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ISAR SUMMIT

Polymer Free Everolimus Eluting Coronary Stent System

Instructions for Use

Manufacturing Facility

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Contents

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1. **Product Description:**
The ISAR SUMMIT Polymer Free Everolimus Eluting Coronary Stent System consist of a L605 Cobalt Chromium Coronary stent mounted on a stent delivery system. The Stent is coated with a formulation of Everolimus in a Polymer Free drug delivery matrix of lipophilic carrier Probucol.

2. **Contents of Sterile Package**
1 nos. Polymer Free Everolimus Eluting Coronary Stent System consisting of a Cobalt Chromium (L605) Coronary stent mounted on a Stent Delivery System.

3. **Device Component Description:**
The device Polymer Free Everolimus Eluting Coronary Stent System consist of Cobalt Chromium stent mounted on a delivery System. The range of stent diameter made possible by varying the number of circumferential cells on the stent. The stent is crimped on various sizes of stent delivery system, which are sizes 2.00 mm to 4.00 mm. The term "Polymer- Free" explicity refers to the absence of synthetic polymers traditionally used in DES coating, such as PLLA, PDLLA, and PLGA. Instaed, the drug is delivered using a non- polymeric carrier and stabilized with, a naturally derived resin that does not form a synthetic polymer film.This ensures no synthetic polymer remains on the device during implantation or drug elution, supporting biocompatibility and controlled release without long- term inflammatory response.

Table 1 Device Component Description

Available Stent Lengths (mm)	8, 12, 16, 18, 21, 24, 28, 32, 36, 40, 44 & 48mm
Available Stent Diameters (mm)	2.00, 2.25, 2.50, 2.75, 3.00, 3.50, 4.00 mm
Stent Material	L605 Cobalt Chromium Alloy Stent
Strut Thickness (µm)	Small Vessel - 68µm, Medium Vessel - 79µm
Strut Width (µm)	Small Vessel - 78µm, Medium Vessel - 88µm
Drug Component	Everolimus Drug
Delivery System Workable Length	143cm (1430 mm)
Stent Delivery System (SDS)	The delivery system is a rapid exchange catheter with a balloon located at the distal tip. The distal shaft comprises of two lumens, one is used for the inflation of the balloon and the other permits the use of a guide wire to enable advancement of the catheter to and through the stenosis to be stented. The balloon provides an expandable segment of known diameter at specific pressure. The proximal shaft is made of a stainless-steel hypotube. Proximal visual markers locate approximately 90 cm to 100 cm from the distal aid catheter positioning without fluoroscopy assistance.
Stent Delivery Balloon	A Semi-Compliant polyamide balloon, nominally about 1 mm longer than stent with two platinum iridium radiopaque marker located in the catheter shaft to indicate balloon positioning and expanded stent length.
Balloon Inflation Pressure	Nominal Inflation Pressure: $9.1/10^5$ Pa or 9 atm / 9.12 Bar Rated Burst Pressure: $16/10^5$ Pa or 15.79 atm / 16 Bar
Guiding Catheter Inner Diameter	5F (1.67mm) (Inner Lumen ⩾0.058")
Guide wire Compatibility (max)	0.014"
Catheter Shaft Outer Diameter	Proximal 1.9 F (0.65mm) Distal 2.7 F (0.90mm)

Drug Component Description

A brief description of the drug and the therapeutic class to which it belongs.

Everolimus

Active pharmaceutical ingredient (API): Everolimus Drug is a novel semisynthetic macrolide immunosuppressant, synthesized by chemical modification of Rapamycin Everolimus

Appearance: white to off-white powder.

Solubility: Soluble in ethanol, chloroform, and Methanol

Molecular Formula: C53H83NO14

Molecular Weight: 958.240g/mol

CAS Registry no.159351-69-6

Chemical name: 40-O-(2-hydroxyethyl)-rapamycin

The drug and hydrophobic carrier coating is adhered to the abluminal surface of the stent.

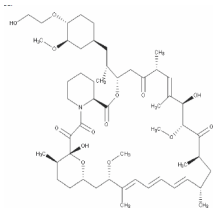

Figure 1: Structural Formula of Everolimus

Mechanism of Action
On a cellular level, everolimus inhibits, in a reversible manner, growth factor-stimulated cell proliferation. On a molecular level, everolimus forms a complex with the cytoplasmic protein FKBP-12. In the presence of everolimus, the growth factor-stimulated phosphorylation of p70 S6 kinase and 4E-BP1 is inhibited. The latter proteins are key proteins involved in the initiation of protein synthesis. Since phosphorylation of both p70 S6 kinase and 4E-BP1 is under the control of FRAP (FKBP-12-rapamycin associated protein, also called mTOR, mammalian target of rapamycin), this finding suggests that the everolimus-FKBP-12 complex binds to and thus interferes with the function of FRAP. FRAP is a key regulatory protein which governs cell metabolism, growth and proliferation. Disabling FRAP function explains the cell cycle arrest at the late G1 stage caused by everolimus.

Balloon Delivery Catheter:
The delivery catheter is a high pressure, semi- compliant balloon delivery catheter that has two radiopaque markers, which fluoroscopically mark the ends of the stent to facilitate proper stent placement. The Nominal pressure for inflation is 9 atm and Rated Burst Pressure is 16 atm. The active balloon length is closely sized to the length of the stent to prevent over- expansion of the tissue proximal or distal to the stent. At the proximal end of the system is a female Luer lock connector hub. This hub connects to the balloon inflation lumen. The guide wire enters the distal tip of the catheter and exists 25cm proximal to the trip. The surface of the catheter is partially coated with hydrophilic polymer coating which generates lubricity when wet.
ISAR SUMMIT Polymer Free Everolimus Eluting Coronary Stent System has a coating consisting of single layer. The drug Coating and drug carrier matrix is expected to degrade within 30 days for release. The drug coating is applied abluminal, leaving the luminal side of the stent free from drug as such enhancing endothelial coverage.

