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RANGER™ Drug-Coated Balloon
for the Value Analysis Committee

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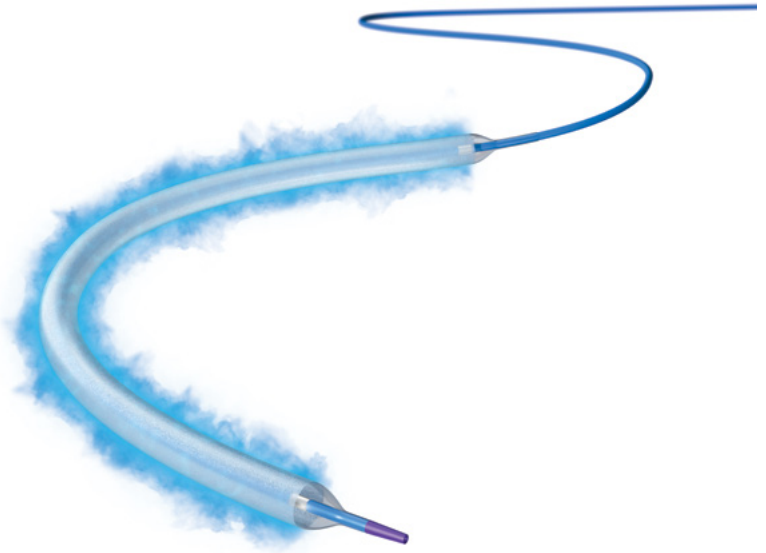
RANGER™ Paclitaxel-Coated PTA Balloon Catheter

Ranger Drug-Coated Balloon for the Treatment of Peripheral Artery Disease



What is the Ranger Drug-Coated Balloon (DCB)?

Ranger is a balloon catheter with drug applied to the balloon. Drug-coated balloons are inflated inside blood vessels to treat blockages and prevent re-narrowing while simultaneously delivering a therapeutic dose of drug to help keep the vessel open longer.

What Makes Ranger Unique?

Clinical Outcomes

Ranger demonstrated similar primary patency as IN.PACT DCB[1] with half the total drug dose[2]. Ranger has demonstrated consistent results with nearly 90% primary patency at 12-months in the RANGER II SFA and COMPARE Trials.[3]

Balloon Platform

Ranger is built on the market leading .018" Sterling™ Balloon Platform[4] with .018"/.014" guidewire compatibility and the lowest tip entry profile.[5]

Drug Transfer

TransPax™ (Citrate Ester + Low Dose Paclitaxel[6]) is a next generation coating that efficiently transfers drug into the tissue, resulting in high primary patency[3] while reducing downstream particulates[7] and systemic drug exposure for the patient.[8]

1. COMPARE Clinical Trial 12-Month Full Cohort Results presented by Sabine Steiner, MD. LINC 2020. K-M Primary Patency = 88.4%. 2. Based on total drug dose for (4mmx60mm) or (averages for full size matrix) per the Ranger and INPACT DCB Directions for Use 3. COMPARE Clinical Trial 12-Month Full Cohort Results presented by Sabine Steiner, MD. LINC 2020. K-M Primary Patency: Ranger = 88.4% versus IN.PACT = 89.4% (p= 0.81). RANGER II SFA Pivotal Trial 12-Month Results presented by Marianne Brodmann. LINC 2020. K-M Primary Patency: Ranger = 89.8% versus PTA = 74.0% (p = 0.0005). Log-rank p-value compares the entire K-M curves from time zero to full one year follow-up window 4. Boston Scientific Data on File. Ranger Catheter Competitive Testing Report, 92517674. Tip entry profile measurements taken from 6 x 120 devices. 5. Drug dose density = 2 µg/mm2 6. DRG data, CY 2019, 0.018" PTA Balloons. 7. Gongora et al. Comparative Drug-Coated Balloon Study. JACC Cardiovasc Interv. 2015 doi.org/10.1016/j.jcin.2015.03.020 8. RANGER II SFA PK Substudy presented by Ravish Sachar, MD. VIVA 2019.

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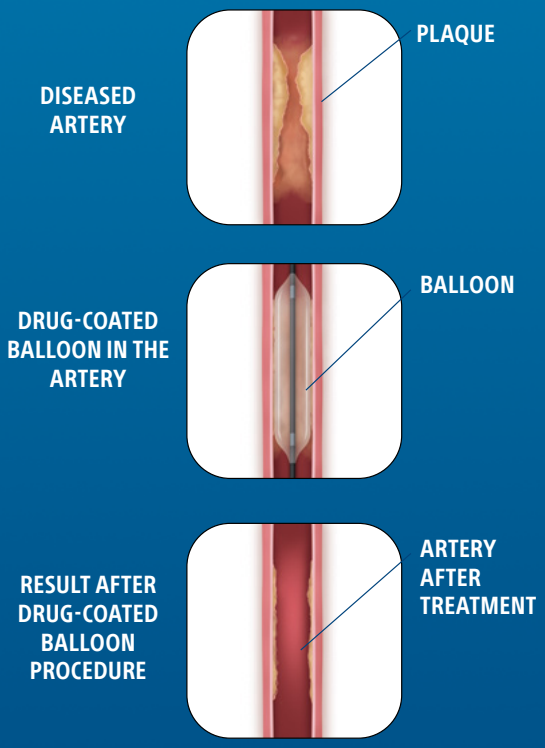
TECHNOLOGY OVERVIEW

Ranger DCB was developed for the treatment of patients with peripheral artery disease (PAD) in the superficial femoral artery (SFA) and proximal popliteal artery (PPA).

What Happens During a Typical Drug-Coated Balloon Procedure?

1. A small puncture is made in the patient's groin to gain access to the artery. A wire and catheter are inserted and moved to the narrowed section of the artery.
2. The narrowed section of the artery may need to be enlarged to make room for the drug-coated balloon. To do this, the doctor may use other devices to push the plaque to the side or remove plaque buildup inside the artery.
3. When the physician is satisfied with the size of the lumen, the drug-coated balloon will be inserted.
4. After the drug-coated balloon is inserted, it is inflated to make contact with the artery wall, allowing the drug to be released. The devices are removed and the puncture site in the patient's groin is closed. The drug from the balloon is absorbed into the artery and is designed to help keep the artery open and prevent future narrowing of the artery.



Images courtesy of Boston Scientific. Images are for illustration purposes only, and are not necessarily to scale.

