA version 16.1.

Note that AEs that occurred through 180 days for each subject are included.
Note that N=110 subjects.
*Arteriovenous Fistula refers to a site reported event of an abnormal connection from the arteriovenous graft near the arterial anastomosis to the brachial vein.
**Vascular Graft Complication includes events such as: access pain, AV access dysfunction, AVG dysfunction, AVG circuit issues, decreased blood flow, decreased access flow rate in AVG circuit, difficult puncture of AVG circuit, high venous pressures, increased pulsatility, infiltration of vascular access, intra-graft dissection and vessel dissection of synthetic graft, poor thrill progression and wound over upper cannulation site.

Table 10: CEC Adjudicated Device and/or Procedure Related Adverse Events through 6 months (inclusive of reported Safety Events in Table 9) (All Treated Subjects)

	Device Related			Procedure Related		
AEs by Type	**Definitely n (%)**	**Possibly n (%)**	**Not Related n (%)**	**Definitely n (%)**	**Possibly n (%)**	**Not Related n (%)**
Subject with at Least One AE	**1 (0.9)**	**8 (7.3)**	**23 (20.9)**	**7 (6.4)**	**4 (3.6)**	**21 (19.1)**
Arteriovenous Graft Site Infection	0	1 (0.9)	2 (1.8)	0	1 (0.9)	2 (1.8)
Paraesthesia	0	1 (0.9)	0	0	1 (0.9)	0
Steal Syndrome	0	2 (1.8)	1 (0.9)	0	2 (1.8)	1 (0.9)
Vascular Graft Complication*	0	3 (2.7)	17 (15.5)	2 (1.8)	1 (0.9)	17 (15.5)
Vasospasm	1 (0.9)	1 (0.9)	3 (2.7)	5 (4.5)	0	0

Note that n=subjects with at least one event.
Note that events were coded using MedDRA version 16.1.
Note that AEs that occurred through 180 days for each subject are included.
Note that N=110 Subjects.
*The three events associated with Vascular Graft Complication were reported as access pain. One of the events was adjudicated as possibly related to device and procedure, and the other two were adjudicated as possibly related to device and definitely related to procedure.

Summary of Effectiveness

Effectiveness was evaluated using multiple endpoints, with TLPP being an important endpoint as it was used as the primary endpoint for previous studies of the same indication. To provide clinical context, the 6-month TLPP rates from the pivotal and post market (RENOVA) studies of the Flair® device are provided in Table 11 below. The results of the AVeVA study demonstrate that the TLPP rates for the Covera™ device are similar to results from the study device arm of the previous studies and greater than the patency rates for PTA from these studies.

Table 11: TLPP Rates in AV Grafts at 6 Months

Study	N	Study Device	90% Confidence Intervals	Randomized PTA	90% Confidence Intervals
Flair® Pivotal Study	91	51%*	(42%, 60%)	23% (N=86)	(16%, 32%)
RENOVA Study (Flair®)	138	66%	(59%, 73%)	40% (N=132)	(33%, 48%)
AVeVA Study (Covera™)	**100****	**71%**	**(61%, 80%)**	-	-

* Physicians unfamiliar with the study device enrolled "roll-in" patients before starting the randomized phase of the trial. This resulted in 37 "roll-in" Flair® patients, resulting in a 60% TLPP rate for those patients at 6 months.
** Nine subjects were excluded from the denominator due to discontinuation or abandonment of the index AV access circuit prior to day 150 of their follow-up. One additional subject was excluded due to a major protocol deviation; refer to Table 17, Footnote [1] for additional detail.

Figure 11 presents the Kaplan-Meier curve for TLPP through 6 months for all treated subjects.

Figure 11: Kaplan Meier Analysis of TLPP (All Treated Subjects)

Table 12: Kaplan-Meier Analysis of TLPP (All Treated Subjects)

Time Point	#of Subjects Left	#of Subjects Censored	#of Subjects with TLPP Failure	TLPP Rate (95% CI) [1]
30 Days	99	1	8	92.6% (85.7%, 96.2%)
90 Days	90	5	13	87.8% (79.9%, 92.7%)
180 Days	70	9	29	71.7% (61.9%, 79.4%)

[1] The rates are estimated using the Kaplan-Meier method and the 95% confidence intervals are estimated using Greenwood's formula.

ACPP and secondary patency are also important effectiveness endpoints evaluated in this study. ACPP and secondary patency are inclusive of all patency events including those that occurred at the target lesion (i.e. inclusive of TLPP). The 6-month ACPP and secondary patency rates from the pivotal and post market (RENOVA) studies of the Flair® device are provided in Table 13 and Table 14 below. The results of the AVeVA study demonstrate that the ACPP rates for the Covera™ device are similar to results from the study device arm of the previous studies and greater than the ACPP rates for PTA from these studies. Furthermore, the secondary patency rates are proportionate for the study devices across these studies.

