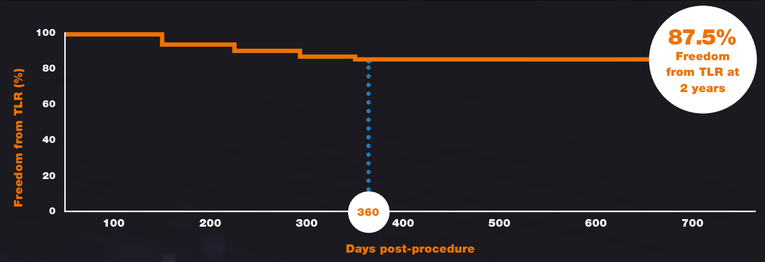
Delivering Long-Term Clinical Benefits in Peripheral Artery Disease[4]

SELUTION SFA – First-in-Man Clinical Trial

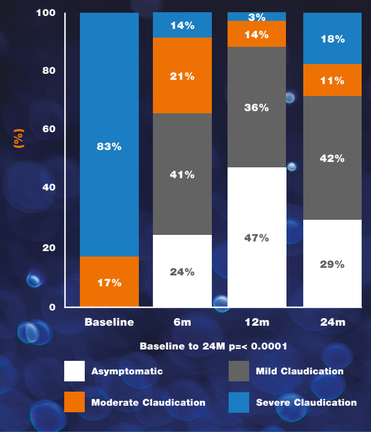
Principal Investigator: Thomas Zeller, MD, Germany (ClinicalTrials.gov ID: NCT02941224)

- Prospective, controlled, multi-center, open, single-arm clinical investigation
- 50 patients in 4 German Centers
- Met Primary Endpoint of Late Lumen Loss at 6 Months with 0.19mm**

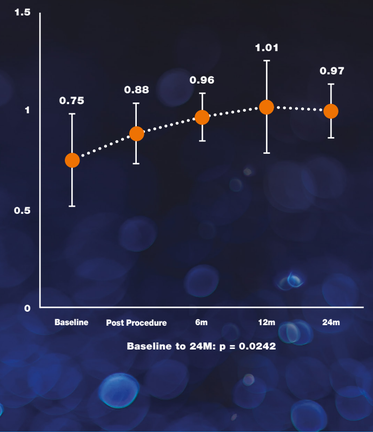
SELUTION SFA – Freedom from TLR



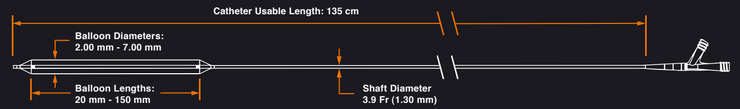
84% of patients improved in Rutherford Classification out to 24M



Clinical Improvement in ABI



Technical Specification



Feature	Specification
Sirolimus Drug Dose	1.0 $\mu g/mm^2$
Drug Carrier	Cell Adherent Technology (CAT™) Amphipathic Lipid Carrier
Catheter Design	Over-the-Wire (OTW)
Shaft Diameter	3.9 Fr (1.30 mm)
Catheter Usable Length	135 cm
Guidewire Compatibility	0.018"
Introducer Sheath Compatibility	5 Fr for balloon diameters 2.00 – 3.00 mm 6 Fr for balloon diameters 3.50 – 5.00 mm 7 Fr for balloon diameters 6.00 – 7.00 mm

Balloon	
Nominal Balloon Pressure (NP)	6 bar
Rated Burst Pressure (RBP)	20 – 40 mm: RBP 12 bar 60 – 150 mm: RBP 10 bar
Balloon Diameter	2.00 mm – 7.00 mm
Balloon Lengths	20, 40, 60, 80, 100, 120, 150 mm

Ordering Information

SELUTION SLR™ Sirolimus Eluting PTA Balloon Catheter

Balloon Diameter (mm)	Balloon Length (mm)						
	20	40	60	80	100	120	150
2.00	SE18-020020	SE18-020040	SE18-020060	SE18-020080	SE18-020100	SE18-020120	SE18-020150
2.50	SE18-025020	SE18-025040	SE18-025060	SE18-025080	SE18-025100	SE18-025120	SE18-025150
3.00	SE18-030020	SE18-030040	SE18-030060	SE18-030080	SE18-030100	SE18-030120	SE18-030150
3.50	SE18-035020	SE18-035040	SE18-035060	SE18-035080	SE18-035100	SE18-035120	SE18-035150
4.00	SE18-040020	SE18-040040	SE18-040060	SE18-040080	SE18-040100	SE18-040120	SE18-040150
5.00	SE18-050020	SE18-050040	SE18-050060	SE18-050080	SE18-050100	SE18-050120	SE18-050150
6.00	SE18-060020	SE18-060040	SE18-060060	SE18-060080	SE18-060100	SE18-060120	SE18-060150
7.00	SE18-070020	SE18-070040	SE18-070060	SE18-070080	SE18-070100	SE18-070120	SE18-070150

** Presented as median value. 1. Drug concentration evident in MicroReservoirs and tissue. - Data on file at M.A. Med Alliance SA.
2. Data on file at M.A. Med Alliance SA. 3. Granada. J - Oral Presentation CRT 2014. 4. Zeller. T - Oral Presentation VIVA 2019.

Indication, contraindications and warnings can be found in the instructions for use supplied with each device.
SELUTION SLR Sirolimus Eluting PTA Balloon Catheter - CE Mark Approved. Not available for sale in United States.

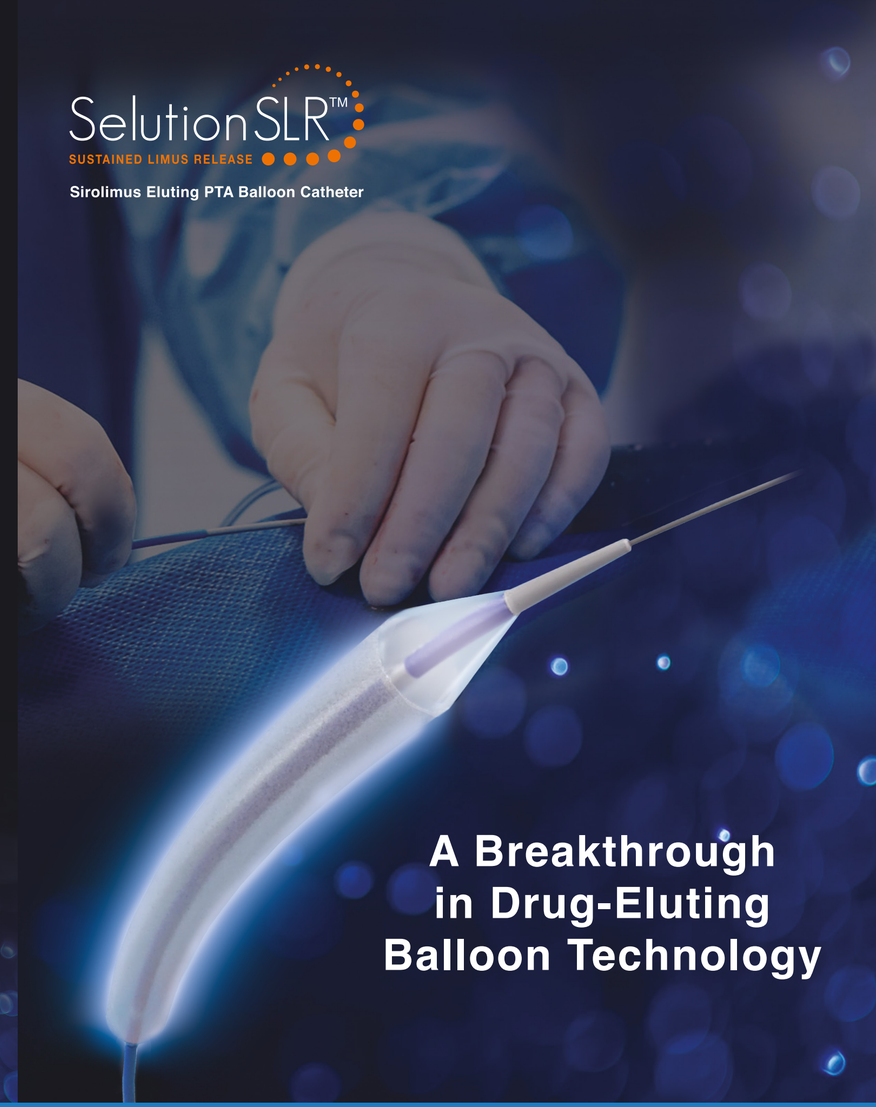
CE 0344

M.A. Med Alliance SA, Rue de Rive 5, 1260 Nyon, Switzerland
T: + 41 22 363 78 90 | E: info@medalliance.com | W: www.medalliance.com

SAM-0002 Rev.E

SelutionSLR™
SUSTAINED LIMUS RELEASE

Sirolimus Eluting PTA Balloon Catheter



A Breakthrough in Drug-Eluting Balloon Technology

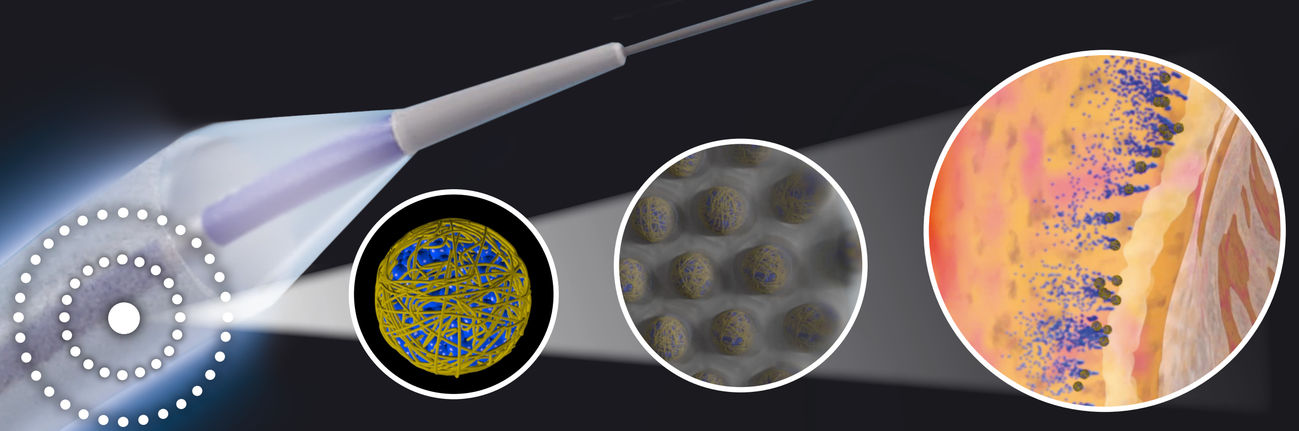
SelutionSLR™
SUSTAINED LIMUS RELEASE

MedAlliance

MedAlliance

The First Sirolimus Drug Eluting Balloon Specifically Designed to Treat Peripheral Artery Disease.