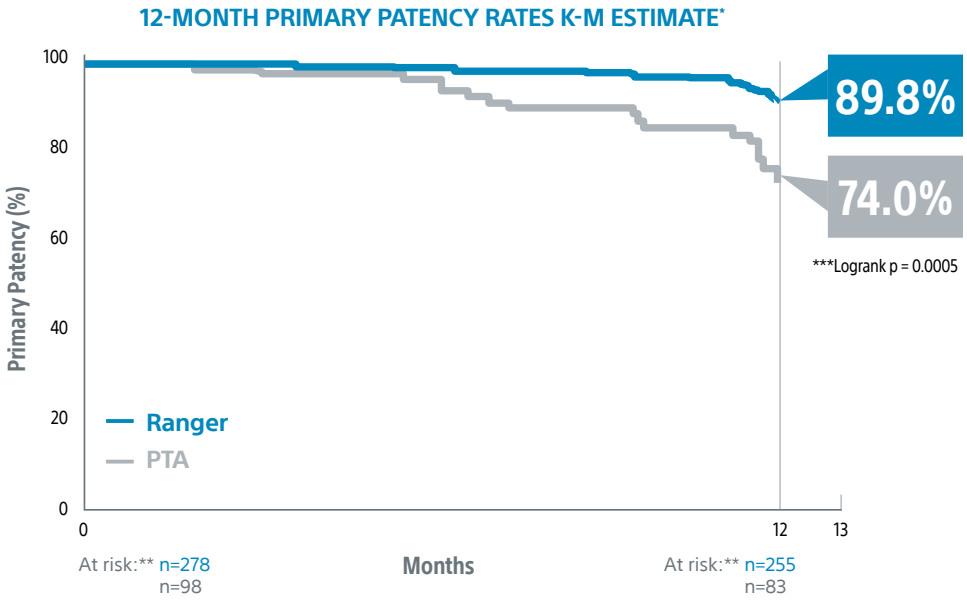
RANGER™ Paclitaxel-Coated PTA Balloon Catheter

General Specifications	
Indication For Use	The Ranger Drug-Coated Balloon (DCB) is indicated for percutaneous transluminal angioplasty (PTA) of de novo or restenotic lesions up to 180 mm in length located in native superficial femoral and proximal popliteal arteries (SFA/PPA) with reference vessel diameters of 4 mm to 8 mm
Drug & Dose Density	Paclitaxel 2µg/mm^2
Excipient	TransPax — Citrate Ester
Platform	Ranger DCB is built on the .018" Sterling Balloon Platform
Guidewire Compatibility	Ranger DCB is compatible with .014" and .018" guidewires
Balloon Diameters	4 mm, 5 mm, 6 mm, 7 mm
Balloon Lengths	40 mm, 60 mm, 80 mm, 100 mm, 120 mm, 150 mm, 200 mm
Catheter Working Lengths	80 cm, 90 cm, 135 cm, 150 cm
Sheath Compatibility	4 mm, 5 mm, and 6 mm Balloon Diameters = 5Fr 7 mm Balloon Diameters = 6Fr
Marker Bands	The Ranger DCB has two 1.3 mm radiopaque marker bands (one proximal and one distal)
Deployment Pressure	6 ATM Nominal / 14 ATM Burst
Inflation Time	3 minutes is recommended
Shelf Life	18 Months

RANGER II SFA PIVOTAL TRIAL[1]

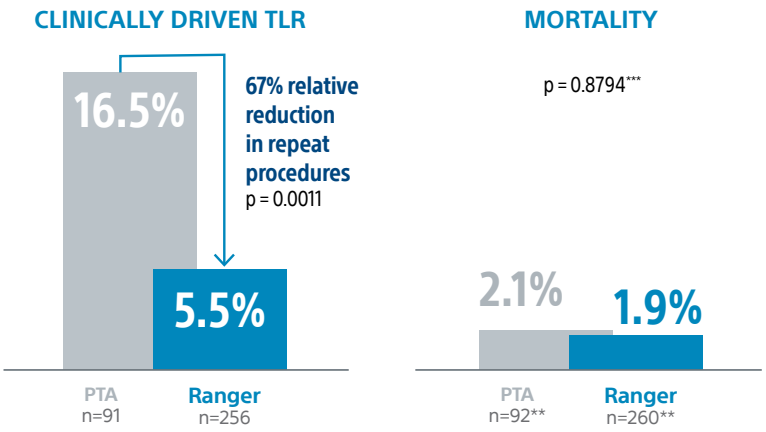
Prospective, Multi-Center, Randomized Controlled Trial
Ranger™ Drug-Coated Balloon vs. Uncoated Balloon (3:1). Follow-up through 5 years

Ranger demonstrated nearly 90% primary patency at 12 months



Clinically-Driven TLR (CD-TLR) & Mortality

Ranger demonstrated significantly lower CD-TLR and no difference in mortality vs. PTA at 12 months



*Kaplan-Meier Estimate: Primary patency as determined by duplex ultrasound (DUS) Peak Systolic Velocity Ratio (PSVR) is ≤2.4 at the 12-month follow-up visit, in the absence of clinically driven TLR or bypass of the target lesion.
** At risk denotes the number of subjects entered in the calculation at the time interval.
*** Logrank p-value compares the entire K-M curves from time zero to full 1-year follow-up.

1. RANGER II SFA Pivotal Trial 12-Month Results presented by Marianne Brodmann. LINC 2020.

RANGER II SFA PIVOTAL TRIAL

PRIMARY ENDPOINT RESULTS	Ranger™ DCB (n=207)	PTA (n=98)	p-value
Primary Safety Endpoint (Freedom from MAE)	94.1% (241/256)	83.0% (75/91)	$P_{non\text{-}inferiority}<0.0001$
Primary Effectiveness Endpoint (Binary Primary Patency)	82.9% (194/234)	66.3% (57/86)	0.0017

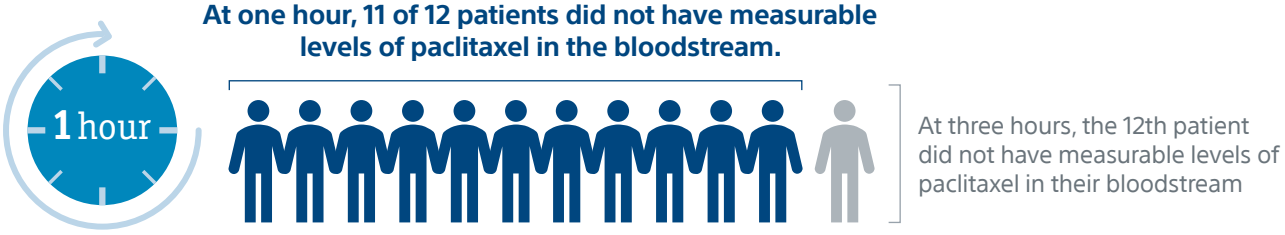
KEY BASELINE CHARACTERISTICS	Ranger DCB (n=207)	PTA (n=98)	p-value
Age (year)	70.6	69.1	0.189
Current/Former Smoker*	85.3%	84.7%	see footnote
Current Diabetes Mellitus	42.4%	43.9%	0.806
Target Lesion Length (mm)**	82.5	79.9	0.655
Calcium: PACSS Grade 3/4***	47.8%	62.2%	see footnote

* Current smokers: Ranger 31.3%, PTA 45.9%, p-value=0.009. Previous smokers: Ranger 54.0%, PTA 38.8%, p-value=0.010.
** Core lab.
*** PACSS Grade 3/4 may be considered similar to moderate/severe calcification. Grade 3: 36.3% Ranger, 52.0% PTA, p=0.006, Grade 4: 11.5% Ranger, 10.2% PTA, p=0.724.