4. **Individualization of Treatment**
The risks and benefits of Polymer Free Everolimus- eluting stent should be considered for each patient before (using) implanting ISAR SUMMIT Polymer Free Everolimus Eluting Coronary Stent System. Physicians are responsible for assessing patient appropriateness for undergoing stent implantation prior to procedure. When estabilishing patient exclusion criteria, the risk associated with antiplatelet therapy should be taken into consideration.Special consideration is required to be taken for patients with recent active gastritis, peptic ulcer disease, hemorrhagic diathesis or other disease conditions such gastro- intestinal ulceration or cerebal circulatory disorders which restrict use of platelet aggregation inhibition therapy and anti- coagulant therapy. Judicious selection of patients is necessary since Percutaneous Coronary Intervention with the use of stent implantation is influenced by various anatomical and procedure dependent factors. These include small vessel diameter, complex vessel anatomy, intra- procedural thrombosis and dissection after stent implantation. Continued presence of thrombosis or dissection should be treated as a sign of subsequent thrombotic occlusion ans should be closely monitored for the first month after treatment as a sign of subsequent thrombotic occlusion and should be closely monitored for the first month after treatment. Patients should be maintained on clinically adequate post- procedural antiplatelet therapy (aspirin and Thienopyridine, or appropriate antiplatelet agents).

5. **Indications of use**
ISAR SUMMIT – Polymer Free Everolimus Eluting Coronary Stent System used for treatment of;
- Symptomatic coronary artery disease due to discrete de novo or restenosis lesion in native coronary artery.
- Symptomatic coronary artery disease due to culprit lesion in saphenous vein graft.
- Treatment of coronary lesion in patients undergoing primary or rescue PCI for acute ST segment elevation myocardial infarction (STEMI)
- Treatment of coronary lesion having athero thrbotic appearance in patients with non-ST-elevation acute coronary syndromes (unstable angina and non-ST-segment elevation myocardial infarction).

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6. Intended User Group
Healthcare Professionals and Cardiologists who are trained in performing Cardiovascular Procedures.

7. Intended Uses
The ISAR SUMMIT Polymer Free Everolimus Eluting Coronary Stent System is indicated for improving coronary luminal diameter in patients with symptomatic heart disease due to de novo native coronary artery lesions in native coronary artery ranging from 2.00 to 4.00 mm.

8. Intended Patient Population
Patients with CAD (including patients with stable angina, unstable angina or silent ischemia and acute coronary syndromes) of either gender, 18 years or older planned for PCI.

9. List of Intended Clinical Benefits
- Revascularization of the stenosed vessel.
- Alleviation of symptoms due to ischemic coronary artery disease.
- Microporous surface has been developed in order to achieve the possibility of a faster re- endothelialization of the stent struts therefore it potentially improves the biocompatibility and reduces the susceptibility to re stenosis.

10. Contraindications
The ISAR SUMMIT Polymer Free Everolimus Eluting Coronary Stent System is contraindicated in the following patient groups;
- Patients in whom anti-platelet and/or anti-coagulation therapy is contraindicated.
- Patients with lesions that possibly cannot be treated successfully with PTCA or stent implantation.
- Patients with known sensitivity to Everolimus and its derivatives, the carrier Probucol and procedural co-medication.
- Patients with known allergy to components of L605 Alloy used for Stent (including major elements like Cobalt, Chromium, Nickel and Tungsten).
- Patients with known sensitivity to contrast agents.
- Patients who have heavily calcified lesion or such lesions that prevents complete inflation of an angioplasty balloon or proper placement of stent or delivery catheter.
- Patients with extreme vessel tortuosity that may impair stent placement.

Recommendations: It is strongly recommended not to implant Polymer Free Everolimus Eluting Coronary Stent System in pregnant women. Effects of Everolimus drug during lactation have not been evaluated, therefore it is strongly recommended to avoid breast feeding when this stent is implanted.

11. Warnings & Precaution Measure
- Judicious selection of patients is necessary since Percutaneous Coronary Intervention with the use of stents carries the risk of stent thrombosis, vascular complications and/or bleeding events. Hence, patients should be maintained on clinically adequate post-procedural antiplatelet therapy (Aspirin and Thienopyridine, or appropriate antiplatelet agents).
- Only physicians who have received appropriate training should perform stent implantation.
- Any advancement after introduction of the delivery catheter into the vessel should be done under high resolution fluoroscopy. When resistance is felt during manipulation, determine the cause of the resistance before proceeding.
- Proper judgment is necessary to select lesion for direct stenting since insufficiently prepared lesion may lead to stent dislodgement.
- Ensure that the Aluminium pack and Tyvek pouch have not been damaged or opened as this may compromise the stability and the sterile barrier.
- Store the device at 25°C in the original package. The Device is packed in Aluminium Foil Pouch. After opening of Aluminium pouch, use the device within 12 hours. Do not store the device only in Tyvek pouch as it may affect the Device.
- The device should only be used at medical facilities by Interventional Cardiologist who are adequately trained and experienced in performing vascular interventions (including (including cases of life-threatening complications).
- The DES should only be considered for implantation in lesions which do not show any signs of severe narrowing after balloon dilation.
- This device carries an associated risk of thrombosis, vascular complications and/or bleeding events. Therefore, careful selection of patients is critical. The long-term effects effects of DES and the risks associated with these implants are unknown. The limited availability of long-term clinical data should be considered before making a risk/benefit assessment for the patient prior to implantation.
- Stent thrombosis is a low-frequency event that is frequently associated with myocardial infarction (MI) or death. The rate of stent thrombosis for DES does not differ significantly from expectations for a current generation DES.
  The patient's exposure to the drug and drug delivery matrix is directly related to the number of stents and the stent length implanted.
- Potential interactions of our system with other DES have not been evaluated and should be avoided whenever possible.
- The product should be used only by Interventional Cardiologist with experience of angiography, percutaneous transluminal coronary angioplasty (PTCA) and of implanting stents in coronary vessels.
- ISAR SUMMIT should only be considered for implantation in lesions which do not show any signs of severe narrowing after balloon deflation.
- Ensure that the inner package has not been opened or damaged as this may indicate the sterile barrier has been breached. Care needs to be taken that the stent coating does not get affected or manipulated and stent does not dislocate from the balloon. Direct touching of the stent or contact with liquids should be strictly avoided, since this can cause negatively effects on coating. Do not inflate or create a vacuum in a balloon catheter prematurely as it may lead to stent dislodgement. The recommended inflation pressure should not exceed for ISAR SUMMIT. If the balloon rupture occurs before complete stent expansion is achieved, the defective balloon should be pulled back and stent should be completely embedded in the vessel wall by the use of additional balloon catheter.
- If any resistance become apparent at any point of time during the stent system insertion procedure, highest care has to be taken as this resistance can indicate damage to the stent. Before taking any further step, the cause has to be found immediately. If resistance occurs while advancing through the guiding catheter, the entire delivery system should be pulled back. If resistance occurs after the stent has left the guiding catheter, or if the stent cannot be advanced to corresponding target lesion, there is an increased risk of stent dislodgement. This may lead to vascular embolization. The stent system should be then pulled back as follows;
- Using fluoroscopy, navigate the stent back into the distal end of guiding catheter.
- Pull the guiding catheter together with the stent back into ascending aorta, without changing the position of guide wire.
- If necessary, fill the balloon slightly, in order to reduce likelihood of the stent slipping off or being pulled off the balloon.
- Pull the guiding catheter and the stent together back through the introducer.
- When placing more than one stent, it is recommended that the distal stent placed first. If a further stent has to be placed distally, care must be taken to ensure that the guide wire is not positioned between vascular wall & the stent