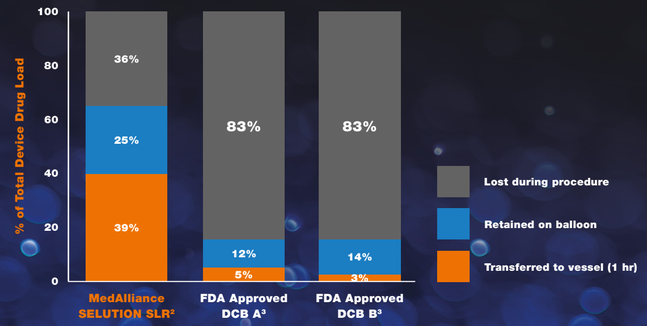
SELUTION SLR™ uniquely combines the proven safety and efficacy of sirolimus with advanced MicroReservoir and Cell Adherent Technology (CAT™) to offer a sustained therapeutic effect for up to 90 days.[1]



Breakthrough* Technology to Deliver Sustained Limus Release for up to 90 days[1]

SELUTION SLR – Drug Transfer Efficiency

The CAT amphipathic coating maximises drug bioavailability



MicroReservoirs form millions of precision-engineered drug delivery systems, combining sirolimus with a biodegradable polymer, achieving consistent and predictable drug release;

- Optimizing MicroReservoir size to achieve a pharmaco-kinetic release profile comparable to the latest generation DES technology.

Cell Adherent Technology (CAT™) is a proprietary amphipathic lipid technology which binds the MicroReservoirs to the balloon surface, protecting them during balloon insertion and inflation;

- Enhancing drug retention and bioavailability, allowing for a lower drug dose concentration on the balloon surface (1μg/mm²).
- Optimizing transfer of MicroReservoirs to the tissue and maximizing the cellular uptake of sirolimus.

Latest Generation of PTA Balloon

- Offering a broader portfolio for peripheral indications with balloon diameters ranging from 2.00 mm to 7.00 mm and lengths from 20 mm to 150 mm.

* MedAlliance is the first drug-eluting balloon (DEB) company in the world to be awarded US Food and Drug Administration (FDA) Breakthrough Device Designation Status.

SelutionSLR™
SUSTAINED LIMUS RELEASE

MedAlliance

SELUTION SLR™ PTA Balloon Catheter

Sustained Limus Release Drug Eluting PTA Balloon Catheter

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ENGLISH

SYMBOLS

REF	Reference Number
SN	Serial Number
	Date of Manufacture
	Use By
	Manufacturer
NP	Nominal Pressure
RBP	Rated Burst Pressure
OTW	Over the Wire
STERILE R	Sterilized Using Irradiation
	Consult Instructions for Use
	Caution
	Do Not Re-Use
	Keep Dry
	Keep Away from Sunlight
	Temperature Limit
	Do Not Use if Package is Damaged
	Diameter
MINIMUM INTRODUCER 	Minimum Size of Introducer
	Do not re-sterilize
CONTENT	Content
Sirolimus Dose Density	Sirolimus Dose Density
USABLE LENGTH	Usable Length
BALLOON LENGTH	Balloon Length
GUIDEWIRE DIAMETER	Guidewire Diameter
SHAFT DIAMETER	Shaft Diameter
BALLOON DIAMETER Ø	Balloon Diameter
BALLOON PRESSURE P	Balloon Pressure

SELUTION SLR™ PTA Balloon Catheter
Sustained Limus Release Drug Eluting PTA Balloon Catheter

Device Description
The SELUTION SLR™ 018 PTA Balloon Catheter is a Drug-Eluting Balloon (DEB) catheter for Percutaneous Transluminal Angioplasty (PTA) procedures. It is a 3.9 Fr (1.3 mm) diameter Over-The-Wire (OTW) catheter that is 0.018" (0.46 mm) guidewire compatible and has a usable length of 135 cm. The balloon that is affixed to the distal portion of the catheter includes a surface coating containing Sirolimus, a drug that acts both as an anti-proliferative agent and as an anti-inflammatory immunosuppressant.
The catheter incorporates a dual-lumen shaft design. One lumen is used for balloon inflation and is accessed through the side port of the Y- hub. The second lumen, accessed through the straight port of the Y-hub, allows passage of a guidewire. Two radiopaque markers, located under the proximal and distal ends of the balloon, delineate the working length of the balloon and facilitate fluoroscopic visualization of the balloon during delivery and positioning.
The SELUTION SLR™ PTA DEB is available in an assortment of balloon sizes. Nominal balloon diameters and lengths are printed on the strain relief that is bonded to the Y-hub. Each device is packaged with a protector sheath over the balloon and a disposable wire stylet in the distal tip; both of which are to be removed prior to use.

Drug Coating Description
The drug coating on the balloon part of the SELUTION SLR™ PTA DEB is a proprietary formulation, consisting of Sirolimus (also known as Rapamycin) as the Active Pharmaceutical Ingredient (API) and four excipients. The first excipient is a biodegradable polymer (Poly(lactic-co-glycolic acid) – PLGA) that encapsulates the Sirolimus into micro-reservoirs which regulate drug release via matrix degradation. The remaining three excipients constitute a phospholipid blend, all of which aim to reduce wash-off of the micro-reservoirs into the bloodstream and help to adhere the drug coating to the surrounding tissues when the SELUTION SLR™ 018 PTA DEB balloon is inflated inside the diseased vessel. The drug coating is evenly distributed across the working length of the balloon with a Sirolimus dose density of 1 µg/mm².

Summary of Characteristics

Catheter Design	Over-the-wire PTA
Usable Catheter Length	135 cm
Balloon Inflation Pressure	Nominal Pressure: 600 kPa (= 6 bar) Rated Burst Pressure (RBP): 20-40 mm length balloons: 1200 kPa (= 12 bar) 60-150 mm length balloons: 1000 kPa (= 10 bar)
Introducer Sheath Compatibility (minimum size)	5F/1.67mm for diameters 2.0 - 3.0 mm 6F/2.00mm for diameters 4.0 - 5.0 mm 7F/2.33mm for diameters 6.0 - 7.0 mm
Guidewire Compatibility	Compatible with 0.018 inch (0.46 mm) guidewires
Active Pharmaceutical Ingredient	Sirolimus at 1.0 µg/mm² dose density

Tables included at the end of this document provide information about each available size of SELUTION SLR™ 018 PTA Balloon Catheter:
- **Drug Dosage Chart**: nominal dose of Sirolimus present on each balloon size
- **Reference Numbers Chart**: Reference Number REF or order code for each balloon size.
- **Compliance Chart**: effective balloon diameter corresponding to each inflation pressures.

Intended Use / Indications for Use
The SELUTION SLR™ PTA DEB is intended for use as a Percutaneous Transluminal Angioplasty (PTA) balloon catheter to dilate de novo or restenotic vascular lesions, for the purpose of improving limb perfusion and decreasing the incidence of restenosis.

Contraindications
The SELUTION SLR™ PTA DEB is contraindicated for use in:
- Patients with known allergies or hypersensitivities to Sirolimus (or analogues).
- Patients who cannot receive recommended antiplatelet and/or anticoagulant therapy.
- Patients with known sensitivity to contrast agents.
- Pregnant or breast-feeding women.
- Lesions that cannot be crossed with a guidewire.

Warnings
- Contents are supplied STERILE using an E-beam irradiation sterilization process.
  DO NOT USE IF sterile barrier is damaged or opened prior to intended use.
- The SELUTION SLR™ PTA DEB is intended for SINGLE USE only. DO NOT RESTERILIZE AND/OR REUSE. Resterilization and/or reuse may create a risk of contamination of the device and/or cause patient infection or cross-infection, including the transmission of infectious disease(s) from one patient to another. Contamination of the device may lead to patient injury, illness, or death. Reuse and/or resterilization may compromise the structural integrity of the device and/or lead to device failure, which in turn, may result in patient injury, illness, or death.
- The drug coated balloon surface is effective for a single inflation only.
- Inspect the SELUTION SLR™ PTA DEB prior to the procedure to verify that the device is intact and functional. DO NOT USE if the outer or the inner packaging is damaged or opened or if any information on the package is obscured or damaged.
- DO NOT USE after the labelled "Use By" date.
- DO NOT EXCEED the Rated Burst Pressure (RBP) recommended for this device. Balloon rupture may occur if the RBP rating is exceeded. To prevent over-pressurization, use of a pressure-monitoring device is recommended.
- Use the recommended balloon inflation medium of contrast and sterile saline (≤50% contrast). Never use air or any gaseous medium to inflate the balloon.
- Do not use in the coronary arteries

Precautions
Device Handling Precautions
- The SELUTION SLR™ PTA DEB should only be used by physicians trained in PTA procedures.
- Replace any device where the balloon has come into contact with organic solvents (e.g. alcohol).
- The coated balloon portion should be handled with dry sterile gloves whenever possible prior to use. Care should be taken to minimize unnecessary contact with the coated balloon portion of the SELUTION SLR™ 018 PTA DEB during preparation and insertion.
- The balloon protector sheath and disposable wire lumen stylet must stay in place during preparation of the SELUTION SLR™ PTA DEB and not be removed until just prior to placing the device over the guidewire.
- If difficulty is encountered while removing the balloon protector sheath, a new SELUTION SLR™ PTA DEB must be utilized.
- It is recommended that an introducer sheath be used to facilitate placement. Refer to the product label for information on the appropriate sheath size.
- After insertion, do not over-tighten the haemostasis valve (if used) around the SELUTION SLR™ PTA DEB shaft as lumen constriction may occur, affecting inflation/ deflation of the balloon.
- To ensure therapeutic drug delivery:
  - Open the haemostasis valve sufficiently to allow an easy passage of the drug coated balloon through the valve during catheter insertion
  - Do not inflate the SELUTION SLR™ PTA DEB prior to reaching the target lesion.