Table 13: ACPP Rates in AV Grafts at 6 Months

Study	N	Study Device	95% Confidence Intervals	Randomized PTA	95% Confidence Intervals
Flair® Pivotal Study	91	38%*	(28%, 49%)	20% (N=86)	(12%, 30%)
RENOVA Study (Flair®)	138	41%	(33%, 50%)	25% (N=132)	(18%, 33%)
AVeVA Study (Covera™)	**101****	**40%**	**(30%, 50%)**	-	-

* Physicians unfamiliar with the study device enrolled "roll-in" patients before starting the randomized phase of the trial. This resulted in 37 "roll-in" Flair® patients, resulting in a 43% ACPP rate for those patients at 6 months.

**One subject from the ten excluded from TLPP was included in the AC[illegible]ysis because the subject was a failure for ACPP only.

Table 14: Secondary Patency Rates in AV Grafts at 6 Months

Study	N	Study Device	95% Confidence Intervals	Randomized PTA	95% Confidence Intervals
Flair® Pivotal Study	91	81%*	(72%, 89%)	86% (N=85)	(77%, 92%)
RENOVA Study (Flair®)	138	75%	(67%, 82%)	79% (N=132)	(71%, 85%)
AVeVA Study (Covera™)	**100****	**92%**	**(85%, 97%)**	-	-

* Physicians unfamiliar with the study device enrolled "roll-in" patients before starting the randomized phase of the trial. This resulted in 37 "roll-in" Flair® patients, resulting in a 91% secondary patency rate for those patients at 6 months.
**Nine subjects were excluded from the denominator due to discontinuation or abandonment. One additional subject was excluded due to a major protocol deviation; refer to Table 17, Footnote [1] for additional detail.

Subgroup analyses were performed on evaluable subjects (Table 15). Per these analyses it is likely that there are no differences in effectiveness outcomes for sex, race, age, target lesion characteristics, outflow vessel, and presence of secondary lesion(s). A difference that is likely significant was observed between subjects that presented with thrombosis at the time of the index procedure comparing to subjects without thrombosis (p-value 0.0093, note this is not adjusted for multiplicity) where subjects presenting with thrombosis were observed to have 47.8% TLPP versus 76.9% TLPP for the non-thrombotic group. A similar trend between the two subgroups of subjects was also observed when subjects that had been treated for thrombosis within 30 days of the index procedure were included (multiplicity unadjusted p-value 0.0.0254).

Table 15: Analysis of TLPP at 6 Months by Subgroup (All Treated Subjects)

Subgroup	Proportion n/N (%)	95% CI (%) [2]	P-Value [1]
Target Lesion Characteristics			
de novo	17/26 (65.4)	(44.3, 82.8)	0.4644
Re-stenotic	54/74 (73.0)	(61.4, 82.6)	
Outflow Vessel			
Axillary Vein	33/49 (67.3)	(52.5, 80.1)	0.2914
Basilic Vein	31/40 (77.5)	(61.5, 89.2)	
Presence of Secondary Lesion(s)			
Yes	26/40 (65.0)	(48.3, 79.4)	0.2821
No	45/60 (75.0)	(62.1, 85.3)	
Presence of Thrombus Prior to Treatment at Index Procedure			
Yes	11/22 (50.0)	(28.2, 71.8)	0.0169
No	60/78 (76.9)	(66.0, 85.7)	
Presence of Thrombus at and /or within 30 days of Index Procedure			
Yes	15/27 (55.6)	(35.3, 74.5)	0.0418
No	56/73 (76.7)	(65.4, 85.8)	

[1] P-values are calculated using the chi squared test and are not adjusted for multiplicity.
[2] The 95% confidence interval is calculated using the exact binomial method. Confidence intervals are unadjusted for multiple comparisons.

The subgroup analysis for ACPP for subjects that presented with thrombosis at the time of the index procedure and within 30 days prior to the index pro[15]re is shown in Table 16.

Table 16: ACPP by Subgroup at 6 months of Follow-Up (All Treated Subjects)

Subgroup	Proportion n/N (%)	95% CI (%) [2]	P-Value [1]
Presence of Thrombus Prior to Treatment at Index Procedure?			
Yes	7/23 (30.4)	(13.2, 52.9)	0.3092
No	33/78 (42.3)	(31.2, 54.0)	
Presence of Thrombus at and /or within 30 days of Index Procedure?			
Yes	9/28 (32.1)	(15.9, 52.4)	0.3442
No	31/73 (42.5)	(31.0, 54.6)	

[1] P-values are calculated using the chi squared test and are not adjusted for multiplicity.
[2] The 95% confidence interval is calculated using the exact binomial method. Confidence intervals are unadjusted for multiple comparisons.