11.1 Stent Handling Precautions
- For single use only. Do not re-sterilize or reuse this device. Note the “Use Before” date on the product label.
- Avoid exposure of device to fluids before implantation, this can affect the Drug coating on the Device.
- Do not remove the stent from the delivery balloon as removal may damage the stent and/or lead to stent embolization. The stent system is intended to perform as a system.
- Do not induce a vacuum on the delivery system prior to reaching the target lesion.
- Special care must be taken not to handle or in any way disrupt the stent on the balloon. This is most important during stent system removal from packaging, placement over guide wire, and advancement through rotating haemostatic valve adaptor and guiding catheter hub.
- Do not “roll” the mounted stent with your fingers as this action may loosen the stent from the delivery balloon and may damage the coating.
- Use only the appropriate balloon inflation media. Do not use air or any gaseous medium to inflate the balloon as this may cause uneven expansion and difficulty in deployment of the stent.
- In the event the ISAR SUMMIT Polymer Free Everolimus Eluting Coronary Stent system is not deployed, follow product return procedures and avoid handling of the stent with hands.

11. 2 Stent Placement Precautions
- Do not prepare or pre-inflate balloon prior to stent deployment other than as directed.
- Use balloon purging technique described in section 14.0 Direction for Use
- The vessel should be pre-dilated with an appropriately sized balloon.
- W hen treating multiple lesions, the distal lesion should be initially stented, followed by stenting of the proximal lesion. Stenting in this order obviates the need to cross the proximal stent in placement of the distal stent and reduces the chances for dislodging the proximal stent. Implanting a stent may lead to dissection of the vessel distal and/or proximal to the stent and may cause acute closure of the vessel requiring additional intervention (CABG, further dilatation, placement of additional stents, or other).
  Do not expand the stent if it is not properly positioned in the vessel. (See 11.3 Stent/System Removal Precautions.)
- Placement of a stent has the potential to compromise side branch patency. The vessel should be pre- dilate with an appropriately sized balloon.
- Balloon pressures should be monitored during inflation. Do not exceed rated burst pressure as indicated on the product label, use of pressures higher than those specified on the product label may result in a ruptured balloon with possible intimal damage and dissection.
- Do not attempt to pull an unexpanded stent back through the guiding catheter, as dislodgement of the stent from the balloon may occur.
- Remove as a single unit per instructions in (*Precautions – 11.3 Stent/System Removal Precautions).
- An unexpanded stent should be introduced into the coronary arteries one time only. An unexpanded stent should not be subsequently moved in and out through the distal end of the guiding catheter as stent damage or stent dislodgement from the balloon may occur.
- Stent retrieval methods (use of additional wires, snares and/or forceps) may result in additional trauma to the coronary vasculature and/or the vascular access site. Complications may include bleeding, hematoma or Pseudoaneurysm.
- Ensure full coverage of the entire lesion/dissection site so that there are no gaps between stents.

11.3 Stent / System Removal Precautions
- Should unusual resistance be felt at any time during either lesion access or removal of the Delivery System post-stent implantation, the entire system should be removed as a single unit.
- Do not attempt to pull an unexpanded stent back through the guiding catheter while engaged in the coronary arteries, as stent damage or stent dislodgement from the balloon may occur.

- When removing the Delivery System as a single unit.
- DO NOT retract the Delivery System into the guiding catheter.
- Position the proximal balloon marker just distal to the tip of the guiding catheter.
- Advance the guide wire into the coronary anatomy as far distally as safely possible.
- Tighten the rotating haemostatic valve to secure the Delivery System to the guiding catheter; then remove the guiding catheter, guiding wire and Delivery System as a single unit.
- Failure to follow these steps and/or applying excessive force to the Delivery System can potentially result in loss or damage to the stent and/or Delivery System components.
- If it is necessary to retain guide wire position for subsequent artery/lesion access, leave the guide wire in place and remove all other system components.

11.4 Post Implantation Precautions

- Great care must be exercised when crossing a newly deployed stent with a coronary guide wire or balloon catheter to avoid disrupting the stent geometry and stent coating.
- Patients should be maintained on clinically adequate post-procedural antiplatelet therapy (Aspirin, Thienopyridine or other appropriate antiplatelet agents) according to the current guidelines. In case of need, dual antiplatelet therapy can be discontinue earlier, but not before one month.
- Do not perform a Magnetic resonance imaging (MRI) scan on patient's post-stent implantation until the stent has completely endothelialized to minimize the potential for migration. The stent may cause artifacts in MRI scan due to distortion of the magnetic field.
- Prescribe an antiplatelet therapy for a period of 6 months to reduce the risk of stent thrombosis

11.5 Magnetic Resonance Imaging (MRI)- Stent Migration

Non-Clinical testing has demonstrated that the metallic platform of ISAR SUMMIT Polymer Free Everolimus Eluting Coronary Stent system is MR-conditional. They can be scanned safely, post implantation under following conditions:

- Static Magnetic field strength of 1.5and 3.0 Tesla
- Spatial Gradient field of 36T/m and less

An MRI scan should not be performed on a patient after stent implantation until there is adequate neointimal growth of the stent because of a potential for stent migration. For a conventional drug coated stent this period is usually considered to be eight weeks. Because of the reduced neointimal formation associated with the ISAR SUMMIT Polymer Free Everolimus Eluting Coronary Stent system, the period of vulnerability may be longer, but there is currently insufficient information to provide a specific recommendation.