Ranger PK Substudy[2]

Study Method:

- Designed to evaluate the levels of paclitaxel in the systemic circulation of 12 subjects who were treated with Ranger DCB
- Protocol required blood draws: Baseline, 10 minutes, 30 minutes, 1, 3, 6, 24 or 48 hours, 7 days and 30 days after last Ranger DCB treatment and removal
- The limit of quantification was defined as < 1 ng/mL
- Average number of DCBs used per patient: 1.75



2. RANGER II SFA PK Substudy presented by Ravish Sachar, MD. VIVA 2019.

COMPARE CLINICAL TRIAL[1]

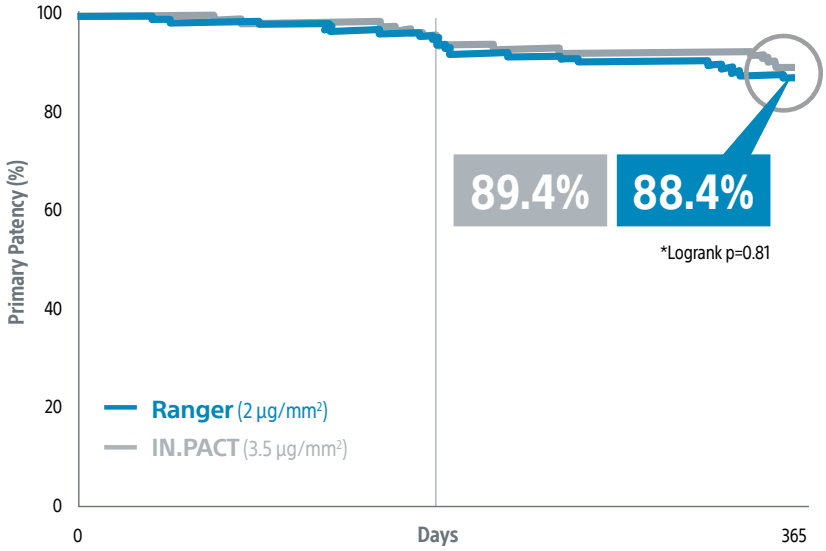
COMPARE is the world's first head-to-head prospective, RCT (1:1) comparing low dose Ranger™ DCB (2 µg/mm²) to higher dose IN.PACT™ DCB (3.5 µg/mm²)

Ranger demonstrated similar primary patency as IN.PACT with half the total drug dose[2] at 12 months[1] and 24 months[3]

24-Month K-M Primary Patency[3]:
Ranger = 75% vs IN.PACT = 77%

1. COMPARE Clinical Trial 12-Month Results presented by Sabine Steiner, MD. LINC 2020.
2. Based on total drug dose for 4mm x 60mm or averages for full size matrix per the IN.PACT™ Admiral™ Drug-Coated Balloon Instructions for Use, www.medtronic.com and the Ranger™ Paclitaxel-Coated PTA Balloon Catheter Instructions for Use.
3. Results from the 150-patient COMPARE-1 Pilot phase. LINC 2019. 75% Ranger Patency (n=62) vs. 77% IN.PACT Patency (n=61) at 24 months. K-M estimate, p= 0.57 (logrank test).

12-MONTH PRIMARY PATENCY KAPLAN-MEIER ESTIMATE



Ranger n=207 **IN.PACT** n=207

*Logrank p-value compares the entire K-M curves from time zero to full 1-year follow-up window.

BASELINE CHARACTERISTICS	RANGER (n=207)	IN.PACT (n=207)	p-value
Age	68.2	68.4	0.79
Female	38.2%	36.2%	0.68
Current/Former Smoker	77.3%	75.3%	0.63*
Total Occlusions	41%	43%	0.62
Total Occlusion Length	131 mm	113 mm	0.23
Target Lesion Length	124 mm	128 mm	0.65
Moderate to Severe Calcification**	50%	57%	***
Diabetics	31%	37%	0.18

* p-value based on entire distribution Never, Former or Current Smokers
** PACSS Grade 3/4 may be considered similar to moderate/severe calcification.
*** p-value for entire distribution of PACSS Calcium Grades 0, 1, 2, 3, 4 calcium for RANGER vs. IN.PACT. p-value was 0.20.

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COMPARE CLINICAL TRIAL[1]

COMPARE TRIAL DETAILS	RANGER™ (n=207)	IN.PACT™ (n=207)	p-value
Excipient	TransPax™ citrate ester	Urea	
Paclitaxel dose density	2.0 µg/mm^2	3.5 µg/mm^2	
Average total paclitaxel dose per patient in trial	6,971 µg	13,035 µg	**<0.0001**

12-MONTH KEY RESULTS	RANGER (n=207)	IN.PACT (n=207)	p-value
Binary Primary Patency*	83.0% (156/188)	81.5% (141/173)	$P_{non\text{-}inferiority}$<0.01
Freedom from Major Adverse Events*	91.0% (182/200)	92.6% (175/189)	$P_{non\text{-}inferiority}$<0.01
Mortality: All Cause	2.5%	1.6%	0.73
Mortality: Device or Procedure Related	0%	0%	N/A
CD-TLR	9.0%	7.4%	0.59

* Primary Endpoint Met

12-Month Results Published in the European Heart Journal

COMPARE: prospective, randomized, non-inferiority trial of high vs. low dose paclitaxel drug-coated balloons for femoropopliteal interventions. January 2020. doi.org/10.1093/eurheartj/ehaa049

Definitions:

Primary safety endpoint: composite of freedom from device and procedure-related death through 30 days and freedom from major target limb amputation and CD-TLR through 12 months post index-procedure.

Primary efficacy endpoint: primary patency at 12 months defined as absence of clinically driven target lesion revascularization (CD-TLR) or binary restenosis determined as a peak systolic velocity ratio > 2.4 evaluated by duplex ultrasound core laboratory analysis.

CD-TLR: a reintervention performed for ≥ 50% diameter stenosis (confirmed by angiography) within ± 5 mm proximal and/or distal to the target lesion after documentation of recurrent clinical symptoms of PAD (increase of 1 Rutherford class or more) and/or drop of ABI (≥20% or >0.15 when compared to maximum early post-procedural level).