ADDITIONAL ENDPOINTS

Table 17 presents information on additional endpoints with proportional values for all available follow-up time points. The 12-month data are site reported and have not been verified and therefore are subject to minor changes at completion of the study (24-month follow-up). Acute Technical Success was defined as successful deployment, based on the operator's opinion, of the implant to the intended location assessed at the time of the index procedure. Procedure Success was defined as anatomic success and resolution of the pre-procedural clinical indicator(s) (clinical success) of a hemodynamically significant stenosis as further defined by Anatomic and Clinical Success. Anatomic Success was determined during the primary procedure and was defined as the achievement of a post-procedure residual stenosis of less than or equal to 30%, measured at the narrowest point of the lumen when compared to the adjacent non-stenosed venous segment. Whereas Clinical Success was defined as resolution of pre-procedural clinical indicators of access malfunction in the opinion of the investigator prior to hospital discharge which could include an abnormal physical exam, abnormal pressure monitoring parameters, decreased access flow, difficulty with dialysis needle puncture, pulling thrombus, prolonged bleeding, increased recirculation, and/or inadequate dialysis clearance.

Table 17: Additional Endpoints, Proportional Values (All Treated Subjects)

	Procedure n/N (%)	30 days n/N (%)	90 days n/N (%)	6 months n/N (%)	12 months n/N (%)
Acute Technical Success [1]	110/110 (100)	N/A	N/A	N/A	N/A
Acute Procedure Success [1]	110/110 (100)	N/A	N/A	N/A	N/A
TLPP	N/A	100/108 (92.6)	91/104 (87.5)	71/100 (71.0)	46/90 (51.1)
ACPP	N/A	96/108 (88.9)	72/105 (68.6)	40/101 (39.6)	15/96 (15.6)
Secondary Patency	N/A	106/108 (98.1)	100/104 (96.2)	92/100 (92.0)	76/87 (87.4)
Proportion Free From Device and Procedure Related AEs [2]	N/A	101/110 (91.8)	96/108 (88.9)	93/105 (88.6)	86/95 (90.5)

[1] One (1) subject presented with a clotted graft at the time of the index procedure and a 100% stenosis at the target lesion. During the initial inflation of the target lesion, rupture of the vessel occurred. After the urgency of resolving the rupture had passed, the investigator determined that there was an additional lesion about 1 cm peripheral to the stent graft. Because the first target lesion segment was stenosed to 100%, it is unlikely the additional lesion would have been seen until after pre-dilatation. A major protocol deviation was required as the remaining segment had to be treated with an adjunctive therapy as placement of a secondary study device in an overlapped configuration was not allowed per the protocol. This deviation does not implicate the technical and procedural success of the device as the study device was placed as initially intended as assessed by the investigator, however the subject was excluded from the follow up patency analysis due to the major protocol deviation.

[2] Refer to Table 10 for a complete list of device and procedure r

AEs at 6 months.

Table 18 presents information on additional endpoints with mean values for all available follow-up time points. Total Number of AV Access Circuit Reinterventions was defined as the number of reinterventions to the AV access circuit until access abandonment or through study completion. Total Number of Target Lesion Reinterventions was defined as the number of reinterventions to maintain target lesion patency. Index of Patency Function (IPF) was defined as the time from the index study procedure to study completion or access abandonment divided by the number of visits for reinterventions performed on the AV access circuit in order to maintain vascular access for hemodialysis. A visit was defined as one (1) procedural event, regardless of the number or type of interventions performed during the visit. The index procedure was counted as the first visit to ensure all subjects have a denominator of at least one. Index of Patency Function – Target Lesion (IPF-T) was defined as the time from the index study procedure to study completion or complete access abandonment divided by the number of visits for a reintervention performed at the target lesion in order to maintain vascular access for hemodialysis.

Table 18: Additional Endpoints, Mean Values (All Treated Subjects)

Total Number of AV Access Circuit Reinterventions	**n**	**mean (SD)***
30 Days	15	0.1 (0.44)
90 Days	48	0.5 (0.74)
6 Months	108	1.1 (1.23)
12 Months	215	2.3 (2.24)
Total Number of Target Lesion Reinterventions	**n**	**mean (SD)***
30 Days	9	0.1 (0.34)
90 Days	15	0.1 (0.43)
6 Months	41	0.4 (0.74)
12 Months	78	0.9 (1.40)
Index of Patency Function (days)	**mean (SD)**	
30 Days	28.23 (5.32)	
90 Days	72.58 (25.81)	
6 Months	110.58 (57.84)	
12 Months	147.59 (105.24)	
Index of Patency Function – Target Lesion (days)	**mean (SD)**	
30 Days	28.88 (4.29)	
90 Days	83.72 (17.86)	
6 Months	146.98 (52.07)	
12 Months	254.50 (127.39)	

* Mean (SD) is the average number of reinterventions per subject.