11.6 Special Retrival Techniques and Precautions

When removing the delivery system and guiding catheter as a single unit:

- Do not attempt to retract an unexpanded stent into the guiding catheter while engaged in the coronary arteries. Stent damage or dislodgement may occur.
- Position the proximal balloon marker just distal to the tip of the guiding catheter.
- Advance the guide wire into the coronary anatomy as far distally as safely possible.
- Tighten the rotating haemostatic valve to secure the delivery system to the guiding catheter, then remove the guiding catheter and delivery system as a single unit.
- Failure to follow these steps and/or applying excessive force to the delivery system can potentially result in stent dislodgementor damage to the stent and/or delivery system components.
- It is necessary to retain guide wire position for subsequent artery/lesion access, leave the guide wire in place and remove all other system components.

Removal of an Unexpanded Stent

- If removal of the stent system is required prior to deployment, ensure that the guiding catheter is coaxially positioned relative to the delivery system and avoid any acute angle between the floppy part of the delivery system and the guiding catheter.
- Slowly pull back the stent system into the guiding catheter. The entry of the stent into the guiding catheter must be performed slowly under fluoroscopic control to avoid dislodgement of the stent from its position on the delivery system balloon.
- Caution: If resistance is felt when pulling the stent system into the guiding catheter, remove the stent system and the guiding catheter as a single unit (proceed as directed).
- The lesion must be pre-dilated again or otherwise prepared before a second attempt at stenting is undertaken using a new stent system.

11.7 Use of Multiple Stents

- The patient's risk factors are related to exposure to Everolimus, Probucol and are also related to the number of stents implanted.
- Use of more than two stents has not received adequate clinical evaluation. With use of more than two stents, the patient will receive larger amounts of drug than the experience and is reflected in the product testing.
- To avoid the possibility of dissimilar metal corrosion, do not implant stents of different materials in tandem where overlap or contact is possible.
- The possible interactions of ISAR SUMMIT Stent with other drug-eluting or coated stents have not been evaluated and should be avoided whenever possible.
- When placing more than one stent, it is recommended that the distal stent is placed first. If a further stent has to be placed distally, care must be taken to ensure that the guidewire is not positioned between the vascular wall and the stent.

If additional ISAR SUMMIT stents are implanted, please make sure that a stent-end overlap is avoided. Overlapping stents may lead to a delayed re-endothelization.

11.8 Pre and Post Antiplatelet Therapy Recommendations

- Antiplatelet/anticoagulation medication should be used in combination with ISAR SUMMIT Polymer Free Everolimus Eluting Coronary Stent System.
- Physicians should consider the information from the current drug-eluting stent literature and the current ACC/AHA guideline recommendations on PCI concerning the selection, dosage, duration and combination of different antithrombotic drugs. Specific needs and the risk profile of individual patients may influence the antiplatelet/ anticoagulation regime to be used.
- Dual Antiplatelet Therapy (DAPT) with aspirin and a P2Y12 inhibitor administration is recommended prior to the index procedure and then continued for a minimum of 6 months.The DAPT protocol is highly recommended for continuing DAPT for 12 months in patients who are not at a high risk of bleeding. Aspirin is recommended to be continued indefinitely to reduce the risk of thrombosis.
- The optimal duration of antiplatelet therapy, specifically P2Y12 inhibitor therapy, is unknown and DES thrombosis may still occur despite continued therapy. Provided herein are recent recommendations for post-procedural antiplatelet therapy from the 2016 ACC/AHA Guideline Focused Update on Duration of Dual Antiplatelet Therapy in Patients with Coronary Artery Disease; see the “Oral Antiplatelet Therapy” section below. Also refer to the “Warnings” Section and Clinical Studies mentioned in DAPT usage for more information.

11.9 Oral Antiplatelet Therapy

Dual antiplatelet therapy (DAPT) using a combination treatment of aspirin with a P2Y12 platelet inhibitor after percutaneous coronary intervention (PCI) reduces the risk of stent thrombosis and ischemic cardiac events but increases the risk of bleeding complications. The optimal duration of DAPT (specifically, a P2Y12 platelet inhibitor in addition to aspirin) following DES implantation is unknown, and DES thrombosis may still occur despite continued therapy. It is very important that the patient is compliant with the post procedural antiplatelet recommendations.

Per 2016 ACC/AHA guidelines1, a daily aspirin dose of 81 mg is recommended indefinitely after PCI. A P2Y12 platelet inhibitor should be given daily for at least 6 months in stable ischemic heart disease patients and for at least 12 months in patients with acute coronary syndrome (ACS). Consistent with the DAPT Study2 and the 2016 ACC/AHA guidelines, longer duration of DAPT may be considered in patients at higher ischemic risk with lower bleeding risk. In patients at higher risk of bleeding, DAPT discontinuation may be reasonable after 3 months in stable patients or 6 months in ACS patients. Decisions about duration of DAPT are best made on an individual basis and should integrate clinical judgment, assessment of the benefit/risk ratio, and patient preference.

Premature discontinuation or interruption of prescribed antiplatelet medication could result in a higher risk of stent thrombosis, MI or death. Prior to PCI, if premature discontinuation of antiplatelet therapy is anticipated, physicians should carefully evaluate with the patient whether a DES and its associated recommended DAPT regimen is the appropriate PCI choice. Following PCI, if elective non-cardiac surgery requiring suspension of antiplatelet therapy is considered, the risks and benefits of the procedure should be weighed against the possible risk associated with interruption of antiplatelet therapy. Patients who require premature DAP discontinuation should be carefully monitored for cardiac events. At the discretion of the patient's treating physician(s), the antiplatelet therapy should be restarted as soon as possible.