- Ensure that there is full contact of the inflated balloon with the lesion across the entire length of the treated area.
- Maintain balloon inflation for a minimum of 2 minutes. Use the maximum balloon inflation time per your institution's standard of care.

- Maintain tight Luer connections and always advance and retrieve the SELUTION SLR™ PTA DEB under negative pressure.
- The SELUTION SLR™ PTA DEB should always be manipulated under fluoroscopic observation when in the body.
- Do not continue to use the SELUTION SLR™ PTA DEB if the shaft has been bent or kinked.
- Whenever possible, the SELUTION SLR™ PTA DEB should be the final treatment of the vessel; however, if post-dilatation is required, use of a new SELUTION SLR™ PTA DEB is recommended.
- The use of the SELUTION SLR™ PTA DEB should be used in a medical environment which affords timely access to open surgery conversion, and acute peri-procedural access to percutaneous reintervention.
- After use, the SELUTION SLR™ PTA DEB may be a biohazard. Handle and dispose of all such devices in accordance with accepted medical practice and applicable hospital, administrative, and government regulations.

Use in Conjunction with Other Devices

- The SELUTION SLR™ PTA DEB should not be used in conjunction with other drug coated balloons or drug eluting stents to treat the same lesion in the same procedure. The safety of combinations of different drug-device products has not been assessed.

Pre- and Post-Procedure Antiplatelet Regimen

- Pre-procedure:
- Note: Flush the guide wire lumen of the SELUTION PTA catheter with sterile heparinized saline or a similar isotonic solution
- Post-Procedure
- Following the procedure, dual antiplatelet therapy should be given for at least 4 weeks; follow-on therapy should be given per hospital standards for PTA procedures.

Drug Information

Mechanism of Action

Sirolimus is a macrocyclic lactone, also known as Rapamycin. It is known that Sirolimus inhibits T and B- lymphocyte activation and smooth muscle and endothelial cell proliferation in response to cytokine and growth factor stimulation. In cells, Sirolimus binds to the immunophilin, FK Binding Protein-12 (FKBP-12). The Sirolimus-FKBP-12 complex binds to and inhibits activity of the mechanistic Target of Rapamycin (mTOR). mTOR is a serine/threonine protein kinase that regulates cell growth, cell proliferation, cell motility, cell survival, protein synthesis, autophagy, and transcription. Inhibition of mTOR stops cell cycle progression from the G1 to the S phase.

Metabolism

Sirolimus is extensively metabolized by the hepatic CYP3A4 enzyme and is also a substrate for the P-glycoprotein (P-gp) transmembrane efflux pump found in the intestinal epithelium, liver cells, proximal tubule of the kidney and capillary endothelial cells. The clearance of Sirolimus is affected by both of these pathways and displays a large inter- patient variability. The majority of the metabolites, including demethyl and hydroxydemethyl Sirolimus are formed via O- demethylation and hydroxylation. Sirolimus is the major component in human whole blood and contributes to more than 90% of the immunosuppressive activity. The metabolites account for less than 10% of the immunosuppressant activity of Sirolimus. Biliary and faecal pathways serve as the primary routes of Sirolimus elimination. The half-life of Sirolimus ranges from 57 to 63 hours in the bloodstream.

Drug Interactions

Consideration should be given to the potential for drug interaction when deciding to use a SELUTION SLR™ PTA DEB in a patient who is taking a drug that could interact with Sirolimus. The effect of drug interactions on the safety or efficacy of the SELUTION SLR™ PTA DEB has not been determined; however, since the SELUTION SLR™ PTA DEB exhibits its treatment effect locally and at a low dosage, it is not expected that concomitant treatment with other drugs will affect the effectiveness or safety of the SELUTION SLR™ PTA DEB.

There is no specific clinical data available for the interactions of Sirolimus with other drugs. However, drugs like Tacrolimus that may act through the same binding proteins (FKBP-12) may interfere with the efficacy of Sirolimus.

Co-administration of Sirolimus with strong inhibitors of CYP3A4 and/or P-gp (such as ketoconazole, voriconazole, itraconazole, erythromycin, telithromycin, or clarithromycin) or strong inducers of CYP3A4 and/or P-gp (such as rifampin or rifabutin) is not recommended. Exercise caution with weaker modulators. Grapefruit juice should be avoided as it also inhibits CYP3A4-mediated metabolism.

Potential Adverse Events

Potential adverse events, which may be associated with a PTA procedure, include, but are not limited to:

- Allergic reaction to contrast medium, anticoagulants and antiplatelets
- Amputation/loss of limb
- Aneurysm or pseudoaneurysm
- Arteriovenous (AV) fistula
- Arrhythmias
- Death
- Embolization
- Fever
- Hematoma
- Haemorrhage, incl. bleeding at puncture site
- Hypotension/hypertension
- Increased Procedure Time/Additional Interventions
- Inflammation
- Occlusion
- Pain or tenderness
- Pneumothorax or haemothorax
- Renal failure
- Sepsis/infection
- Shock
- Stroke
- Thrombosis
- Vessel dissection, occlusion, perforation, recoil, restenosis, rupture, or spasm

Potential adverse events that may be unique to the SELUTION SLR™ PTA DEB Sirolimus drug coating include, but are not limited to:

- Abnormal liver function tests
- Anaemia
- Arthralgias
- Diarrhoea
- Hypercholesterolemia
- Hypersensitivity, including anaphylactic/anaphylactoid type reactions
- Hypertriglyceridemia
- Hypokalaemia
- Infections
- Interstitial lung disease
- Leukopenia
- Lymphoma and other malignancies
- Thrombocytopenia

The potential adverse events listed above are related to the oral administration of Sirolimus at significantly higher doses than what would be delivered by the SELUTION SLR™ PTA DEB locally to the vessel wall. Therefore, due to the local administration and low dosage, these pharmacological interactions are not expected.

Procedure

Prior to angioplasty, carefully examine all equipment and materials to be used during the procedure, including the SELUTION SLR™ 018 PTA DEB, to verify proper functioning. Verify that the SELUTION SLR™ 018 PTA DEB size is suitable for the specific procedure for which it is intended.

In addition to the SELUTION SLR™ 018 PTA DEB, the following standard materials may also be required:

- 0.018" (0.46 mm) guidewire
- Torque device
- Haemostasis valve with 7 Fr inner lumen
- Introducer sheath (5, 6, or 7 Fr)
- Contrast medium
- Sterile saline
- Inflation device with manometer
- Luer lock syringe for purging

Handle the SELUTION SLR™ 018 PTA DEB with extreme caution in order to avoid any damage to the folded balloon. Avoid exposing the balloon's drug coating to excessive handling or contact with liquids prior to preparation and delivery, as the coating may be susceptible to damage or premature drug release.

1. Inflation Device Preparation
   a. Prepare the inflation device according to the manufacturer's instructions.
2. SELUTION SLR™ 018 PTA DEB Selection
   a. The chosen nominal balloon size should be equal to the reference vessel diameter. The balloon should extend at least 5 mm beyond the lesion both proximally and distally. If multiple SELUTION SLR™ 018 PTA DEB are required to complete the treatment of a lesion, the sequentially used devices should be minimally sized and angiographically positioned so that the balloon marker bands of consecutively placed devices overlap by at least 5 mm. The use of a radiopaque ruler is recommended to ensure appropriate placement of the SELUTION SLR™ 018 PTA DEB.
   b. Pre-dilatation with a standard PTA balloon having not more than one size smaller than the reference vessel diameter is required.
3. SELUTION SLR™ 018 PTA DEB Preparation
   a. Prior to use, verify that neither the unit's carton nor the sterile packaging have been damaged in shipment.
   b. Carefully remove the device from the packaging, and examine it to verify it is not damaged.
   c. Purge the SELUTION SLR™ PTA DEB of air prior to use. Keep the balloon protector sheath in place during the purging procedure. Begin by pointing the distal tip of the SELUTION SLR™ PTA DEB downward while holding it vertically. Connect a stopcock and Luer lock syringe partially filled with the saline-contrast mixture to the inflation side port of the SELUTION SLR™ 018 PTA DEB Y-hub. Apply negative pressure until air is completely evacuated and release the plunger.
      Repeat this operation until migration of air bubbles towards the syringe stops. Close the stopcock while vacuum is being applied to the device.
   d. While the device is under vacuum, remove the stylet and the protector sheath from the balloon and discard. Do not use the balloon protector sheath as an introduction aid or rewrapping tool.
   e. Flush the wire lumen thoroughly through the Luer lock on the straight port of the SELUTION SLR™ DEB Y-hub.
4. Inflation Device Connection
   a. To remove any air lodged in the distal Luer fitting of the inflation device, purge approximately 1 ml (cc) of diluted contrast medium.
   b. With the stopcock in the closed position, disconnect the syringe used in preparation, slightly applying positive pressure. A meniscus of contrast medium will appear in the inflation side port of the SELUTION SLR™ 018 PTA DEB Y-hub when the syringe is removed. Verify that a meniscus of contrast medium is evident in both the inflation side port of the SELUTION SLR™ 018 PTA DEB Y-hub and the inflation device's connection. Securely couple the inflation device to the inflation side port of the SELUTION SLR™ 018 PTA DEB Y-hub.
5. Use of the SELUTION SLR™ 018 PTA DEB
   a. Load the distal tip of the SELUTION SLR™ 018 PTA DEB onto the guidewire.
   b. Open the haemostasis valve to allow for easy passage of the balloon and to prevent damage to the balloon coating. With the

balloon fully deflated, advance the SELUTION SLR™ 018 PTA DEB through the haemostasis valve of the introducer sheath. To avoid kinking, advance the SELUTION SLR™ 018 PTA DEB slowly, in small increments, until the proximal end of the guidewire emerges from the catheter. Close the haemostasis valve of the introducer sheath only as much as is needed to prevent blood return while permitting easy movement of the SELUTION SLR™ 018 PTA DEB. If the SELUTION SLR™ 018 PTA DEB encounters resistance, do not advance it through the haemostasis valve of the introducer sheath.