ORDERING INFORMATION

RANGER™ Paclitaxel-Coated PTA Balloon Catheter

Ranger UPN	Product Description
H74939419400410	RANGER GLOBAL DCB OTW 4.0 X 40 MM 135 CM
H74939419400480	RANGER GLOBAL DCB OTW 4.0 X 40 MM 80 CM
H74939419400610	RANGER GLOBAL DCB OTW 4.0 X 60 MM 135 CM
H74939419400680	RANGER GLOBAL DCB OTW 4.0 X 60 MM 80 CM
H74939419400810	RANGER GLOBAL DCB OTW 4.0 X 80 MM 135 CM
H74939419400880	RANGER GLOBAL DCB OTW 4.0 X 80 MM 80 CM
H74939419401010	RANGER GLOBAL DCB OTW 4.0 X 100 MM 135 CM
H74939419401080	RANGER GLOBAL DCB OTW 4.0 X 100 MM 80 CM
H74939419401210	RANGER GLOBAL DCB OTW 4.0 X 120 MM 150 CM
H74939419401510	RANGER GLOBAL DCB OTW 4.0 X 150 MM 150 CM
H74939419401590	RANGER GLOBAL DCB OTW 4.0 X 150 MM 90 CM
H74939419402010	RANGER GLOBAL DCB OTW 4.0 X 200 MM 150 CM
H74939419402090	RANGER GLOBAL DCB OTW 4.0 X 200 MM 90 CM
H74939419500410	RANGER GLOBAL DCB OTW 5.0 X 40 MM 135 CM
H74939419500480	RANGER GLOBAL DCB OTW 5.0 X 40 MM 80 CM
H74939419500610	RANGER GLOBAL DCB OTW 5.0 X 60 MM 135 CM
H74939419500680	RANGER GLOBAL DCB OTW 5.0 X 60 MM 80 CM
H74939419500810	RANGER GLOBAL DCB OTW 5.0 X 80 MM 135 CM
H74939419500880	RANGER GLOBAL DCB OTW 5.0 X 80 MM 80 CM
H74939419501010	RANGER GLOBAL DCB OTW 5.0 X 100 MM 135 CM
H74939419501080	RANGER GLOBAL DCB OTW 5.0 X 100 MM 80 CM
H74939419501210	RANGER GLOBAL DCB OTW 5.0 X 120 MM 150 CM
H74939419501510	RANGER GLOBAL DCB OTW 5.0 X 150 MM 150 CM
H74939419501590	RANGER GLOBAL DCB OTW 5.0 X 150 MM 90 CM
H74939419502010	RANGER GLOBAL DCB OTW 5.0 X 200 MM 150 CM
H74939419502090	RANGER GLOBAL DCB OTW 5.0 X 200 MM 90 CM

Ranger UPNs continued on second page

ORDERING INFORMATION

RANGER™ Paclitaxel-Coated PTA Balloon Catheter

Ranger UPN	Product Description
H74939419600410	RANGER GLOBAL DCB OTW 6.0 X 40 MM 135 CM
H74939419600480	RANGER GLOBAL DCB OTW 6.0 X 40 MM 80 CM
H74939419600610	RANGER GLOBAL DCB OTW 6.0 X 60 MM 135 CM
H74939419600680	RANGER GLOBAL DCB OTW 6.0 X 60 MM 80 CM
H74939419600810	RANGER GLOBAL DCB OTW 6.0 X 80 MM 135 CM
H74939419600880	RANGER GLOBAL DCB OTW 6.0 X 80 MM 80 CM
H74939419601010	RANGER GLOBAL DCB OTW 6.0 X 100 MM 135 CM
H74939419601080	RANGER GLOBAL DCB OTW 6.0 X 100 MM 80 CM
H74939419601210	RANGER GLOBAL DCB OTW 6.0 X 120 MM 150 CM
H74939419601510	RANGER GLOBAL DCB OTW 6.0 X 150 MM 150 CM
H74939419601590	RANGER GLOBAL DCB OTW 6.0 X 150 MM 90 CM
H74939419602010	RANGER GLOBAL DCB OTW 6.0 X 200 MM 150 CM
H74939419602090	RANGER GLOBAL DCB OTW 6.0 X 200 MM 90 CM
H74939419700410	RANGER GLOBAL DCB OTW 7.0 X 40 MM 135 CM
H74939419700480	RANGER GLOBAL DCB OTW 7.0 X 40 MM 80 CM
H74939419700610	RANGER GLOBAL DCB OTW 7.0 X 60 MM 135 CM
H74939419700680	RANGER GLOBAL DCB OTW 7.0 X 60 MM 80 CM
H74939419700810	RANGER GLOBAL DCB OTW 7.0 X 80 MM 135 CM
H74939419700880	RANGER GLOBAL DCB OTW 7.0 X 80 MM 80 CM
H74939419701010	RANGER GLOBAL DCB OTW 7.0 X 100 MM 135 CM
H74939419701080	RANGER GLOBAL DCB OTW 7.0 X 100 MM 80 CM
H74939419701210	RANGER GLOBAL DCB OTW 7.0 X 120 MM 150 CM
H74939419701510	RANGER GLOBAL DCB OTW 7.0 X 150 MM 150 CM
H74939419702010	RANGER GLOBAL DCB OTW 7.0 X 200 MM 150 CM

RANGER™ DRUG-COATED BALLOON

CODING AND REIMBURSEMENT GUIDE

The procedure codes listed below are applicable to Femoral/Popliteal cases involving the Ranger™ Drug-Coated Balloon.

HOSPITAL OUTPATIENT

CPT®	Abbreviated Description	APC	Payment	MD-In Facility
37224	Femoral/Popliteal PTA	**5192**	$4,679	$466
37225	Femoral/Popliteal PTA + Atherectomy	**5193**	$9,669	$635
37226	Femoral/Popliteal PTA + Stent			$547
37227	Femoral/Popliteal PTA, Atherectomy + Stent	**5194**	$15,355	$763

C-Codes are used to report devices used in combination with device-related procedures for hospital outpatient services.

- The applicable C-Code to report the use of Ranger™ is C2623, defined as "catheter, transluminal angioplasty, drug-coated, non-laser."