Vessel Ruptures

During the index procedure, two (2) subjects experienced vessel rupture at the target lesion during pre-dilation prior to study device implantation. The protocol allowed for vessel rupture at the target lesion to be treated using the study device and as such, the ruptures were resolved after implantation of the COVERA™ Vascular Covered Stent. The investigators deeme[17] procedures a success and no further AEs were

reported for these subjects through the 6-month follow-up period.

Summary of Deaths

There were six (6) deaths reported in the 6-month follow-up period. Two (2) deaths were cardiac-related and two (2) subjects expired due to voluntary termination of dialysis. The remaining two (2) primary causes of death were reported as volume overload (1), and worsening terminal cerebrovascular disease (1). Deaths were not considered to be related to the study device or index procedure.

Observed Device Malfunctions

There were zero (0) device malfunctions reported.

Conclusions Drawn from Pre-specified Endpoints

The prospective, multi-center, non-randomized, single-arm study of the Bard® COVERA™ Vascular Covered Stent in the treatment of stenotic lesions at the graft-vein anastomosis of hemodialysis patients dialyzing with an AV graft (AVeVA) evaluated safety and effectiveness measures.

The proportion of subjects free from primary safety events at 30-days was 96.4%, meeting the performance goal of 88% (p-value=0.0021). Additionally, results from the study demonstrate a TLPP rate of 71.0% at 6-months.

Data from the clinical trial provide a reasonable assurance that the Covera™ Vascular Covered Stent is safe and effective for the treatment of stenoses at the venous anastomosis of ePTFE or other synthetic arterio-venous (AV) access grafts when used in accordance with its labeling.

Symbols used on Labeling

Rx Only — CAUTION: Federal (USA) law restricts this device to sale by or on the order of a physician

Consult Instructions For Use

Keep Away From Sunlight

Keep Dry

Do Not Use If Package Is Damaged

Single Use

Do Not Resterilize

Contents: (1)

MR Conditional

Not Made With Natural Rubber Latex

Non-Pyrogenic

Catalogue Number

Lot Number

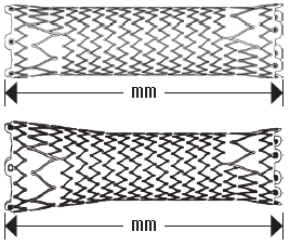
Sterilized Using Ethylene Oxide

Use By

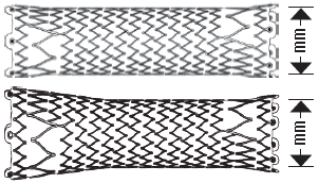
Manufacturer

Minimum Introducer Size

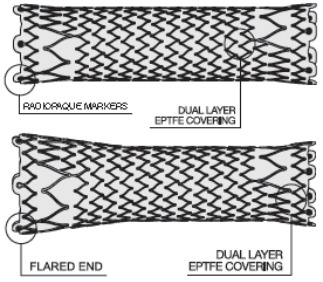
Guidewire Compatibility



Length



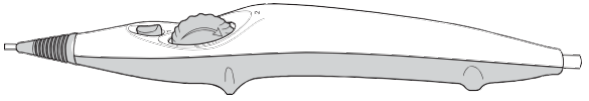
Diameter



Radiopaque Markers

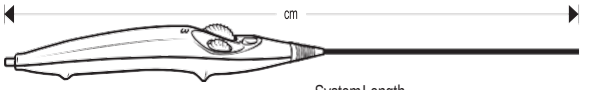
Dual Layer ePTFE Covering

Flared End



Triaxial Delivery System

Working Length



System Length

Labeling issue date: 2018-05

COVERA™

Vascular Covered Stent

Distributed by:

Bard Peripheral Vascular, Inc.
1625 West 3rd Street
Tempe, AZ 85281
USA
Tel: 1-480-894-9515
1-800-321-4254
Fax: 1-480-966-7062
1-800-440-5376
www.bardpv.com

Manufacturer:

Angiomed GmbH & Co. Medizintechnik KG
Wachhausstrasse 6
76227 Karlsruhe
Germany

BARD | PERIPHERAL VASCULAR

B05872 Rev.3/05-18