c. Under fluoroscopy, use the balloon's radiopaque markers to position the balloon within the lesion to be dilated; then inflate the balloon to between 90% and 110% of reference vessel diameter using the appropriate pressure (refer to the balloon compliance chart included on the product label and do not exceed the RBP of the balloon). Once inflation has begun, do not move or reposition the SELUTION SLR™ 018 PTA DEB.
d. Maintain balloon inflation for a minimum of 2 minutes. Use the maximum balloon inflation time per your institution's standard of care.
Note: The SELUTION SLR™ 018 PTA DEB is intended for a single inflation only.
e. Apply negative pressure to fully deflate the SELUTION SLR™ 018 PTA DEB. Prior to removal, confirm under fluoroscopy that the balloon is fully deflated.
f. Perform angiography to confirm dilatation of the lesion.
Note: In case the vessel requires post-dilatation after the initial treatment with the SELUTION SLR™ 018 PTA DEB, use of a new SELUTION SLR™ 018 PTA DEB is recommended.
g. Open the haemostasis valve and withdraw the SELUTION SLR™ 018 PTA DEB from the body under negative pressure. Maintain the guidewire across the stenosis.
h. After confirming that a satisfactory dilatation was achieved, remove all equipment from the body and close the access site per standard clinical practice. If greater than 30% residual stenosis if present by visual estimate after using the SELUTION SLR™ 018 PTA DEB, it is recommended to use a bailout procedure per hospital standards to further increase the lumen diameter inside the lesion.

How Supplied

The SELUTION SLR™ PTA DEB is supplied sterile and for single use only. It is sterilized by E-beam irradiation. If left unopened and stored properly, the device will remain stable through the labelled Use By date.

The sterile packaging contains one (1) SELUTION SLR™ PTA DEB that is stored inside a catheter dispenser coil, which is placed inside a sealed aluminium foil pouch along with an oxygen absorber and desiccant.

Storage

The SELUTION SLR™ PTA DEB should be stored in its original packaging in a dry and dark location, at room temperature of 21°C (70°F); excursions are permitted to 15-25°C (59-77°F).

Warranty / Liability

The manufacturer warrants that each component of the SELUTION SLR™ PTA DEB has been designed, manufactured, packaged and tested with standard reasonable care. However, the manufacturer has no control over the conditions under which the device is used and a partial or complete failure of the intended function of the device may occur for various reasons. In this respect, the warnings in these Instructions for Use are expressly to be considered as an integral part of this Disclaimer and provide more detailed information.

THEREFORE, TO THE EXTENT ALLOWABLE BY APPLICABLE LAW, THIS WARRANTY IS EXCLUSIVE AND IS EXPRESSLY IN LIEU OF ANY OTHER EXPRESS OR IMPLIED WARRANTY OF MERCHANTABILITY OR FITNESS FOR ANY PARTICULAR PURPOSE AND OF ANY OTHER OBLIGATION OF THE MANUFACTURER.

Clinical Data Summary

The safety and Effectiveness of the SELUTION SLR™ 018 PTA DEB has been established through the pivotal European CE mark trial of the SELUTION SLR™ 018 PTA DEB device. A brief summary of the study design, data and conclusions is provided below.

Title of the study: Prospective, Controlled, Multi-Center, Open, Single-Arm Clinical Investigation of the Treatment of Patients with Femoropopliteal Artery Lesions with a Novel Drug Coated Balloon (SELUTION SLR™ 018 PTA DEB).

Primary Objective: To assess the clinical safety and the inhibition of restenosis of the SELUTION™ DCB in the treatment of de-novo occluded/stenotic or re-occluded/restenotic lesions of the superficial femoral and/or popliteal arteries.

Design: Prospective, controlled, multi-center, open, single arm clinical investigation

Primary Endpoint: Late Lumen Loss (LLL) of the target lesion, as measured by Quantitative Vascular Angiography (QVA) at 6 months post-index procedure.

Study follow-up: 6 months (primary endpoint), 12 and 24 months

Full details of inclusion/exclusion criteria, secondary objectives and secondary endpoints can be accessed on ClinicalTrials.gov, where this study is registered with the identifier (NCT number): NCT02941224

Patient population: n=50, average age of 70 years, 58% male and 42% female, 98% hyperlipidaemia, 80% hypertensive, 28% diabetic, all patients on anti-coagulant during procedure, 22% on heparin, all others on clopidogrel,22% renal insufficiency, 58% history of smoking, 26% previous percutaneous or surgical coronary revascularization, 22% had had anticoagulant therapy (5 were still on anticoagulant therapy during the clinical investigation).

Data Summary:

Primary Endpoint –

Mean late lumen loss (LLL) at 6 months in the Intention To Treat (ITT) population was 0.29 mm, significantly lower than the Objective Performance Criteria (OPC) of 1.0 mm ($p<0.0001$). In the Per Protocol (PP) population the mean LLL at 6 months was 0.50 mm ($p=0.0478$).

Secondary Endpoints -

Device success (successful delivery, inflation and retrieval): 98.8%.

Procedural success (residual stenosis ≤ 30% of the target lesion measured by QVA): 58% when measured by the Core laboratory versus 92% when measured by the investigators during the procedure.

Primary patency by Duplex UltraSound (DUS): At discharge 98%, at 6 months 88.4%.

Freedom from Angiographic Binary Restenosis (ABR): at 6 months 91% in the ITT population and 92.9% in the PP population.

Rutherford Classification (baseline to 6 months): 30% of the patients improved by 3 grades, 33% by 2 grades and 20% by 1 grade.

Ankle-Brachial Index (baseline to 6 months): Increased by 0.16 ($p < 0.0001$).

Change in Walking Impairment Questionnaire (WIQ) (baseline to 6 months): patients reporting much or great difficulty in walking decreased by 30% in the right leg ($p<0.0001$) and 23% in the left leg ($p=0.0019$).

Change in EQ-5D-5L (baseline to 6 months): perception of pain and mobility both improved

User acceptance: ratings were "good" or "excellent" in at least 82% of cases. The crossability and flexibility of the device, and the general impression of the device, all had "good" or "excellent" ratings in 100% of cases.

Safety Results

Clinical success: No MAEs (cardiovascular mortality, index limb amputation, target late thrombosis) within 24hrs post-index procedure. No device or procedure related deaths through 30 days. No MAE at 6 months and only 1 clinically driven Target Lesion Revascularisation (TLR) at 6 months post-index procedure. One device deficiency was reported (balloon burst) with no clinical consequences.

SELUTION SLR™ 018 PTA Balloon Catheter – Sirolimus Drug Dosage Chart

Balloon Diameter Ø [mm]	Balloon Length ⟷ [mm]						
	20	**40**	**60**	**80**	**100**	**120**	**150**
2.0	126 µg	251 µg	377 µg	503 µg	628 µg	754 µg	942 µg
3.0	188 µg	377 µg	565 µg	754 µg	942 µg	1131 µg	1414 µg
4.0	251 µg	503 µg	754 µg	1005 µg	1257 µg	1508 µg	1885 µg
5.0	314 µg	628 µg	942 µg	1257 µg	1571 µg	1885 µg	2356 µg
6.0	377 µg	754 µg	1131 µg	1508 µg	1885 µg	2262 µg	2827 µg
7.0	440 µg	880 µg	1319 µg	1759 µg	2199 µg	2639 µg	3299 µg

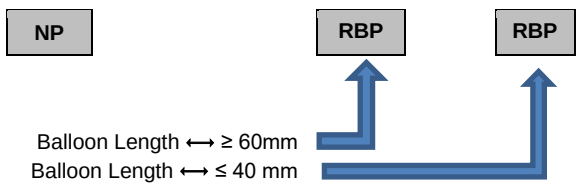
$$\underset{[\mu g]}{\text{Sirolimus Drug Dose}} = \underset{[mm]}{\text{Balloon Diameter Ø}} \times \underset{[mm]}{\text{Balloon Length} \leftrightarrow} \times \pi \approx 3.1415 \times \underset{[\mu g/mm^2]}{\text{Sirolimus Dose Density } 1.0}$$

SELUTION SLR™ 018 PTA Balloon Catheter – Reference Numbers Chart

Balloon Diameter Ø [mm]	Balloon Length ⟷ [mm]						
	20	**40**	**60**	**80**	**100**	**120**	**150**
2.0	SE18-020020	SE18-020040	SE18-020060	SE18-020080	SE18-020100	SE18-020120	SE18-020150
3.0	SE18-030020	SE18-030040	SE18-030060	SE18-030080	SE18-030100	SE18-030120	SE18-030150
4.0	SE18-040020	SE18-040040	SE18-040060	SE18-040080	SE18-040100	SE18-040120	SE18-040150
5.0	SE18-050020	SE18-050040	SE18-050060	SE18-050080	SE18-050100	SE18-050120	SE18-050150
6.0	SE18-060020	SE18-060040	SE18-060060	SE18-060080	SE18-060100	SE18-060120	SE18-060150
7.0	SE18-070020	SE18-070040	SE18-070060	SE18-070080	SE18-070100	SE18-070120	SE18-070150