HOSPITAL INPATIENT

CPT®	Abbreviated Description	MS DRG	Payment	MD-In Facility
37224	Femoral/Popliteal PTA			$466
37225	Femoral/Popliteal PTA + Atherectomy	● **252** ● **253** ● **254**	$20,548 $16,327 $11,401	$635
37226	Femoral/Popliteal PTA + Stent			$547
37227	Femoral/Popliteal PTA, Atherectomy + Stent			$763

● Denotes DRG assigned to patient w/ MCC

● Denotes DRG assigned to patient w/ CC

● Denotes DRG assigned to patient w/o MCC or CC

REIMBURSEMENT INFORMATION

CPT® CODES:

CPT®	Description
37224	Revascularization, endovascular, open or percutaneous, femoral, popliteal artery(s), unilateral; with transluminal angioplasty
37225	Revascularization, endovascular, open or percutaneous, femoral, popliteal artery(s), unilateral; with atherectomy, includes angioplasty within the same vessel, when performed
37226	Revascularization, endovascular, open or percutaneous, femoral, popliteal artery(s), unilateral; with transluminal stent placement(s), includes angioplasty within the same vessel, when performed
37227	Revascularization, endovascular, open or percutaneous, femoral, popliteal artery(s), unilateral; with transluminal stent placement(s) and atherectomy, includes angioplasty within the same vessel, when performed

ICD-10 PCS CODES:

ICD-10	Description
047K3Z1	Dilation of Right Femoral Artery using Drug-Coated Balloon, Percutaneous Approach
047L3Z1	Dilation of Left Femoral Artery using Drug-Coated Balloon, Percutaneous Approach
047M3Z1	Dilation of Right Popliteal Artery using Drug-Coated Balloon, Percutaneous Approach
047N3Z1	Dilation of Left Popliteal Artery using Drug-Coated Balloon, Percutaneous Approach

Boston Scientific Reimbursement Support: 1.800.CARDIAC (227.3422)

IMPORTANT INFORMATION: Health economic and reimbursement information provided by Boston Scientific Corporation is gathered from third-party sources and is subject to change without notice as a result of complex and frequently changing laws, regulations, rules and policies. This information is presented for illustrative purposes only and does not constitute reimbursement or legal advice. Boston Scientific encourages providers to submit accurate and appropriate claims for services. **It is always the provider's responsibility to determine medical necessity, the proper site for delivery of any services and to submit appropriate codes, charges, and modifiers for services that are rendered.** It is also always the provider's responsibility to understand and comply with Medicare national coverage determinations (NCD), Medicare local coverage determinations (LCD) and any other coverage requirements established by relevant payers which can be updated frequently. Boston Scientific recommends that you consult with your payers, reimbursement specialists and/or legal counsel regarding coding, coverage and reimbursement matters.

FDA APPROVAL LETTER

U.S. FOOD & DRUG ADMINISTRATION

October 30, 2020

Boston Scientific Corporation
Matt Beauchane
Principal Regulatory Affairs Specialist
Three Scimed Place
Maple Grove, Minnesota 55311

Re: P190019
Trade/Device Name: Ranger™ Paclitaxel-Coated PTA Balloon Catheter
Product Code: ONU
Filed: July 22, 2019
Amended: April 6, 2020; June 16, 2020

Dear Mr. Beauchane:

The Center for Devices and Radiological Health (CDRH) of the Food and Drug Administration (FDA) has completed its review of your premarket approval application (PMA) for the Ranger™ Paclitaxel-Coated PTA Balloon Catheter. This device is indicated for percutaneous transluminal angioplasty (PTA) of de novo or restenotic lesions up to 180 mm in length located in native superficial femoral and proximal popliteal arteries (SFA/PPA) with reference vessel diameters of 4 - 7 mm. We are pleased to inform you that the PMA is approved. You may begin commercial distribution of the device in accordance with the conditions of approval described below. Although this letter refers to your product as a device, please be aware that some approved products may instead be combination products. The Premarket Approval Database located at https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMA/pma.cfm identifies combination product submissions.

The sale and distribution of this device are restricted to prescription use in accordance with 21 CFR 801.109 and under section 515(d)(1)(B)(ii) of the Federal Food, Drug, and Cosmetic Act (the act). The device is further restricted under section 515(d)(1)(B)(ii) of the act insofar as the labeling must specify the specific training or experience practitioners need in order to use the device. FDA has determined that these restrictions on sale and distribution are necessary to provide reasonable assurance of the safety and effectiveness of the device. Your device is therefore a restricted device subject to the requirements in sections 502(q) and (r) of the act, in addition to the many other FDA requirements governing the manufacture, distribution, and marketing of devices.

Expiration dating for this device has been established and approved at 18 months.

Continued approval of the PMA is contingent upon the submission of periodic reports, required under 21 CFR 814.84, at intervals of one year (unless otherwise specified) from the date of approval of the original PMA. This report, identified as "Annual Report" and bearing the applicable PMA reference number, should be submitted to the address below. The Annual Report should indicate the beginning and ending date of the period covered by the report and should include the information required by 21 CFR 814.84.

U.S. Food & Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993
www.fda.gov

Doc ID: 040017.04.18

In addition to the above, and in order to provide continued reasonable assurance of the safety and effectiveness of the PMA device, the Annual Report must include, separately for each model number (if applicable), the number of devices sold and distributed during the reporting period, including those distributed to distributors. The distribution data will serve as a denominator and provide necessary context for FDA to ascertain the frequency and prevalence of adverse events, as FDA evaluates the continued safety and effectiveness of the device.

In addition to the Annual Report requirements, you must provide the following data in post-approval study (PAS) reports for each PAS listed below. Separate PAS Progress Reports must be submitted for each study.

1. *RANGER II SFA Continued Follow-Up Study:* This study will evaluate the long-term safety and effectiveness of the Ranger DCB in 376 subjects from the premarket study (RANGER II SFA trial). The RANGER II SFA trial was designed as a global, single-blind, multicenter, randomized (3:1 Ranger DCB to PTA) trial. Subjects will be followed annually through 5 years post-procedure with no more than 15% attrition.

   The primary effectiveness endpoint is primary patency of the target lesion at 24 months. The primary safety endpoint is a composite of freedom from device- and procedure-related death at 30 days and freedom from target limb major amputation and clinically-driven target lesion revascularization (CD-TLR) at 24 months.

   The endpoints to be assessed through 5 years post-procedure are rate of: (1) major adverse events (MAE), (2) clinically-driven target lesion revascularization (CD-TLR), (3) all TLR, (4) clinically-driven target vessel revascularization (CD-TVR), (5) target limb major amputation, (6) arterial thrombosis and (7) mortality status. The endpoints to be assessed at 2 and 3 years post-procedure are: (1) patency, (2) change in ankle-brachial index (ABI), (3) change in walking impairment questionnaire (WIQ), (4) change in walking distance, (5) change in Rutherford classification, and (6) change in quality of life assessment by EQ-5D questionnaire.

   Robust independent adjudication of events (i.e., Clinical Events Committee) will be maintained throughout the PAS study, unmodified from the pivotal portion of the study. In addition, COVID-19 testing and adjudication of COVID-19 related events will be included. RANGER II SFA updates will be provided semi-annually for 2 years and annually thereafter until all subjects have completed the 5 year follow-up visit, are discontinued prior to the 5 year follow-up visit, have died, or the 5 year follow-up window has closed.

2. *Ranger Long Balloon, Ranger China, and COMPARE I Follow-Up Studies:* These studies will provide additional safety and effectiveness data for the Ranger DCB. Updates will be provided on the following ongoing clinical studies:

   Ranger Long Balloon Substudy: The Ranger Long Balloon Substudy is a non-blinded, non-randomized, single-arm Long Balloon (LB) Sub Study to fulfill the post-market clinical follow-up requirement by DEKRA in Europe and New Zealand regions following enrolled patients for one year. Semi-annual updates, including mortality status, will be provided for the Ranger Long Balloon Sub study until all subjects have completed the 12 month follow-up visit, are discontinued prior to the 12 month follow-up visit, have died, or the 12 month follow-up window has closed.

