DES Sirolimus Eluting Coronary Stent System

A Description

The GENOSS DES Sirolimus Eluting Coronary Stent System (GENOSS DES) is intended for use in improving coronary luminal diameter in patients with symptomatic ischemic heart disease due to coronary artery lesions. The GENOSS DES consists of a balloon expandable stent pre-mounted on a fast exchange delivery system. The stent body is intended as a permanent implant. It is made from a cobalt chromium alloy (L-605) and it is completely covered parylene coating because it is extremely inert and blocked metal ion release when inside the human body.
The stent body is asymmetrically coated by a matrix consisting of the carrier PLGA [poly (lactic-co-glycolic acid), PLA (polylactic c acid) and the active substance Sirolimus. The nominal drug content on the GENOSS DES is 1.02μg Strolimus per mm2 of the stents 2 of the stent surface area, with a maximum amount of 160μg on the largest stent (04.0-38mm). The delivery system is a fast-exchange PTCA catheter. It has a working length of 145cm.
To facilitate fluoroscopic visualization and positioning, the s stent is cent ered between two radiopaque markers. The proximal shaft of the stent syst em is a hypotube. It has a single Luer port for connecting an inflation/ defla tion device to inflate/deflate the balloon that can be connected to a stand ard inflation device. The guide wire lumen starts at the delivery system tip and ends at the guide wire exit point, 28cm from the distal end." The stent system is compatible with guide wires of 0.014 (0.36mm) diameter and gu iding catheters with an inner diameter of 20.056"(1.42mm). To indicate when the delivery system tip exits from the guiding catheter, shaft exit mar kers are located on the hypotube 90cm(brachial technique) and 100cm (femoral technique) from the distal end of the delivery system.

B How Supplied

Device is sterilized with ethylene oxide. DO NOT use if the package is ope ned or damaged, or if any information provided is obscured or damaged.

C Contents

- One (1) GENOSS DES Sirolimus Eluting Coronary Stent System in a
- sealed, peel-open pouch.
- One (1) Instructions for Use Manual.
- One (1) Compliance Chart.

D Storage

Store the device between 15 ~ 30°C in the aluminum pack.

E Indications

The GENOSS DES Sirolimus 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 with reference vessel diameters of 2.25 mm to 4.0 mm.

F Contraindications

The GENOSS DES Sirolimus Eluting Coronary Stent System is contraindi cated for use in patients with:

- Who cannot receive antiplatelet and/or anticoagulant therapy.
- With lesions that prevent complete angioplasty balloon inflation or proper placement of the stent or stent delivery system.
- With hypersensitivity or contraindication to contrast agents, sirolimus or structurally-related compounds, cobalt, chromium, nickel, tungsten, PLGA [poly(lactic-co-glycolic acid)]polymer, and PLA(polylactic acid) polymer.
- Transplant patients
- Patient who The safety and efficacy have not been established with GENOSS DES Sirolimus Eluting Coronary Stent System

G ⚠ Warnings

- This device carries an associated risk of subacute thrombosis, vascular complications and/or bleeding events. Therefore patients should be carefully selected (see Section: Patient Selection. Individualization of Treatment.) The long-term effects of drug eluting stents and the risk associated with these implants are unknown. The lack of knowledge should be considered making a risk/benefit assessment for the patient prior to implantation. Implantation.
- This device is designed and intended for single use only. DO NOT resterilize and/or reuse. Reuse of single-use devices creates a potential risk of patient or user infections. Contamination of the device may lead to injury, illness or death of the patient. Cleaning, disinfection and sterilization may compromise essential material and design characteristics leading to device failure. GENOSS will not be responsible for any direct, incidental or consequential damages resulting from resterilization or reuse.
- DO NOT use the stent system if the outer package or inner package is damaged or opened, or any information provided is obscured.
- DO NOT use device after the "Use by" date indicated on the label.
- DO NOT attempt to remove or readjust the stent on the delivery system as it may damage the stent, polymer system and/or lead to stent embolization. The stent cannot be removed and placed on another balloon catheter.
- DO NOT expose the stent system to organic solvents, e.g. alcohol. The GENOSS DES Sirolimus Eluting Coronary Stent System must not be exposed to contact with liquids prior to preparation or delivery as the drug carrier coating may be susceptible to damage or premature drug elution.
- Administration of appropriate anticoagulant, antiplatelet and vasodilatation therapy is critical to successful stent implantation.
- When the stent system is in the body it should be manipulated while under high quality fluoroscopy.
- When multiple stents are required to treat the lesion, stents should be similar composition as the risk of corrosion increases when stents of differing metals contact one another.
- Potential interactions of the GENOSS DES Sirolimus Eluting Coronary Stent System with other drug eluting stents have not been evaluated and should be avoided whenever possible.
- The use of GENOSS DES Sirolimus Eluting Coronary Stent System in patients with chronic total occlusions or in patients with poor flow distal to the identified lesion is not recommended.
- To reduce the potential for vessel damage, the inflated diameter of the balloon should NOT exceed the original diameter of the vessel proximal and distal to the lesion.
- Balloon pressure should not exceed the Rated Burst Pressure. Use of a pressure-monitoring inflation/deflation device is mandatory to prevent over-pressurization.
- Use only an appropriate balloon inflation medium (e.g. 50:50 mixture by volume of contrast medium and saline.) NEVER use air or any gaseous medium to inflate the balloon.
- Subsequent restenosis may require repeat dilatation of the arterial segment containing the stent. The long-term outcomes following repeat dilatation of endothelialized stents are unknown.