SELUTION SLR™ 018 PTA Balloon Catheter – Compliance Chart

Balloon Diameter Ø [mm]	Balloon Pressure P									
	kPa (bar)	**400** (4)	**500** (5)	**600** (6)	**700** (7)	**800** (8)	**900** (9)	**1000** (10)	**1100** (11)	**1200** (12)
2.0	1.94	1.97	2.00	2.02	2.03	2.05	2.06	2.08	2.09
3.0	2.91	2.96	3.00	3.02	3.05	3.07	3.09	3.11	3.14
4.0	3.88	3.94	4.00	4.03	4.06	4.09	4.12	4.15	4.18
5.0	4.90	4.95	5.00	5.04	5.08	5.11	5.15	5.19	5.23
6.0	5.88	5.93	6.00	6.05	6.09	6.14	6.18	6.23	6.27
7.0	6.86	6.93	7.00	7.05	7.11	7.16	7.21	7.26	7.32



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M.A. Med Alliance SA
Rue de Rive 5
1260 Nyon
SWITZERLAND
Tel.: +41 22 363 78 90
Fax: +41 22 363 78 99

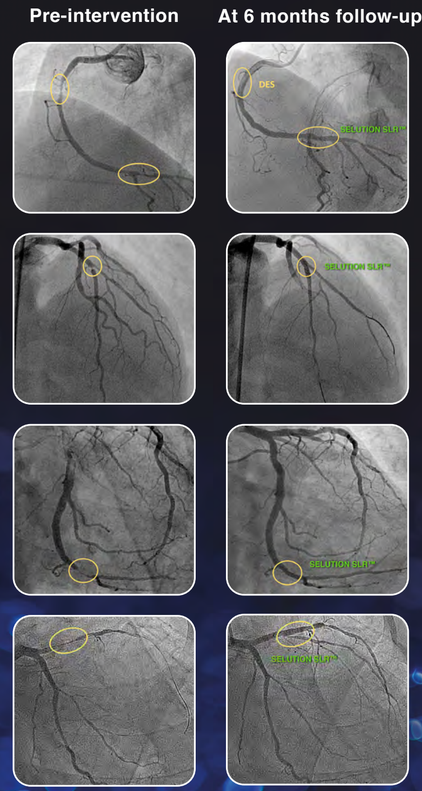
CE 0344

C1028 Rev I

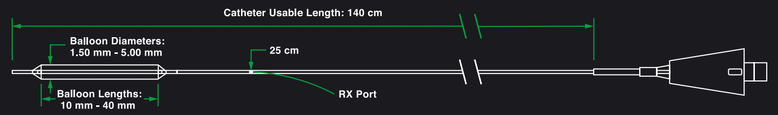
SELUTION SLR™ drug-eluting balloon (DEB) demonstrates safety and efficacy in First-in-Human coronary study[4] and is designed to deliver similar performance as drug-eluting stents (DES)[5].

- Primary endpoint - 100% Freedom from device and procedure-related mortality through 30 days.
- Low overall MACE rate of 2% at 12 months.

Case examples from First-in-Human Coronary Study



Technical Specification



Feature	Specification
Sirolimus Drug Dose	1.0 µg/mm²
Drug Carrier	Cell Adherent Technology (CAT™) Amphipathic Lipid Carrier
Catheter Design	Rapid Exchange (RX)
Catheter Usable Length	140 cm
Guidewire Compatibility	0.014"
Minimum Guide Catheter Compatibility (Fr)	≥ 5 Fr: 1.50 – 3.75 mm balloon diameter ≥ 6 Fr: 4.00 – 5.00 mm balloon diameter

Balloon	
Nominal Balloon Pressure (NP)	6 bar
Rated Burst Pressure (RBP)	12 bar
Balloon Diameters	1.50 mm – 5.00 mm
Balloon Lengths	10, 15, 20, 25, 30, 35, 40 mm

Ordering Information

SELUTION SLR™ Sirolimus Eluting PTCA Balloon Catheter

Balloon Diameter (mm)	Balloon Length (mm)						
	10	15	20	25	30	35	40
1.50	SC14-150010	SC14-150015	SC14-150020	SC14-150025	SC14-150030	SC14-150035	SC14-150040
2.00	SC14-200010	SC14-200015	SC14-200020	SC14-200025	SC14-200030	SC14-200035	SC14-200040
2.25	SC14-225010	SC14-225015	SC14-225020	SC14-225025	SC14-225030	SC14-225035	SC14-225040
2.50	SC14-250010	SC14-250015	SC14-250020	SC14-250025	SC14-250030	SC14-250035	SC14-250040
2.75	SC14-275010	SC14-275015	SC14-275020	SC14-275025	SC14-275030	SC14-275035	SC14-275040
3.00	SC14-300010	SC14-300015	SC14-300020	SC14-300025	SC14-300030	SC14-300035	SC14-300040
3.25	SC14-325010	SC14-325015	SC14-325020	SC14-325025	SC14-325030	SC14-325035	SC14-325040
3.50	SC14-350010	SC14-350015	SC14-350020	SC14-350025	SC14-350030	SC14-350035	SC14-350040
3.75	SC14-375010	SC14-375015	SC14-375020	SC14-375025	SC14-375030	SC14-375035	SC14-375040
4.00	SC14-400010	SC14-400015	SC14-400020	SC14-400025	SC14-400030	SC14-400035	SC14-400040
4.50	SC14-450010	SC14-450015	SC14-450020	SC14-450025	SC14-450030	SC14-450035	SC14-450040
5.00	SC14-500010	SC14-500015	SC14-500020	SC14-500025	SC14-500030	SC14-500035	SC14-500040

1,5. To achieve optimum performance from SELUTION SLR as a possible alternative to DES, follow the instructions for Use in your implant procedure, and reference "How to use the drug-eluting balloon: recommendations by the German consensus group", EuroIntervention 2011;7-K125-K128

2. MedAlliance is the first drug-eluting balloon (DEB) company in the world to be awarded US Food and Drug Administration (FDA) Breakthrough Device Designation Status.

3. Drug concentration evident in MicroReservoirs and tissue - Data on file at MedAlliance CardioVascular SA.

4. Windecker. S - Oral Presentation TCT 2019.

Indication, contraindications and warnings can be found in the instructions for use supplied with each device.
SELUTION SLR Sirolimus Eluting PTCA Balloon Catheter - CE Mark Approved. Not available for sale in United States.

CE 0344

Legal Manufacturer: MedAlliance Cardiovascular SA, Rue de Rive 5, 1260 Nyon, Switzerland
T: + 41 22 363 78 90 | E: info@medalliance.com | W: www.medalliance.com

SAM-0004 Rev.C

SelutionSLR™
SUSTAINED LIMUS RELEASE

Sirolimus Eluting PTCA Balloon Catheter

The New Paradigm for Coronary Interventions

SelutionSLR™
SUSTAINED LIMUS RELEASE

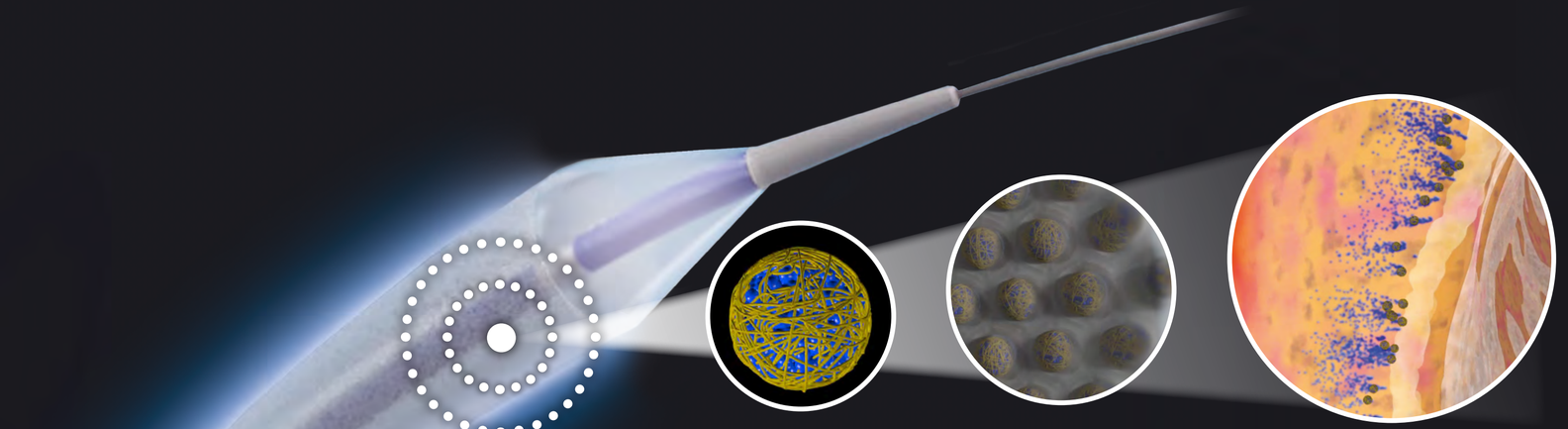
MedAlliance

MedAlliance

The new Paradigm for Coronary Interventions.

Don’t compromise on your treatment standard…
SELUTION SLR™ is the latest generation of Drug-Eluting Balloon technology.

- Offering you a greater choice of options for your coronary interventions.
- Designed to deliver the same safety and performance as the best-in-class DES technology[1] with the added benefit of “leaving nothing behind”.



Breakthrough[2] Technology to Deliver Sustained Limus Release for up to 90 days[3]

Cell Adherent Technology (CAT™) is a proprietary amphipathic lipid technology which binds the MicroReservoirs to the balloon surface, protecting them during balloon insertion and inflation;

- Enhancing drug retention and bioavailability, allowing for a lower drug dose concentration on the balloon surface (1 $\mu g/mm^2$).
- Optimizing transfer of MicroReservoirs to the tissue and maximizing the cellular uptake of sirolimus.

MicroReservoirs form millions of precision-engineered drug delivery systems, combining sirolimus with a biodegradable polymer, achieving consistent and predictable drug release;

- Optimizing MicroReservoir size to achieve a pharmaco-kinetic release profile comparable to the latest generation DES technology.

Latest Generation of PTCA Balloon

- Offering a broader portfolio for coronary indications with balloon diameters ranging from 1.50 mm to 5.00 mm and lengths from 10 mm to 40 mm.