Ranger China Study: The Ranger China study, is a prospective, non-randomized, multi-center, premarket clinical study to demonstrate acceptable safety and performance of Ranger DCB used for angioplasty of femoropopliteal artery lesions. This study will enroll 123 subjects at up to 15 sites in China that will follow patients through 12 months. Annual updates, including mortality status, will be provided.

COMPARE I Study: the COMPARE I Study (NCT02701543), an investigator sponsored, prospective, multi-center, 1:1 randomized trial comparing Ranger and IN.PACT™ DCBs in the treatment of high grade stenotic or occluded lesions in the SFA and/or PPA in PAD patient with Rutherford class 2-4 This European post-market study enrolled 414 subjects (approximately 207 Ranger DCB) at up to 18 sites with a follow-up period 24 months to assess patency by duplex ultrasound (DUS) and major adverse events (MAEs). Annual updates, including mortality status up to 5 years, will be provided.

You must obtain approval of your PAS protocol(s) within 60 days from the date of this order. Within 30 days of your receipt of this letter, you must submit a PMA supplement that includes a complete protocol of your post-approval study described above. Your PMA supplement should be clearly labeled as a "PMA Post-Approval Study Protocol" as noted above and submitted to the address below. Please reference the PMA number above to facilitate processing. If there are multiple protocols being finalized after PMA approval, please submit each protocol as a separate PMA supplement.

Each PAS report should be submitted to the address below identified as a "PMA Post-Approval Study Report" in accordance with how the study is identified above and bearing the applicable PMA reference number.

Be advised that failure to comply with any post-approval requirement, including completion requirements outlined above constitutes grounds for FDA withdrawal of approval of the PMA in accordance with 21 CFR 814.82(c) and 814.46(a)(2).

Be advised that the failure to conduct any such study in compliance with the good clinical laboratory practices in 21 CFR part 58 (if a non-clinical study subject to part 58) or the institutional review board regulations in 21 CFR part 56 and the informed consent regulations in 21 CFR part 50 (if a clinical study involving human subjects) may be grounds for FDA withdrawal of approval of the PMA in accordance with 21 CFR 814.46(a)(3)-(4).

Be advised that protocol information, interim and final results will be published on the Post Approval Study Webpage https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMA/pma_pas.cfm.

In addition, the results from any post approval study should be included in the labeling as these data become available. Any updated labeling must be submitted to FDA in the form of a PMA Supplement. For more information on post-approval studies, see the FDA guidance document entitled, "Procedures for Handling Post-Approval Studies Imposed by PMA Order" (https://www.fda.gov/media/71327/download).

This is a reminder that as of September 24, 2014, class III devices are subject to certain provisions of the final Unique Device Identification (UDI) rule. These provisions include the requirement to provide a UDI on the device label and packages (21 CFR 801.20), format dates on the device label in accordance with 21 CFR

801.18, and submit data to the Global Unique Device Identification Database (GUDID) (21 CFR 830 Subpart E). Additionally, 21 CFR 814.84 (b)(4) requires PMA annual reports submitted after September 24, 2014, to identify each device identifier currently in use for the subject device, and the device identifiers for devices that have been discontinued since the previous periodic report. It is not necessary to identify any device identifier discontinued prior to December 23, 2013. Combination Products may also be subject to UDI requirements (see 21 CFR 801.30). For more information on these requirements, please see the UDI website, https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/unique-device-identification-udi-system.

Before making any change affecting the safety or effectiveness of the PMA device, you must submit a PMA supplement or an alternate submission (30-day notice) in accordance with 21 CFR 814.39. All PMA supplements and alternate submissions (30-day notice) must comply with the applicable requirements in 21 CFR 814.39. For more information, please refer to the FDA guidance document entitled, "Modifications to Devices Subject to Premarket Approval (PMA) - The PMA Supplement Decision-Making Process" https://www.fda.gov/media/81431/download.

You are reminded that many FDA requirements govern the manufacture, distribution, and marketing of devices. For example, in accordance with the Medical Device Reporting (MDR) regulation, 21 CFR 803.50 and 21 CFR 803.52 for devices or post-marketing safety reporting (21 CFR 4, Subpart B) for combination products, you are required to report adverse events for this device. Manufacturers of medical devices, including in vitro diagnostic devices, are required to report to FDA no later than 30 calendar days after the day they receive or otherwise becomes aware of information, from any source, that reasonably suggests that one of their marketed devices:

1. May have caused or contributed to a death or serious injury; or

2. Has malfunctioned and such device or similar device marketed by the manufacturer would be likely to cause or contribute to a death or serious injury if the malfunction were to recur.

Additional information on MDR, including how, when, and where to report, is available at https://www.fda.gov/medical-devices/medical-device-safety/medical-device-reporting-mdr-how-report-medical-device-problems and on combination product post-marketing safety reporting is available at (see https://www.fda.gov/combination-products/guidance-regulatory-information/postmarketing-safety-reporting-combination-products).

In accordance with the recall requirements specified in 21 CFR 806.10 for devices or the post-marketing safety reporting requirements (21 CFR 4, Subpart B) for combination products, you are required to submit a written report to FDA of any correction or removal of this device initiated by you to: (1) reduce a risk to health posed by the device; or (2) remedy a violation of the act caused by the device which may present a risk to health, with certain exceptions specified in 21 CFR 806.10(a)(2). Additional information on recalls is available at https://www.fda.gov/safety/recalls-market-withdrawals-safety-alerts/industry-guidance-recalls.

CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading. CDRH will notify the public of its decision to approve your PMA by making available, among other information, a summary of the safety and effectiveness data

upon which the approval is based. The information can be found on the FDA CDRH Internet Home Page located at https://www.fda.gov/medical-devices/device-approvals-denials-and-clearances/pma-approvals. Written requests for this information can also be made to the Food and Drug Administration, Dockets Management Branch, (HFA-305), 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852. The written request should include the PMA number or docket number. Within 30 days from the date that this information is placed on the Internet, any interested person may seek review of this decision by submitting a petition for review under section 515(g) of the act and requesting either a hearing or review by an independent advisory committee. FDA may, for good cause, extend this 30-day filing period.

Failure to comply with any post-approval requirement constitutes a ground for withdrawal of approval of a PMA. The introduction or delivery for introduction into interstate commerce of a device that is not in compliance with its conditions of approval is a violation of law.

You are reminded that, as soon as possible and before commercial distribution of your device, you must submit an amendment to this PMA submission with a copy of all final labeling. Final labeling that is identical to the labeling approved in draft form will not routinely be reviewed by FDA staff when accompanied by a cover letter stating that the final labeling is identical to the labeling approved in draft form. If the final labeling is not identical, any changes from the final draft labeling should be highlighted and explained in the amendment.