1. Levine GN, et al. 2016 ACC/AHA Guideline Focused Update on Duration of Dual Antiplatelet Therapy in Patients With Coronary Artery Disease: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. J Am Coll Cardiol. 2016; doi:10.1016/j.jacc.2016.03.513. For full text, please refer to the following website:
http://content.onlinejacc.org/article.aspx?doi=10.1016/j.jacc.2016.03.513
2. Mauri L, et al. Twelve or 30 Months of Dual Antiplatelet Therapy after Drug-Eluting Stents. N Engl J Med. 2014; 371:2155–66.

11.10 Brachytherapy

The safety and effectiveness of the ISAR SUMMIT Polymer Free Everolimus Eluting Coronary Stent System in patients with prior brachytherapy of the target lesion have not been established. The safety and effectiveness of use of brachytherapy to treat in-stent restenosis in ISAR SUMMIT Polymer Free Everolimus Eluting Coronary Stent System have not been established. Both vascular brachytherapy and ISAR SUMMIT stent alter arterial biology, and the combined vascular responses of these two treatments have not been determined.

12. Use in Conjunction with Other Procedures

The safety and effectiveness of the ISAR SUMMIT Polymer Free Everolimus Eluting Coronary Stent System in patients with prior brachytherapy of the target lesion have not been established. The safety and effectiveness of use of brachytherapy to treat in-stent restenosis in ISAR SUMMIT Polymer Free Everolimus Eluting Coronary Stent System have not been established. Both vascular brachytherapy and ISAR SUMMIT stent alter arterial biology, and the combined vascular responses of these two treatments have not been determined.

13. Use in Special Population

13.1 Pregnancy

There are no adequate and well-controlled studies in pregnant women or men intending to father children. Systemic levels of everolimus have not been demonstrated in any pre-clinical or clinical trials with the ISAR SUMMIT Polymer Free Everolimus Eluting Coronary Stent System. Effective contraception should be initiated before implanting an ISAR SUMMIT Polymer Free Everolimus Eluting Coronary Stent System and for 12 weeks after implantation. The ISAR SUMMIT Polymer Free Everolimus Eluting Coronary Stent System should be used during pregnancy only if the potential benefit outweighs the potential risk to the embryo or foetus.

13.2 Use during Lactation
It is not known whether Everolimus is excreted in human milk. The pharmacokinetic and safety profiles of Everolimus in infants are not known. Because many drugs are excreted in human milk and because of the potential for adverse reactions in nursing infants, a decision should be made whether to discontinue nursing or to implant the stent, taking into account the importance of the stent to the mother.

13.3 Pediatric Use
The safety and efficacy of the ISAR SUMMIT Polymer Free Everolimus Eluting Coronary Stent System in pediatric patients have not been established.

13.4 Geriatric Use
Clinical studies of the ISAR SUMMIT Polymer Free Everolimus Eluting Coronary Stent System did not find that patients age 65 Years and over differed with regard to safety and efficacy compared to younger patients.

13.5 Gender
Clinical studies of Everolimus based stent are generalizable in safety and effectiveness for both male and female patients.

13.6 Non-Coronary Use
The safety and effectiveness of this product has not been established in the cerebral, carotid or peripheral vasculature.

13.7 Lesion / Vessel Characteristics
The safety and effectiveness of the ISAR SUMMIT Polymer Free Everolimus Eluting Coronary Stent system have not been established in the following patient populations;

- Patients with unresolved vessel thrombus at the lesion site.
- Patients with coronary artery reference vessel diameter < 2.0 mm or >4.0 mm.
- Patients with lesions located in the unprotected left main coronary artery system, ostial lesions, or lesions located at a bifurcation.
- Patients with diffuse disease or poor overflow distal to the identified lesions.
- Patients with tortuous vessels in the region of the obstruction or proximal to the lesion.
- Patients with a recent acute myocardial infarction where there is evidence of thrombus or poor flow.
- Patients with multi vessel disease.
- Patients with lesions longer than 48 mm and requiring more than one ISAR SUMMIT Polymer Free Everolimus Eluting Coronary Stent system
- Patients with chronic total occlusions
- Patients with in-stent restenotic lesions.

14. Direction for use

14.1 Access to Package Holding Sterile Stent Delivery System

- Tear open outer foil pouch to reveal second inner pouch.
- Note: DO NOT drop or hand inner pouch into sterile field.
- Remove inner pouch from outer foil pouch.
- Peel open inner pouch using aseptic technique to reveal sterile package.

14.2 Inspection Prior to Use
Prior to using the ISAR SUMMIT Polymer Free Everolimus Eluting Coronary Stent system, carefully remove the system from the package and inspect for bends, kinks, and other damage. Verify that the stent is located between the radiopaque balloon markers. Do not use if there is any damage to the packaging.

14.3 Materials Required

Quantity	Material
N/A	Appropriate Guiding catheter(s) minimum Size 5F
2-3	10-20 cc syringes
1000u/500cc	Sterile Heparinised Normal Saline (Hep NS)
1	0.014" x 175 cm (minimum length) Guidewire
1	Rotating Haemostatic valve with minimum 0.096" inner diameter
	Contrast medium diluted 1:1 with sterile saline solution
1	Inflation Device with three-way stopcock
1	Torque Device
1	Guidewire Introducer

14.4 Preparation

- AVOID manipulation of stent during flushing of the guidewire lumen, as this may disrupt the placement of the stent on the balloon.
- DO NOT apply negative or positive pressure to the balloon during the delivery system preparation.
- Rinse the catheter with sterile heparinized normal saline solution.
- Flush the guide wire lumen with HepNS.

14.5 Guidewire Lumen Flush

- Remove protective cover from tip.
- Flush guide wire lumen with HepNS until fluid exits guide wire exit notch.
- Avoid manipulation of stent during flushing of the guidewire lumen, as this may disrupt the placement of the stent on balloon.
- DO NOT apply negative or positive pressure to the balloon during the delivery system preparation.
- Rinse the catheter with sterile heparinized normal saline solution.