SelutionSLR™
SUSTAINED LIMUS RELEASE

MedAlliance

ENGLISH

SYMBOLS

REF	Reference Number
SN	Serial Number
	Date of Manufacture
	Use By Date
	Manufacturer
NP	Nominal Pressure
RBP	Rated Burst Pressure
RX	Rapid Exchange
STERILE R	Sterilized Using Irradiation
	Consult Instructions for Use
	Caution
	Do Not Re-Use
	Keep Dry
	Keep Away from Sunlight
	Temperature Limit
	Do Not Use if Package is Damaged
CONTENT	Content
Sirolimus Dose Density	Sirolimus Dose Density
USABLE LENGTH	Usable Length
BALLOON LENGTH ◄►	Balloon Length
GUIDEWIRE DIAMETER	Guidewire Diameter
SHAFT DIAMETER	Shaft Diameter
BALLOON DIAMETER ∅	Balloon Diameter
BALLOON PRESSURE P	Balloon Pressure
	Do Not Re-Sterilize
MIN GUIDE CATHETER OD MIN GUDE CATHETER ID	Minimum Guide Catheter Outer Diameter Minimum Guide Catheter Inner Diameter

SELUTION SLR™ 014 PTCA

Sustained Limus Release Drug Eluting PTCA Balloon Catheter

Device Description

The SELUTION SLR™ 014 PTCA is a Sirolimus-Eluting Balloon catheter for Percutaneous Transluminal Coronary Angioplasty (PTCA) procedures. It is a 1.9 Fr (0.63 mm) diameter Rapid Exchange (RX) catheter that is 0.014" (0.36 mm) guidewire compatible and has a usable length of 140 cm. The balloon that is affixed to the distal portion of the catheter includes a surface coating containing Sirolimus, a drug that acts both as an anti-proliferative agent and as an anti-inflammatory immunosuppressant.

The distal end of the catheter incorporates a coaxial design with two lumens. One lumen is used for balloon inflation and is accessed through the catheter port on proximal side and ends with the balloon. The second lumen is accessed through the RX port system to the distal tip and allows passage of a guidewire. Two radiopaque markers, located under the proximal and distal ends of the balloon, delineate the working length of the balloon and facilitate fluoroscopic visualization of the balloon during delivery, positioning and inflation.

The SELUTION SLR™ 014 PTCA is available in an assortment of balloon sizes. Nominal balloon diameters and lengths are printed on the hub. Each device is packaged with a protector sheath over the balloon and a disposable wire stylet in the distal tip – both of which are to be removed prior to use.

How Supplied

The SELUTION SLR™ 014 PTCA is supplied sterile and for single use only. It is sterilized by E-beam irradiation. If left unopened and stored properly, the device will remain stable through the labeled Use By date.

The sterile packaging contains one (1) SELUTION SLR™ 014 PTCA that is stored inside a catheter dispenser coil, which is placed inside a sealed aluminum foil pouch along with an oxygen absorber and desiccant.

Storage

The SELUTION SLR™ 014 PTCA should be stored in its original packaging in a dry and dark location, at room temperature of 21°C (70°F); excursions permitted to 15-25°C (59-77°F).

Drug Coating Description

The drug coating on the balloon part of the SELUTION SLR™ 014 PTCA is a proprietary formulation, consisting of Sirolimus (also known as Rapamycin) as the Active Pharmaceutical Ingredient (API) and four excipients. The first excipient is a biodegradable polymer (Poly-lactic-co-glycolic acid – PLGA) that encapsulates the Sirolimus into micro-reservoirs which regulate drug release via matrix degradation. The remaining three excipients constitute a phospholipid blend, all of which aim to reduce wash-off of the micro-reservoirs into the bloodstream and help to adhere the drug coating to the surrounding tissues when the SELUTION SLR™ 014 PTCA balloon is inflated inside the diseased vessel. The drug coating is evenly distributed across the working length of the SELUTION SLR™ 014 PTCA balloon with a Sirolimus concentration of 1 µg/mm².

Summary of Characteristics

Catheter Design	Rapid Exchange PTCA
Usable Catheter Length	140 cm
Balloon Inflation Pressure	Nominal Pressure: 600 kPa (= 6 bar) Rated Burst Pressure (RBP): 1200 kPa (= 12 bar)
Minimum Guide Catheter	Outer diameter (OD) ≥ 5Fr (1.67 mm) Inner Diameter (ID) ≥ 0.056" (1.42 mm) for balloon, diameters 1.50 - 3.75 mm Outer diameter (OD) ≥ 6Fr (2.00 mm) Inner Diameter (ID) ≥ 0.070" (1.78 mm) for balloon diameters 4.00 - 5.00 mm
Guidewire Compatibility	Compatible with 0.014" (0.36 mm) guidewires
Active Pharmaceutical Ingredient	Sirolimus at 1.0 µg/mm² dose density

Tables included at the end of this document provide information about each available size of SELUTION SLR™ 014 PTCA:

[1] **Drug Dosage Chart:** nominal dose of Sirolimus present on each balloon size

[2] **Reference Numbers Chart:** Reference Number REF or order code for each balloon size.

[3] **Compliance Chart**: effective balloon diameter corresponding to each inflation pressures.

Intended Use / Indications for Use

The SELUTION SLR™ 014 PTCA is intended for use as a Percutaneous Transluminal Coronary Angioplasty (PTCA) balloon catheter to dilate de novo or restenotic coronary lesions, for the purpose of improving myocardial perfusion and decreasing the incidence of restenosis.

Contraindications

The SELUTION SLR™ 014 PTCA is contraindicated for use in:

- Patients with known allergies or hypersensitivities to Sirolimus (or analogs).
- Patients who cannot receive recommended antiplatelet and/or anticoagulant therapy.
- Patients with known sensitivity to contrast agents.
- Pregnant or breast-feeding women.
- Lesions that cannot be crossed with a guidewire.

Warnings

- Contents are supplied STERILE using an E-beam irradiation sterilization process.
  DO NOT USE if sterile barrier is damaged or opened prior to intended use.
- The SELUTION SLR™ 014 PTCA is intended for SINGLE USE only. DO NOT RESTERILIZE AND/OR REUSE. Resterilization and/or reuse may create a risk of contamination of the device and/or cause patient infection or cross-infection, including the transmission of infectious disease(s) from one patient to another. Contamination of the device may lead to patient injury, illness, or death. Reuse and/or resterilization may compromise the structural integrity of the device and/or lead to device failure, which in turn, may result in patient injury, illness, or death.
- The drug eluting balloon surface is effective for a single inflation only.
- Inspect the SELUTION SLR™ 014 PTCA prior to the procedure to verify that the device is intact and functional. DO NOT USE if the outer or the inner packaging is damaged or opened or if any information on the package is obscured or damaged.
- DO NOT USE after the labeled "Use By" date.
- DO NOT EXCEED the Rated Burst Pressure (RBP) recommended for this device. Balloon rupture may occur if the RBP rating is exceeded. To prevent over-pressurization, use of a pressure-monitoring device is recommended.
- Use the recommended balloon inflation medium of contrast and sterile saline (≤50% contrast). Never use air or any gaseous medium to inflate the balloon.

Precautions

Device Handling Precautions

- The SELUTION SLR™ 014 PTCA should only be used by physicians trained in PTCA procedures.
- Replace any device where the balloon has come into contact with organic solvents (e.g. alcohol).
- Pre-dilatation of the target lesion with an uncoated standard PTCA balloon is required prior to use of the SELUTION SLR™ 014 PTCA. The coated balloon portion should be handled with dry sterile gloves whenever possible prior to use. Care should be taken to minimize unnecessary contact with the coated balloon portion of the SELUTION SLR™ 014 PTCA during preparation and insertion.
- The balloon protector sheath and disposable wire stylet must stay in place during preparation of the SELUTION SLR™ 014 PTCA and not be removed until just prior to flushing with saline and placing the device over the guidewire.
- If difficulty is encountered while removing the balloon protector sheath, a new SELUTION SLR™ 014 PTCA must be utilized.
- It is recommended that a guiding catheter be used to facilitate placement. Refer to the product label for information on the appropriate guiding catheter size.
- During insertion, do not over-tighten the hemostasis valve (if used) around the SELUTION SLR™ 014 PTCA shaft as lumen constriction may occur, affecting inflation/deflation of the balloon.
- To ensure therapeutic drug delivery:
  - Open the hemostasis valve sufficiently to allow an easy passage of the drug eluting balloon through the valve during catheter insertion
  - Do not inflate the SELUTION SLR™ 014 PTCA prior to reaching the target lesion.
  - Ensure that there is full contact of the inflated balloon with the lesion across the entire length of the treated area.

- Maintain balloon inflation for a minimum of 30 seconds and a target of 1 minute if tolerated. Use the maximum balloon inflation time per your institution's standard of care.
- Maintain tight Luer connections and always advance and retrieve the SELUTION SLR™ 014 PTCA under negative pressure.
- The SELUTION SLR™ 014 PTCA should always be manipulated under fluoroscopic observation when in the body.
- Do not continue to use the SELUTION SLR™ 014 PTCA if the shaft has been bent or kinked.
- Whenever possible, the SELUTION SLR™ 014 PTCA should be the final treatment of the vessel
- The use of the SELUTION SLR™ 014 PTCA should be used in a medical environment which affords timely access to open surgery conversion, and acute peri-procedural access to percutaneous reintervention.
- After use, the SELUTION SLR™ 014 PTCA may be a biohazard. Handle and dispose of all such devices in accordance with accepted medical practice and applicable hospital, administrative, and government regulations.

Use in Conjunction with Other Procedures

- The SELUTION SLR™ 014 PTCA should not be used in conjunction with other drug eluting balloons or drug eluting stents to treat the same lesion in the same procedure except in cases of bail-out. The safety of combinations of different drug-device products has not been assessed.
- In the case that a bail-out stent is needed, a limus drug eluting stent (DES) should be used.

Pre- and Post-Procedure Antithrombotic Regimen

Pre-procedure:

The patient should receive an anticoagulant regimen for drug eluting balloons as per hospital standard of care.