All required documents should be submitted, unless otherwise specified, to the address below and should reference the above PMA number to facilitate processing.

U.S. Food and Drug Administration
Center for Devices and Radiological Health
Document Control Center - WO66-G609
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002

If you have any questions concerning this approval order, please contact Hajira Ahmad at 240-402-9925 or Hajira.Ahmad@fda.hhs.gov.

Sincerely,

Brian D. Pullin -S

Brian Pullin
Director
DHT2C: Division of Coronary
and Peripheral Intervention Devices
OHT2: Office of Cardiovascular Devices
Office of Product Evaluation and Quality
Center for Devices and Radiological Health

TWO DRUG-ELUTING SOLUTIONS. ONE TRUSTED PARTNER.

THE ONLY COMPANY WITH HEAD-TO-HEAD RCTs

Eluvia™ Drug-Eluting Stent and Ranger™ Drug-Coated Balloon are the only PAD devices backed by Level-1, Head-to-Head, Randomized Controlled Trials that demonstrate exceptional outcomes with differentiated technology – helping physicians make better, data-driven treatment decisions with a best-in-class drug-eluting portfolio.

Strengthen Quality Outcomes

Boston Scientific is the only company providing Level-1 Head-to-Head Randomized Controlled Clinical Trials in the PAD space for DES and DCB, helping physicians make more informed treatment decisions.

Enhance Patient Experience

Ranger DCB and Eluvia DES were purposely designed to deliver the lowest possible drug dose through efficient drug transfer to achieve high patency with low systemic drug exposure to the patient.

Increase Operational Efficiencies

Ranger DCB is .014" guidewire compatible to help streamline atherectomy procedures. Eluvia DES has shown to reduce hospital length of stay and readmission rates.

Improve Financial Health

Boston Scientific is the only company offering both DES and DCB, with the largest PI portfolio to streamline hospital supply chain management.

RANGER DRUG COATED BALLOON

CAUTION: Federal law (USA) restricts this device to sale by or on the order of a physician. Rx only. Prior to use, please see the complete "Instructions for Use" for more information on Indications, Contraindications, Warnings, Precautions, Adverse Events, and Operator's Instructions.

WARNING: A signal for increased risk of late mortality has been identified following the use of paclitaxelcoated balloons and paclitaxel-eluting stents for femoropopliteal arterial disease beginning approximately 2-3 years post-treatment compared with the use of non-drug coated devices. There is uncertainty regarding the magnitude and mechanism for the increased late mortality risk, including the impact of repeat paclitaxel coated device exposure. Physicians should discuss this late mortality signal and the benefits and risks of available treatment options with their patients. See Section 8.1 (in the eIFU) for further information. INTENDED USE / INDICATIONS FOR USE: The Ranger Drug Coated Balloon (DCB) is indicated for percutaneous transluminal angioplasty (PTA) of de novo or restenotic lesions up to 180 mm in length located in native superficial femoral and proximal popliteal arteries (SFA/PPA) with reference vessel diameters of 4 mm to 7 mm. **CONTRAINDICATIONS:** Use of the Ranger DCB is contraindicated in: • Patients with known hypersensitivity to paclitaxel (or structurally-related compounds). • Patients who cannot receive recommended antiplatelet and/or anticoagulation therapy. • Women who are breastfeeding, pregnant, or men intending to father children. • Patients judged to have a lesion that prevents complete inflation of an angioplasty balloon or proper placement of the delivery system. • Coronary arteries, renal arteries, and supra-aortic/cerebrovascular arteries. **WARNINGS:** • To reduce the potential for vessel damage, the inflated diameter of the balloon should approximate the diameter of the vessel segment to be treated. The inflated length of the balloon (shoulder to shoulder) may exceed the length of the lesion/stenosis by approximately 10 mm on either side within the targeted artery. • The safety of using multiple Ranger DCBs with a total drug dosage exceeding 9266 µg of Paclitaxel in a patient has not been studied. • Using a drug-eluting stent in conjunction with Ranger DCB at the same treatment site has not been studied. **PRECAUTIONS:** • The balloon catheter should be used only by physicians trained in the performance of percutaneous transluminal angioplasty. • The balloon catheter should be used with caution for procedures involving calcified lesions due to the abrasive nature of these lesions. • The balloon catheter is not intended for injection of contrast medium. • Full arterial wall apposition of the Ranger DCB is necessary for proper drug transfer to the vessel. • Do not touch, wipe, bend, or squeeze the balloon. Do not allow it to contact any liquids including organic solvents such as alcohol or detergents prior to insertion. Damage to the balloon coating or premature release of the drug may occur. • This product should not be used in patients with uncorrected bleeding disorders or patients who cannot receive anticoagulation or antiplatelet aggregation therapy. • If treating a long lesion (longer than the maximum balloon length available), each individual segment should be treated only once with a drug-coated balloon. Treat each segment with a new balloon and minimize overlapping of treated segments. **Pregnancy / Lactation** This product has not been tested in pregnant or breastfeeding women or in men intending to father children; effects on the developing fetus have not been studied and the risks and reproductive effects remain unknown. It is not recommended that the Ranger DCB be used in women attempting to conceive, or who are pregnant. Prior to use, careful consideration should be given to the continuation of breastfeeding, taking into account the importance of the procedure to the mother. It is not known whether paclitaxel is distributed in human milk. In lactating rats, milk concentrations appeared to be higher than maternal plasma levels and declined in parallel with the maternal levels. Mothers should be advised of the potential for serious adverse reactions to paclitaxel in nursing infants. **Drug Information** The mechanism of action by which paclitaxel reduces or reverses neointima formation and proliferation, leading to restenosis, as demonstrated in clinical studies has not been established. It is known that paclitaxel promotes the assembly of microtubules from tubulin dimers and stabilizes microtubules by preventing depolymerization. This stability results in the inhibition of the normal dynamic reorganization of the microtubule network that is essential for vital interphase and mitotic cellular functions. **Drug Interaction** Possible interactions of paclitaxel with concomitantly administered medications have not been formally investigated. Drug interactions of systemic chemotherapeutic levels of paclitaxel with possible concomitant medications are outlined in the labeling for finished pharmaceuticals containing paclitaxel, such as TAXOL™. **Carcinogenicity, Genotoxicity, and Reproductive Toxicology** No long-term studies in animals have been published in peer-reviewed literature to evaluate the carcinogenic potential of paclitaxel. Paclitaxel interacts with microtubules; this is the major mechanism by which it inhibits cell growth. One consequence is the loss of whole chromosomes via interactions with spindle microtubules during cell division. As such, paclitaxel is defined as an aneugen (agent causing an alteration in chromosome number). This indirect action is consistent with positive responses in in vitro and in vivo micronucleus genotoxicity assays, which detect DNA fragments. Positive results have also been reported for chromosomal aberrations in primary human lymphocytes. It is not known whether paclitaxel has a separate direct action on DNA in the generation of DNA strand breaks or fragments. It is negative in assays for gene mutation, including salmonella and CHO/HPRT. Paclitaxel administered via IV prior to and during mating produced impairment of fertility in male and female rats at doses > 1 mg/kg. Administration of paclitaxel during the period of organogenesis to rabbits at doses of 3 mg/kg/day caused embryo- and fetotoxicity. Maternal toxicity was also observed at this dose. No teratogenic effects were observed at 1 mg/kg/day; teratogenic potential could not be assessed at higher doses due to extensive fetal mortality. For comparison, the worst-case dose of paclitaxel delivered by the Ranger DCB (assuming maximum size and number of balloons used in a lesion) is 9266 µg, which is approximately 6 and 19 times less than the dose that saw effects in rats and rabbits, respectively, when normalizing to body weight. **Pre and Post Procedure Antiplatelet Therapy** It is strongly advised that the treating physician follow the Inter-Society Consensus (TASC II) Guidelines recommendations (or other applicable country guidelines) for antiplatelet therapy pre- and postprocedure. **ADVERSE EVENTS:** Potential adverse events include, but are not limited to, the following: • Allergic reaction (device, contrast medium, medications) • Arteriovenous fistula • Death • Hematoma • Hemorrhage/Bleeding • Hypotension/Hypertension • Infection/Sepsis • Pseudoaneurysm • Thromboembolic episodes • Vascular thrombosis • Vessel injury (e.g., dissection, perforation, rupture) • Vessel occlusion • Vessel spasm Potential adverse events not captured above that may be unique to the paclitaxel drug coating: • Allergic/immunologic reaction to drug (paclitaxel or structurally-related compounds) or coating or its individual components • Alopecia • Anemia • Blood product transfusion • Gastrointestinal symptoms • Hematologic dyscrasia (including leukopenia, neutropenia, thrombocytopenia) • Hepatic enzyme changes • Histologic changes in vessel wall, including inflammation, cellular damage or necrosis • Myalgia/Arthralgia • Peripheral neuropathy Apart from hypersensitivity reactions (allergic/immunologic reactions), the likelihood of paclitaxel related adverse events is low, due to the low exposure. There may be other potential adverse events that are unforeseen at this time. **92618589 B.3**