14.6 Delivery System Preparation

1. Prepare the inflation device or syringe with diluted contrast medium.
2. Attach the inflation device/syringe to the stopcock; attach to inflation port.
3. With tip down, orient Delivery System vertically.
4. Open stopcock to Delivery System; pull negative for 30 seconds; release to neutral for contrast fill.
5. Close stopcock to Delivery System; purge inflation device/syringe of all air.
6. Repeat steps 3 to 5 until all air is expelled.
7. Note: If air is seen in shaft, repeat Balloon Preparation steps 3 to 5 to prevent uneven stent expansion.
8. If a syringe was used, attach a prepared inflation device to stopcock.
9. Open stopcock to Delivery System.
10. Leave on neutral.

14.7 Delivery Procedure

1. Prepare the vascular access site according to standard practice.
2. Predilate the lesion with a PTCA catheter.
3. Maintain neutral pressure on the inflation device. Open the rotating hemostatic valve as widely as possible.
4. Backload the delivery system onto the proximal portion of the guidewire while maintaining the guide wire position across the target lesion.
5. Advance the stent delivery system over the guidewire to the target lesion. Use the radiopaque balloon markers to position thestent across the lesion; perform angiography to confirm the position of the stent.

NOTE. If during the process of moving the Delivery System into position you notice the stent has moved on the balloon, do not deploy the stent. The entire system should be removed as a single unit. See Precautions – 11.3 Stent/System Removal Precautions for specific Delivery System removal instructions.

6. Tighten rotating hemostatic valve. Stent is now ready to be deployed.

14.8 Deployment Procedure

1. Before deployment, reconfirm the correct position of the stent relative to the target lesion via radiopaque balloon markers.
2. Attach the inflation device (only partially filled with contrast media) to a three-way stopcock and apply negative pressure to purge the air bubble if any.
3. Turn the stopcock on the catheter to the off position and purge the inflation device of air. Close the side port of the stopcock.
4. Under fluoroscopic visualization, inflate the balloon to at least the nominal pressure to deploy the stent, but do not exceed the labelled rated burst pressure of 16 bar. Maintain inflation pressure for 15-30 seconds for full expansion of the stent. Optimal expansion requires the stent to be in full contact with the artery wall, with the stent internal diameter matching the size of the reference vessel diameter. Stent wall contact should be verified through routine angiography or intravascular ultrasound.
5. Fully cover by entire lesion and balloon treated area (including dissection) with the ISAR SUMMIT Polymer Free Everolimus stent coverage into healthy tissue proximal and distal to lesion. Eluting Coronary Stent system, allowing for adequate
6. If more than one ISAR SUMMIT Polymer Free Everolimus Eluting Coronary Stent system is needed to cover the lesion and balloon treated area, adequately overlap the stents, taking into account stent foreshortening.
7. Ensure no gaps between to stents by positioning the balloon marker bands of the second ISAR SUMMIT Polymer Free Everolimus Eluting Coronary Stent system inside the deployed stent prior to expansion.

8. Deflate the balloon by pulling a vacuum with the inflation device. Make certain that the balloon is fully deflated stent prior to move the catheter.
9. Confirm that the stent is adequately expanded by angiographic injection through the guiding catheter.

NOTE: The inner diameter of the stent should not be less than the reference diameter of the target vessel. The Stent should be expanded to a diameter slightly above one of the neighboring non-diseased vessels, or one which corresponds it.

14.9 Further Dilation of Stented Segments

Precautions: Do not dilate the stent beyond

Nominal Stent Diameter	Dilation Limits
2.00 mm - 2.50 mm	3.00 mm
2.75 mm- 3.50mm	4.00 mm
4.00 mm	4.50 mm

The following limits;

All efforts should be taken to assure that the stent is not under dilation. If the deployed stent size is still inadequate with respect to vessel diameter or if full contact with the vessel wall is not achieved, a larger balloon may be used to expand the stent further.

The stent may be further expanded using a low profile, and non- complaint balloon catheter. If this is required, the stented segment should be recrossed carefully with a prolapsed guidewire to aviod dislodging the stent. The balloon should be centered within the stent and should not external outside of the stented region.

14.10 Removal Procedure

1. Ensure that the balloon is fully deflated.
2. Fully open rotating haemostatic valve
3. While maintaining guide wire position and negative pressure on inflation device, withdraw Delivery System.

NOTE. Should unusual resistance be felt at any time during either lesion access or removal of Delivery System post-stent implantation, the entire system should be removed as a single unit. See Precautions - Stent/System Removal Precautions for specific Delivery System removal instructions.

4. Tighten rotating haemostatic valve.
5. Repeat angiography to assess stented area. If necessary, post dilates within stent. Balloon inflations should Incorporate balloon size closely matching vessel.
6. Final stent diameter should match reference vessel. ENSURE STENT IS NOT UNDERDILATED

14.11 Disposal Procedure

After use, dispose of product and packaging in accordance with hospital, administrative and/or local government policy.

15. Product Matrix and Part Numbers are mentioned as below:

Ref No.	Length (mm)	Diameter (mm)	Nominal Everolimus Content (µg)	Nominal Probucol Content (µg)
ISIT2008	8	2.00	100	100
ISIT2208	8	2.25	100	100
ISIT2508	8	2.50	100	100
ISIT2708	8	2.75	100	100
ISIT3008	8	3.00	100	100
ISIT3508	8	3.50	100	100
ISIT4008	8	4.00	100	100
ISIT2012	12	2.00	150	150
ISIT2212	12	2.25	150	150
ISIT2512	12	2.50	150	150
ISIT2712	12	2.75	150	150
ISIT3012	12	3.00	150	150
ISIT3512	12	3.50	150	150
ISIT4012	12	4.00	150	150
ISIT2016	16	2.00	200	200
ISIT2216	16	2.25	200	200
ISIT2516	16	2.50	200	200
ISIT2716	16	2.75	200	200
ISIT3016	16	3.00	200	200
ISIT3516	16	3.50	200	200
ISIT4016	16	4.00	200	200
ISIT2018	18	2.00	225	225
ISIT2218	18	2.25	225	225
ISIT2518	18	2.50	225	225
ISIT2718	18	2.75	225	225
ISIT3018	18	3.00	225	225
ISIT3518	18	3.50	225	225
ISIT4018	18	4.00	225	225
ISIT2021	21	2.00	263	263
ISIT2221	21	2.25	263	263
ISIT2521	21	2.50	263	263
ISIT2721	21	2.75	263	263
ISIT3021	21	3.00	263	263
ISIT3521	21	3.50	263	263
ISIT4021	21	4.00	263	263
ISIT2024	24	2.00	300	300