H ⚠ Precautions

General precautions:

- The patient's exposure to the drug and polymer system is directly related to the number of stents and the stent length implanted.
- Prior to procedure, the stent system should be visually examined to verify functionality and ensure that its size is suitable for the specific procedure which it is to be used.
- Only physicians thoroughly trained and experienced in the performance of PCTA and stent implantation should use this device.
- PTCA and stent implantation should only be performed at hospitals where emergency coronary artery bypass graft surgery can be readily performed in the event of a potential injury or life-threatening complication.
- If the GENOSS DES Sirolimus Eluting Coronary Stent System was rem oved prior to expansion, DO NOT RE-INSERT the GENOSS DES Sirolimus Eluting Coronary Stent System as the stent and/or the delivery system may have been damaged during the initial attempt to cross the lesion or during withdrawal.
- Stent thrombosis is a low frequency event that current drug-eluting stent(DES) clinical trials are not adequately powered to fully characterize. Stent thrombosis is frequently associated with MI or death. Data from randomized clinical trials with Sirolimus eluting coronary stents have been prospectively evaluated and adjudicated using both the protocol definition of stent thrombosis and the definition developed by the Academic Research Consortium(ARC), and demonstrate specific patt erns of stent thrombosis that varied depending on the definition used. In those clinical trials with Sirolimus eluting coronary stents, differences on the incidence of stent thrombosis observed with the drug eluting stent when compared to bare metal stents have not been associated with an increased risk of cardiac death myocardial infarction all causes of mortality. Additional data from longer term follow up in randomized clinical trials with Sirolimus eluting coronary stents and analyses of DES-related stent thrombosis are expected and should be considered making treatment decisions as data become available.
- Compared to use within the specified Indications for Use, the use of drug- eluting stents in patients and lesions outside the labeled indic ations may have an increased risk of adverse events, including stent thrombosis, stent embolization, myocardial infarction or death.

Pre-and Post-Procedure Antiplatelet Therapy Recommendations:

- Antiplatelet/anticoagulation medication should be used in combination with GENOSS DES.
- 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.

- In the GENOSS DES Clinical Trial, dual antiplatelet therapy (DAPT) with aspirin and a p2Y12 inhibitor was administration prior to the index procedure and then continued for at least 12 months. The protocol highly recommended continuing DAPT for 12 months in subjects who were not at a high risk of bleeding. Aspirin was 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" and "Clinical Studies" sections for more information on DAPT usage.

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 guidelines 1, 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 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 DAPT 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.

Handling precautions:

- Exercise care during device handling to reduce the possibility of disrupting the delicate placement of the stent on the balloon and accidental breakage, bending, kinking of the stent system shaft. Special care must be taken not to handle or in any way disrupt the polymer from packaging, placement over guidewire, and advancement through rotating haemostatic valve adapter and guide catheter hub.
- Take care when removing the stent system from the spiral packaging, as forceful movements may dislocate the protector and the stent.
- When removing the stent protector, always pull at the very distal end of the protector to avoid dislocation of the stent. DO NOT touch the part of the protector over the stent.
- Avoid excessive manipulation of the stent during flushing of the guidewire lumen. Special care must be taken not to handle or in any way disrupt the stent coating and the stent itself on the balloon. Manipulation, e.g. rolling the mounted stent with your fingers, may loosen the stent from the delivery system balloon and cause dislodgement. Should there be movement of or damage to the stent, DO NOT use.