Post-procedure:
Following the procedure, dual antiplatelet therapy should be given for at least for 4 weeks; follow-on therapy should be given per hospital standards for PTCA procedures.

Drug Information

Mechanism of Action
Sirolimus is a macrocyclic lactone produced by the bacteria Streptomyces hygroscopicus. It is known that Sirolimus inhibits T and B-lymphocyte activation and smooth muscle and endothelial cell proliferation in response to cytokine and growth factor stimulation. In cells, Sirolimus binds to the immunophilin, FK Binding Protein-12 (FKBP-12). The Sirolimus-FKBP-12 complex binds to and inhibits activity of the mechanistic Target of Rapamycin (mTOR). mTOR is a serine/threonine protein kinase that regulates cell growth, cell proliferation, cell motility, cell survival, protein synthesis, autophagy, and transcription. Inhibition of mTOR stops cell cycle progression from the G1 to the S phase.

Metabolism
Sirolimus is extensively metabolized by the hepatic CYP3A4 enzyme and is also a substrate for the P-glycoprotein (P-gp) transmembrane efflux pump found in the intestinal epithelium, liver cells, proximal tubule of the kidney and capillary endothelial cells. The clearance of Sirolimus is affected by both of these pathways and displays a large inter-patient variability. The majority of the metabolites, including demethyl and hydroxydemethyl Sirolimus are formed via O-demethylation and hydroxylation. Sirolimus is the major component in human whole blood and contributes to more than 90% of the immunosuppressive activity. The metabolites account for less than 10% of the immunosuppressant activity of Sirolimus. Biliary and fecal pathways serve as the primary routes of Sirolimus elimination. The half-life of Sirolimus ranges from 57 to 63 hours in the bloodstream.

Drug Interactions
Consideration should be given to the potential for drug interaction when deciding to use a SELUTION SLR™ 014 PTCA in a patient who is taking a drug that could interact with Sirolimus. The effect of drug interactions on the safety or efficacy of the SELUTION SLR™ 014 PTCA has not been determined, however, since the SELUTION SLR™ 014 PTCA exhibits its treatment effect locally and at a low dosage, it is not expected that concomitant treatment with other drugs will affect the effectiveness or safety of the SELUTION SLR™ 014 PTCA.

There is no specific clinical data available for the interactions of Sirolimus with other drugs. However, drugs like Tacrolimus that may act through the same binding proteins (FKBP-12) may interfere with the efficacy of Sirolimus.

Co-administration of Sirolimus with strong inhibitors of CYP3A4 and/or P-gp (such as ketoconazole, voriconazole, itraconazole, erythromycin, telithromycin, or clarithromycin) or strong inducers of CYP3A4 and/or P-gp (such as rifampin or rifabutin) is not recommended. Exercise caution with weaker modulators. Grapefruit juice should be avoided as it also inhibits CYP3A4-mediated metabolism.

Potential Adverse Events
Potential adverse events, which may be associated with a PTCA procedure, include, but are not limited to:

- Allergic reaction to contrast medium, anticoagulants and antiplatelets
- Aneurysm or pseudoaneurysm
- Arteriovenous (AV) fistula
- Arrhythmias
- Death
- Embolization
- Fever
- Hematoma
- Hemorrhage, incl. bleeding at puncture site
- Hypotension/hypertension
- Increased Procedure Time/Additional Interventions
- Inflammation
- Myocardial Infarction
- Occlusion
- Pain or tenderness
- Pneumothorax or hemothorax
- Renal failure
- Sepsis/infection
- Shock
- Stroke
- Thrombosis
- Vessel dissection, occlusion, perforation, recoil, restenosis, rupture, or spasm

Potential adverse events that may be unique to the SELUTION SLR™ 014 PTCA Sirolimus drug coating include, but are not limited to:

- Abnormal liver function tests
- Anemia
- Arthralgias
- Diarrhea
- Hypercholesterolemia
- Hypersensitivity, including anaphylactic/anaphylactoid type reactions
- Hypertriglyceridemia
- Hypokalemia
- Infections
- Interstitial lung disease
- Leukopenia
- Lymphoma and other malignancies
- Thrombocytopenia

The potential adverse events listed above are related to the oral administration of Sirolimus at significantly higher doses than what would be delivered by the SELUTION SLR™ 014 PTCA locally to the vessel wall. Therefore, due to the local administration and low dosage, these pharmacological interactions are not expected.

Procedure

Prior to angioplasty, carefully examine all equipment and materials to be used during the procedure, including the SELUTION SLR™ 014 PTCA, to verify proper functioning. Verify that the SELUTION SLR™ 014 PTCA size is suitable for the specific procedure for which it is intended.

In addition to the SELUTION SLR™ 014 PTCA, the following standard materials may also be required:

- 0.014" (0.36 mm) guidewire
- Torque device
- Guiding Catheter (appropriate size as per label)
- Contrast medium
- Sterile saline
- Inflation device with manometer
- Luer lock syringe for purging

Handle the SELUTION SLR™ 014 PTCA with extreme caution in order to avoid any damage to the folded balloon. Avoid exposing the balloon's drug coating to excessive handling or contact with liquids prior to preparation and delivery, as the coating may be susceptible to damage or premature drug release.

Do not touch the part of the device that is coated with Sirolimus.

1. Inflation Device Preparation
   a. Prepare the inflation device according to the manufacturer's instructions.
   b. Prior to use, carefully examine the carton, pouch, and catheter to verify that neither the SELUTION SLR™ 014 PTCA nor the sterile packaging have been damaged in shipment.
2. SELUTION SLR™ 014 PTCA Selection
   a. The chosen nominal balloon size should be equal to the reference vessel diameter. The balloon should extend ≥ 1 mm beyond the lesion both proximally and distally. If multiple SELUTION SLR™ 014 PTCA are required to complete the treatment of a lesion, the sequentially used devices should be minimally sized and angiographically positioned so that the balloon marker bands of consecutively placed devices overlap by ≥ 1mm.
   b. Predilatation with a standard PTCA balloon inflated to the same size as the reference vessel diameter is required.
3. SELUTION SLR™ 014 PTCA Preparation
   a. Carefully remove the device from the packaging.
   b. Purge the SELUTION SLR™ 014 PTCA of air prior to use. Keep the balloon protector sheath in place during the purging procedure. Begin by pointing the distal tip of the SELUTION SLR™ 014 PTCA downward while holding it vertically. Connect a stopcock and Luer lock syringe partially filled with the saline-contrast mixture to the inflation port of the SELUTION SLR™ 014 PTCA hub. Apply negative pressure until air is completely evacuated and release the plunger. Repeat this operation until migration of air bubbles towards the syringe stops. Close the stopcock while vacuum is being applied to the device.
   c. While the device is under vacuum, remove the stylet and the protector sheath from the balloon and discard. Do not use the balloon protector sheath as an introduction aid or rewrapping tool.
   d. Flush the guidewire lumen thoroughly with sterile heparinized saline or a similar isotonic solution from the distal tip.
4. Inflation Device Connection
   a. To remove any air lodged in the distal Luer fitting of the inflation device, purge approximately 1 ml (cc) of diluted contrast medium.
   b. With the stopcock in the closed position, disconnect the syringe used in preparation, slightly applying positive pressure. A meniscus of contrast medium will appear in the inflation port of the SELUTION SLR™ 014 PTCA hub when the syringe is removed. Verify that a meniscus of contrast medium is evident in both the inflation port of the SELUTION SLR™ 014 PTCA hub and the inflation device's connection. Securely couple the inflation device to the inflation port of the SELUTION SLR™ 014 PTCA hub.
5. Use of the SELUTION SLR™ 014 PTCA
   a. Load the distal tip of the SELUTION SLR™ 014 PTCA onto the guidewire.
   b. Open the hemostasis valve to allow for easy passage of the balloon and to prevent damage to the balloon coating. With the balloon fully deflated, advance the SELUTION SLR™ 014 PTCA through the guiding catheter. To avoid kinking, advance the SELUTION SLR™ 014 PTCA slowly, in small increments, until the proximal end of the guidewire emerges from the catheter. Close the hemostasis valve of the introducer sheath only as much as is needed to prevent blood return while permitting easy movement of the SELUTION SLR™ 014 PTCA. If the SELUTION SLR™ 014 PTCA encounters resistance, do not advance it through the hemostasis valve of the guiding catheter.
   c. Under fluoroscopy, use the balloon's radiopaque markers to position the balloon within the lesion to be dilated; then inflate the balloon to reference vessel diameter using the appropriate pressure (refer to the balloon compliance chart included on the product label and do not exceed the RBP of the balloon). Once inflation has begun, do not move or reposition the SELUTION SLR™ 014 PTCA.
   d. Maintain balloon inflation for a minimum of 30 seconds. Use the maximum balloon inflation time per your institution's standard of care.
   Note: The SELUTION SLR™ 014 PTCA is intended for a single inflation only.
   e. Apply negative pressure to fully deflate the SELUTION SLR™ 014 PTCA. Prior to removal, confirm that the balloon is fully deflated under fluoroscopy.
   f. Perform angiography to confirm successful dilatation of the lesion.
   Note: In case the vessel requires post-dilatation after initial treatment with the SELUTION SLR™ 014 PTCA, use of a new SELUTION SLR™ 014 PTCA is recommended.
   g. Open the hemostasis valve and withdraw the SELUTION SLR™ 014 PTCA from the body under

MedAlliance CardioVascular SA
Rue de Rive, 5
1260 NYON
SWITZERLAND
Tel.: +41 22 363 78 90
Fax: +41 22 363 78 99

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Origin NC

NON-COMPLIANT PTCA BALLOON CATHETER

Controlled **Performance**
Excellent **Deliverability**

MedAlliance

Origin NC is a non-compliant PTCA balloon catheter that combines high pressure tolerance and controlled compliance with an optimal crossing profile for the most challenging cases.