ELUVIA™ DRUG-ELUTING VASCULAR STENT SYSTEM

CAUTION: Federal law (USA) restricts this device to sale by or on the order of a physician. Rx only. Prior to use, please see the complete "Directions for Use" for more information on Indications, Contraindications, Warnings, Precautions, Adverse Events, and Operator's Instructions. **INTENDED USE/INDICATIONS FOR USE:** The ELUVIA Drug-Eluting Vascular Stent System is intended to improve luminal diameter in the treatment of symptomatic de-novo or restenotic lesions in the native superficial femoral artery (SFA) and/or proximal popliteal artery with reference vessel diameters (RVD) ranging from 4.0-6.0 mm and total lesion lengths up to 190 mm. **CONTRAINDICATIONS:** • Women who are pregnant, breastfeeding, or plan to become pregnant in the next 5 years should not receive an ELUVIA Drug-Eluting Stent. It is unknown whether paclitaxel will be excreted in human milk, and there is a potential for adverse reaction in nursing infants from paclitaxel exposure. • Patients who cannot receive recommended anti-platelet and/or anti-coagulant therapy. • Patients judged to have a lesion that prevents proper placement of the stent or stent delivery system. **WARNINGS**: **A signal for increased risk of late mortality has been identified following the use of paclitaxel-coated balloons and paclitaxel-eluting stents for femoropopliteal arterial disease beginning approximately 2-3 years post-treatment compared with the use of non-drug coated devices. There is uncertainty regarding the magnitude and mechanism for the increased late mortality risk, including the impact of repeat paclitaxel-coated device exposure. Physicians should discuss this late mortality signal and the benefits and risks of available treatment options with their patients. See Section 8.1 of the DFU for further information**. • The delivery system is not designed for use with power injection systems. • Only advance the stent delivery system over a guidewire. • The stent delivery system is not intended for arterial blood monitoring. • In the event of complications such as infection, pseudoaneurysm or fistula formation, surgical removal of the stent may be required. • Do not remove the thumbwheel lock prior to deployment. Premature removal of the thumbwheel lock may result in an unintended deployment of the stent. • It is strongly advised that the treating physician follow the Inter-Society Consensus (TASC II) Guidelines recommendations (or other applicable country guidelines) for antiplatelet therapy pre-procedure to reduce the risk of thrombosis. Post-procedure dual antiplatelet therapy is required for a minimum of 60 days. **PRECAUTIONS:** • Stenting across a bifurcation or side branch could compromise future diagnostic or therapeutic procedures. • The stent is not designed for repositioning. • Once the stent is partially deployed, it cannot be "recaptured" or "reconstrained" using the stent delivery system. • The stent may cause embolization from the site of the implant down the arterial lumen. • This product should not be used in patients with uncorrected bleeding disorders or patients who cannot receive anticoagulation or antiplatelet aggregation therapy. • Persons with a known hypersensitivity to paclitaxel (or structurally-related compounds), to the polymer or its individual components (see details in **Primer Polymer and Drug Matrix Copolymer Carrier** section), nickel, or titanium may suffer an allergic response to this implant. • Persons with poor kidney function may not be good candidates for stenting procedures. **PROBABLE ADVERSE EVENTS**: Probable adverse events which may be associated with the use of a peripheral stent include but are not limited to: • Allergic reaction (to drug/polymer, contrast, device or other) • Amputation • Arterial aneurysm • Arteriovenous fistula • Death • Embolization (air, plaque, thrombus, device, tissue, or other) • Hematoma • Hemorrhage (bleeding) • Infection/Sepsis • Ischemia • Need for urgent intervention or surgery • Pseudoaneurysm formation • Renal insufficiency or failure • Restenosis of stented artery • Thrombosis/thrombus • Transient hemodynamic instability (hypotensive/hypertensive episodes) • Vasospasm • Vessel injury, including perforation, trauma, rupture and dissection • Vessel occlusion. Probable adverse events not captured above that may be unique to the paclitaxel drug coating: • Allergic/immunologic reaction to drug (paclitaxel or structurally-related compounds) or the polymer stent coating (or its individual components) • Alopecia • Anemia • Gastrointestinal symptoms • Hematologic dyscrasia (including leukopenia, neutropenia, thrombocytopenia) • Hepatic enzyme changes • Histologic changes in vessel wall, including inflammation, cellular damage or necrosis • Myalgia/Arthralgia • Peripheral neuropathy There may be other potential adverse events that are unforeseen at this time. **92306016 B.3**

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PI-897901-AA