Ref No.	Length (mm)	Diameter (mm)	Nominal Everolimus Content (µg)	Nominal Probucol Content (µg)
ISIT2224	24	2.25	300	300
ISIT2524	24	2.50	300	300
ISIT2724	24	2.75	300	300
ISIT3024	24	3.00	300	300
ISIT3524	24	3.50	300	300
ISIT4024	24	4.00	300	300
ISIT2028	28	2.00	350	350
ISIT2228	28	2.25	350	350
ISIT2528	28	2.50	350	350
ISIT2728	28	2.75	350	350
ISIT3028	28	3.00	350	350
ISIT3528	28	3.50	350	350
ISIT4028	28	4.00	350	350
ISIT2032	32	2.00	400	400
ISIT2232	32	2.25	400	400
ISIT2532	32	2.50	400	400
ISIT2732	32	2.75	400	400
ISIT3032	32	3.00	400	400
ISIT3532	32	3.50	400	400
ISIT4032	32	4.00	400	400
ISIT2736	36	2.75	450	450
ISIT3036	36	3.00	450	450
ISIT3536	36	3.50	450	450
ISIT4036	36	4.00	450	450
ISIT2740	40	2.75	500	500
ISIT3040	40	3.00	500	500
ISIT3540	40	3.50	500	500
ISIT4040	40	4.00	500	500
ISIT2744	44	2.75	550	550
ISIT3034	44	3.00	550	550
ISIT3544	44	3.50	550	550
ISIT4044	44	4.00	550	550
ISIT2748	48	2.75	600	600
ISIT3048	48	3.00	600	600
ISIT3548	48	3.50	600	600
ISIT4048	48	4.00	600	600

The Nominal Drug Content is **2.60µg/mm²**

NOTE: Nominal Probucol content on the Device is same as Everolimus Drug. The Formulation has 1:1 (w/w) proportion of Everolimus to Probucol on the Device.

16. Adverse Events

Potential adverse events associated with a PTCA procedure and/or stent implantation include, but are not limited to:

- Acute/Sub-acute occlusion of treated vessel
- Acute myocardial infarction, cardiogenic shock
- Vascular complications requiring surgical intervention, e.g., coronary artery bypass graft surgery (CABG)

  Intraluminal thrombus formation
- Stent dislocation or failed stent placement at target lesion site
- Restenosis of stented vessel segment
- Haematoma at the access point
- Pseudoaneurysm
- Pulse arrhythmia, ventricular fibrillation
- Cerebral circulatory disorders
- General bleeding and infection

  Distal embolism
- Hypotension
- Palpitations
- Angina pectoris, ischemia
- Arterial perforation, arterial rupture
- Vascular spasm
- Death
- Infection and sepsis

Potential adverse events related to Everolimus

Potential adverse events related to oral administration of Everolimus include, but are not limited to, abnormal liver function tests, anaemia, arthralgia, diarrhoea, hypercholesterolemia, hypersensitivity (including anaphylactic/anaphylactoid type reactions), hypertriglyceridemia, hypokalaemia, infections, interstitial lung disease, thrombocytopenia, leukopenia, lymphoma and other malignancies.

Potential adverse events related to Probucol

Potential adverse event related to oral administration of Probucol, it decreases both LDL and HDL cholesterol. Probucol can have undesired effect of lowering HDL in patients with heart disease. It promotes resolution of cholesterol xanthomata. Potential adverse events related to administration of Probucol are generally mild but are not limited to gastrointestinal discomfort like Diarrhoea, Angioneurotic oedema, cardiac arrhythmias and prolonged QT intervals in ECG. The arrhythmia events are likely to increase in patients who are also taking tricyclic antidepressants or class I or III antiarrhythmic agents or phenothiazines. In rare cases, swelling on face, hands, feet or mouth is observed, Common side-effects of Probucolon patients includes dizziness or fainting.

17. Drug Interaction

A complete study of possible interactions of Everolimus in association with treatment accompanying has not been established. It is rather improbable that interactions with other drugs will occur due to significant lower dosage compared to oncologically indicated Everolimus therapy. For possible interactions within the scope of Everolimus administrated for oncological indications the relevant instructions for use should be consulted.The metabolism of Everolimus is mainly driven by CYP3A4-isoenzyme. If the patient intakes strong inhibitors or inductors of CYP3A4 or further implantation of additional Stents is indicated, local or systemic effect must be taken into consideration.