- Offering a broad portfolio of sizes for all clinical situations in your daily practice, with balloon diameters ranging from 2.00 mm – 5.00 mm and lengths from 8 mm – 20 mm.
- Origin NC's low crossing profile ensures easy crossing, deliverability and controlled balloon expansion to optimize dilatation of challenging, heavily calcified lesions.
- Minimal balloon longitudinal growth (3%) ensures focused dilatation force on the target lesion.[1]

Technical Specification

Feature	Specification
Crossing Profile[2]	From 0.0230" (Ø 2.00 mm) to 0.0310" (Ø 5.00 mm)
Distal Shaft (OD)	From 2.55 Fr (Ø 2.00 – 4.00 mm) to 2.60 Fr (Ø 4.50 – 5.00 mm)
Proximal Shaft (OD)	2.0 Fr
Catheter Design	Rapid Exchange (RX)
Catheter Usable Length	140 cm
Guidewire Compatibility	0.014"
Minimum Guide Catheter Compatibility (Fr)	5 Fr Compatible 6 Fr Kissing Balloon Compatible
Coating	Hydrophilic outer surface coating from tip to guidewire exit port. Hydrophobic coating inside guidewire lumen.

Balloon	
Balloon Diameters	2.00 mm – 5.00 mm
Balloon Lengths	8,10,12,15,18, 20 mm
Nominal Balloon Pressure (NP)	12 bar
Rated Burst Pressure (RBP)	22 bar (Ø 2.00 – 4.00 mm) 20 bar (Ø 4.50 – 5.00 mm)
Average Burst Pressure (ABP)	30 bar
Balloon Material	Nylon
Balloon Pleats	Tri-Fold

MD CE 2797

Ordering Information

Balloon Diameter (mm)	Balloon Length (mm)					
	8	10	12	15	18	20
2.00	ON2008	ON2010	ON2012	ON2015	ON2018	ON2020
2.25	ON2208	ON2210	ON2212	ON2215	ON2218	ON2220
2.50	ON2508	ON2510	ON2512	ON2515	ON2518	ON2520
2.75	ON2708	ON2710	ON2712	ON2715	ON2718	ON2720
3.00	ON3008	ON3010	ON3012	ON3015	ON3018	ON3020
3.25	ON3208	ON3210	ON3212	ON3215	ON3218	ON3220
3.50	ON3508	ON3510	ON3512	ON3515	ON3518	ON3520
3.75	ON3708	ON3710	ON3712	ON3715	ON3718	ON3720
4.00	ON4008	ON4010	ON4012	ON4015	ON4018	ON4020
4.50	ON4508	ON4510	ON4512	ON4515	ON4518	ON4520
5.00	ON5008	ON5010	ON5012	ON5015	ON5018	ON5020

Indication, contraindications and warnings can be found in the instructions for use supplied with each device.
Origin NC Non-Compliant PTCA Balloon Catheter - CE Mark Approved. Not available for sale in United States.
1. Data on file at BrosMed Medical Co. Ltd. 2. In-vitro bench testing – Manufacturer's data on file.

Manufacturer: BrosMed Medical Co. Ltd, 15th building, SMEs Venture Park SongShan Lake Hi-Tech Industrial Development Zone, Dongguan 523808, China Tel: + 86 (769) 2289 2018

Exclusive Distributor: MedAlliance CardioVascular SA, Rue de Rive 5, 1260 Nyon, Switzerland
T: + 41 22 363 78 90 I E: info@medalliance.com I W: www.medalliance.com

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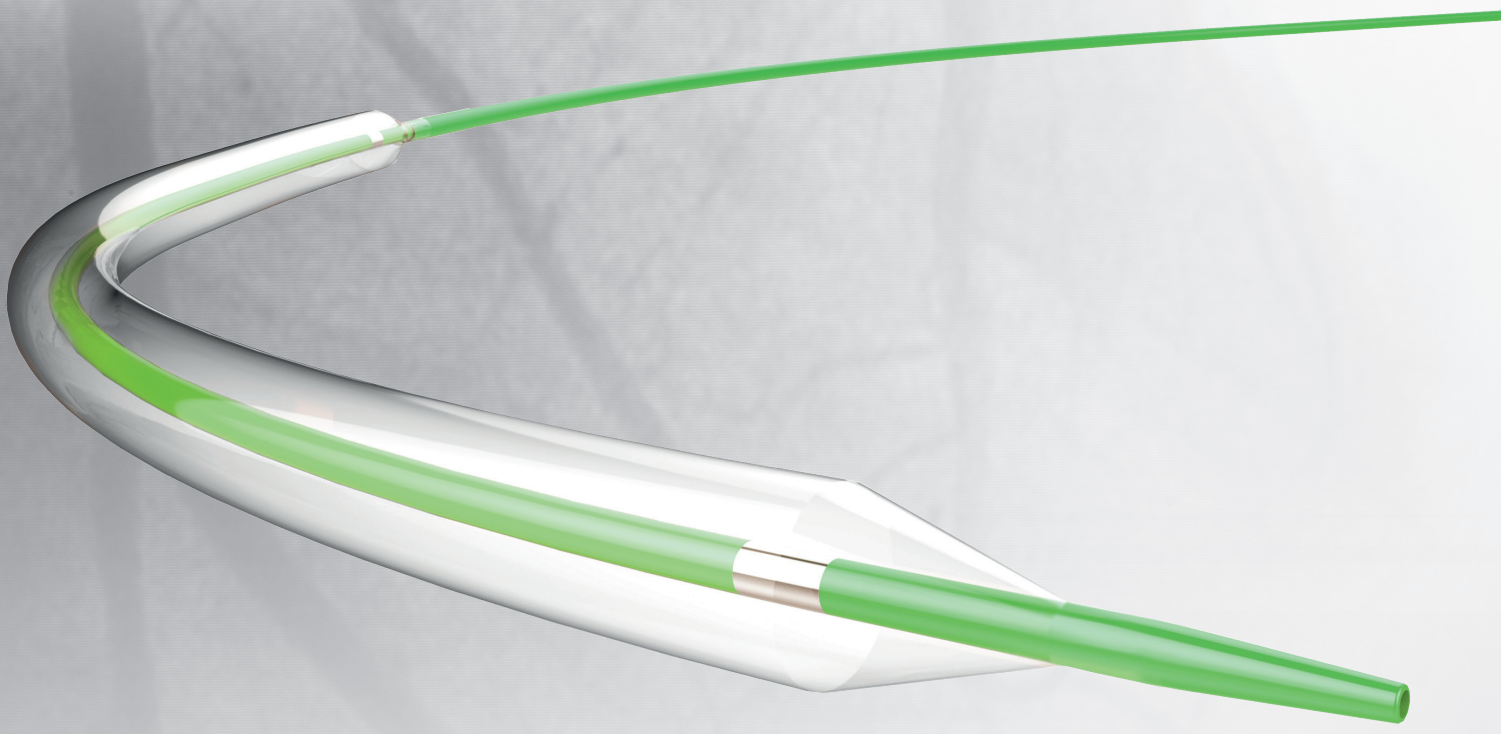
Origin NC
NON-COMPLIANT PTCA BALLOON CATHETER

MedAlliance

Origin SC

SEMI-COMPLIANT PTCA BALLOON CATHETER



Track Cross Push Further

MedAlliance

Origin SC is a very low profile semi-compliant PTCA balloon catheter with enhanced trackability, crossability and pushability to access your most challenging lesions.

- Offering a broad portfolio of sizes, including 1.00 mm, 1.25 mm, 1.50 mm and 1.75 mm balloon diameters to treat very small vessels and complex cases.
- Lowest crossing profile compared to the best-in-class semi-compliant PTCA balloons.[1]

Technical Specification

Feature	Specification
Crossing Profile[2]	From 0.0186" (Ø 1.00 mm) to 0.0223" (Ø 4.00 mm)
Distal Shaft (OD)	2.36 Fr (Ø 1.00 – 1.75 mm) 2.55 Fr (Ø 2.00 – 3.00 mm) 2.70 Fr (Ø 3.25 – 4.00 mm)
Proximal Shaft (OD)	1.9 Fr
Catheter Design	Rapid Exchange (RX)
Catheter Usable Length	140 cm
Guidewire Compatibility	0.014"
Minimum Guide Catheter Compatibility (Fr)	5 Fr Compatible 6 Fr Kissing Balloon Compatible
Coating	Hydrophilic outer surface coating from tip to guidewire exit port. Hydrophobic coating inside guidewire lumen.

Balloon	
Balloon Diameters	1.00 mm – 4.00 mm
Balloon Lengths	10, 12, 15, 20, 30 mm
Nominal Balloon Pressure (NP)	6 bar
Rated Burst Pressure (RBP)	14 bar
Balloon Material	Pebax
Balloon Pleats	Bi-fold for Ø 1.00 mm Tri-fold for Ø 1.25 mm – 4.00 mm

MD CE 2797

Ordering Information

Balloon Diameter (mm)	Balloon Length (mm)				
	10	12	15	20	30
1.00	OS1010	OS1012	OS1015	OS1020	OS1030
1.25	OS1210	OS1212	OS1215	OS1220	OS1230
1.50	OS1510	OS1512	OS1515	OS1520	OS1530
1.75	OS1710	OS1712	OS1715	OS1720	OS1730
2.00	OS2010	OS2012	OS2015	OS2020	OS2030
2.25	OS2210	OS2212	OS2215	OS2220	OS2230
2.50	OS2510	OS2512	OS2515	OS2520	OS2530
3.00	OS3010	OS3012	OS3015	OS3020	OS3030
3.50	OS3510	OS3512	OS3515	OS3520	OS3530
4.00	OS4010	OS4012	OS4015	OS4020	OS4030

Indication, contraindications and warnings can be found in the instructions for use supplied with each device.

Origin SC Semi-Compliant PTCA Balloon Catheter - CE Mark Approved. Not available for sale in United States.

1. Data on file at MedAlliance Cardiovascular SA. 2. In-vitro bench testing – Manufacturer's data on file.

Manufacturer: BrosMed Medical Co. Ltd, 15th building, SMEs Venture Park SongShan Lake Hi-Tech Industrial Development Zone, Dongguan 523808, China Tel: + 86 (769) 2289 2018

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T: + 41 22 363 78 90 I E: info@medalliance.com I W: www.medalliance.com

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