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LIMITLESS POSSIBILITIES

Probucol lowers the level of cholesterol in blood by increasing LDL catabolism. It may inhibit cholesterol synthesis and delay cholesterol absorption. The major interaction of Probucol with various drugs lead to increased risk or severity of QT prolongation. The drug is a lipid modifying agent and it is not recommended to use with following medicines like Bepridil, Cisapride, Dronedarone, Foscarnet, Levomethadyl, Mesoridazine, Pimozide, Piperaquine, Sparfloxacin, Terfenadine, Thioridazine, Ziprasidone. In some cases, using Probucol is not usually recommended but may be required when both medicines are prescribed together. The Dose may be adjusted for each of the Drug by Physician. The List of medicines are given but not limited to them only – Acecainide, Ajmaline, Amiodarone, Amisulpride, Anagrelide, Apomorphine, Aprindine, Aripiprazole, AripiprazoleLauroxil, Arsenic Trioxide, Astemizole, Azimilide, Bretylium, Buprenorphine, Buserelin, Ceritinib, Chloral Hydrate, Chloroquine, Chlorpromazine, Clarithromycin, Clofazimine, Clozapine, Crizotinib, Dabrafenib, Dasatinib, Degarelix, Delamanid, Deslorelin, Deutetrabenazine, Disopyramide, Dofetilide, Dolasetron, Domperidone, Donepezil, Droperidol, Efavirenz, Encorafenib, Enflurane, Entrectinib, Erythromycin, Escitalopram, Fingolimod, Flecainide, Fluconazole, Fluoxetine, Formoterol, Fostemsavir, Gemifloxacin, Glasdegib, Gonadorelin,Goserelin, Halofantrine, Haloperidol, Halothane, Histrelin, Hydroquinidine, Hydroxychloroquine, Hydroxyzine, Ibutilide, InotuzumabOzogamicin, Isoflurane, Isradipine, Ivabradine, Ivosidenib, Ketoconazole, Lefamulin, Lenvatinib, Levofloxacin,Lidoflazine, Lofexidine, Lorcainide, Macimorelin, Mefloquine, Methadone, Metronidazole, Mirtazapine, Moxifloxacin, Nafarelin,Nilotinib, Octreotide, Ondansetron, Osilodrostat, Osimertinib, Oxaliplatin, Ozanimod, Panobinostat, Pasireotide, Pazopanib, Pentamidine, Pimavanserin, Pirmenol, Pitolisant, Posaconazole, Prajmaline, Procainamide, Prochlorperazine, Propafenone, Quetiapine, Quinidine, Ribociclib, Risperidone, Selpercatinib, Sematilide, Sertindole, Sertraline, Sevoflurane, Siponimod, Solifenacin, Sotalol, Spiramycin, Sulfamethoxazole, Sulpiride, Sultopride, Sunitinib, Tacrolimus, Tedisamil, Telithromycin, Trazodone, Triclabendazole, Trifluoperazine, Trimethoprim, Triptorelin, Vandetanib, Vasopressin, Vemurafenib, Vinflunine, Zolmitriptan, Zotepine, Zuclopenthixol. (Data from Mayo Clinic.org website for Probucol and its side-effects).

18. Patient Counselling Information

Cardiologist should consider the following in counselling patient about this product:

- Discuss the risks associated with stent placement
- Discuss the risks associated with an Everolimus eluting stent.
- Discuss the risks/benefits issues for this particular patient
- Discuss alteration to current lifestyle immediately following the procedure and over the long terms.
- Discuss the risks of early discontinuation of the antiplatelet therapy.
- The following stent implantation, the patients are expected to keep the patient implant card that includes product details at all times for procedure/stent identification.

19. Packaging & Storage

- Package contents: One (1) ISAR SUMMIT Polymer Free Everolimus Eluting Coronary Stent system:
- Sterile: This device is sterilized with ETO, Non-pyrogenic, the contents inside the sterile barrier system are sterile.
- Do not use if the package is opened or damaged.
- Do not re-sterilize. Do not reuse.
- Storage: Store in cool and dry place at 25°C, Do not freeze
- Keep away from sunlight

20. Compliance Chart, Inflation Pressure

Balloon Ø [mm]	Inflation Pressure (atm/bar/10^5Pa)														
				*NP							**RBP				
	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
2.00	1.68	1.88	1.94	1.98	2.01	2.05	2.09	2.12	2.15	2.18	2.20	2.23	2.25	2.27	2.29
2.25	2.12	2.16	2.21	2.26	2.29	2.32	2.36	2.40	2.43	2.46	2.49	2.50	2.52	2.54	2.56
2.50	2.17	2.33	2.43	2.47	2.50	2.53	2.56	2.59	2.62	2.65	2.69	2.78	2.81	2.83	2.85
2.75	2.62	2.67	2.72	2.75	2.79	2.84	2.89	2.93	2.96	3.00	3.03	3.06	3.09	3.12	3.14
3.00	2.85	2.90	2.95	3.01	3.07	3.11	3.16	3.19	3.23	3.26	3.29	3.34	3.37	3.40	3.43
3.50	3.18	3.24	3.33	3.46	3.51	3.54	3.59	3.65	3.69	3.74	3.75	3.89	3.93	3.96	3.99
4.00	3.67	3.76	3.84	3.93	3.98	4.03	4.07	4.12	4.17	4.22	4.27	4.44	4.49	4.53	4.57

*Nominal Pressure, ** Rated Burst Pressure

21. Complaint registration information:

Product complaints/ serious incidents that have occured in relation to the device should be reported to the manufactured and/ or the Competent Authority (CA) of the Member State.

Contact details of Manufacturer are provided in table below:

Manufacturer	Translumina Therapeutics Private Limited Plot #12, Pharma City, Selaqui, Dehardun 248011, Uttarakhand, INDIA Customer Care No.: +91-7454804151, Email: customersupport@translumina.in Web: www.translumina.in

22. Patient Information

In addition to this instruction for Use booklet, the following patient specific information regarding the ISAR SUMMIT Polymer Free Everolimus- Eluting Coronary Stent is available:
A patient implant card that includes both patient's and ISAR SUMMIT Polymer Free Everolimus - Eluting Coronary Stent's Specific information.
All patients will be expected to keep this card in their possession at all times for procedure/ stent identification.

23. Conversion Chart

1 cc	1 ml		
1 French	0.0131 inch	0.33 mm	
1 bar	0.99 atm	14.5 psi	10^5 Pa

24. Symbols Meaning

Symbol	Description
Stent	Stent Length
⌀	Stent Diameter
LOT	Batch No.
SN	Serial No.
YYYY MM	Manufacturing Date
YYYY MM	Use by Date (Expiry Date)
STERILE EO	Sterile and method of sterilization using Ethylene Oxide
STERILIZE	Single use only & Do not Re-sterile
REF	Reference No.

Symbol	Description
	Storage Temperature
MD	Medical Device
	Contains a medicinal substance
143cm & 25cm	Catheter Length & Rapid Exchange Length
RBP	Rated Burst Pressure
	Manufacturer
	Pyrogen Free
	Consult Instruction for Use
	Do not Use if package open or damaged

Symbol	Description
	Keep Away from Sun Light
	Keep dry.
NP	Nominal Pressure
	Attention: see Instruction for Use
#	Content of the package
	Single sterile barrier system with protective packaging outside
MR	MR Conditional
0.36mm (0.014")	Guide wire Diameter

25. Disclaimer of Warranty and Limitation of Remedy

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