Stent Placement precautions:

- The GENOSS DES is recommended to use a maximum number of 2 stents to be implanted in single procedure.
- DO NOT apply negative pressure to the stent system at any time prior to placement of the stent across the target lesion. This may cause premature dislodgment of the stent.
- DO NOT suspend the stent within any solution on the sterile field. The GENOSS DES Sirolimus Eluting Coronary Stent System must not be exposed to contact with liquids prior to preparation and delivery as the coating may be susceptible to damage or premature drug elution.
- Use only guidewires with a diameter of 0.014" (0.36mm).
- Use guiding catheters with a minimum inner diameter of ≥ 0.056" (1.42mm).
- When inserting and positioning the stent system, ensure that the haemostatic rotating valve of the guiding catheter is fully open. A partially opened haemostatic rotating valve might damage the stent or dislodge it from the centered location on the balloon.
- If any resistance is felt at any time during lesion access, DO NOT force the passage, stop the procedure and determine the cause of resistance before proceeding. If the stent system is unable to reach the lesion easily, the procedure should be aborted. In this case, refer to the instructions for "Removal of an unexpanded stent"
- During the procedure, make sure that the guide wire exit port of the delivery system, 29cm from the distal tip of the delivery system, remains in the guiding catheter.
- An unexpanded stent should not be subsequently moved in and out through the distal end of the guide catheter as stent or coating damage or stent dislodgement from the balloon may occur.
- DO NOT apply excessive force while attempting to cross the lesion. This may damage the stent and/or dislodge it from the dilatation balloon. If the stent system is unable to cross the lesion easily the unexpanded stent system should be removed according to the instructions. In this case, refer to the instructions for "Removal of an unexpanded stent.
- DO NOT inflate the balloon if vacuum cannot be held, as this indicates a leak in the delivery system. If a vacuum cannot be held, follow the instructions for the "Removal of an unexpanded stent"
- Avoid barotrauma outside the stent margins during post-dilatation.
- Placement of the stent has the potential to compromise side branch patency.
- Implanting stent may lead to dissection of the vessel distal and/or proximal to the stented portion, and may cause acute closure of the vessel requiring additional intervention (e.g. CABG, further dilatation or placement of additional stents)
- DO NOT post-dilate the stent to more than the maximum expanded diameter recommended in the table "Available sizes."
- Additional expansion of a deployed stent may cause a flow limiting dissection. This may be treated by implantation of another stent. When multiple stents are implanted, the ends should overlap slightly.
- When 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.
- 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 can include bleeding, hematoma or pseudoaneurysm.
- The use of brachytherapy treatment, mechanical atherectomy devices (directional atherectomy catheters, rotational atherectory catheters) or laser angioplasty catheters to treat in-stent restenosis of a GENOSS DES Sirolimus Eluting Coronary Stent System is not recommended.

Stent/Delivery System Removal precautions:

- Should unusual resistance be felt at any time during either lesion access, crossing the lesion or removal of the delivery system (pre-or post- implantation), the stent system/delivery system must be removed as directed either in "Removal of an unexpanded stent" or in "Removal of the stent system delivery system and the guiding catheter as a single unit" sections below.
- Failure to follow correct removal steps for the delivery system or for an unexpanded stent system and/or applying excessive force to the stent system can potentially result in loss or damage to the stent and/or delivery system components.

Post-implant precautions:

- Exercise care when crossing a newly deployed stent with an intravascular ultrasound (IVUS) catheter, a coronary guidewire, a balloon catheter or any other device to avoid disrupting the stent placement, apposition, coating or stent geometry of the GENOSS DES Sirolimus Eluting Coronary Stent System.

I Drug Information

Mechanism of Action

- Sirolimus is a drug with potent anti-proliferative, anti-inflammatory and immuno suppressive effects. It acts by binding to the cytosolic receptor FK506-binding-protein-12 (FKBP-12).
- The complex that is formed between sirolimus and FKBP-12 inhibits the activation of mammalian target of rapamycin (mTOR), which in turn causes cell cycle arrest (progression from phase G1 to S). In detail, the sirolimus-FKBP -12-TOR complex inhibits the 70-kD 56 protein kinase p70S6K (the eukaryotic initiation factor binding protein eIF-4E-BP) and cell cycle progression through upregulation of p27kip1 (a cyclin dependent kinase inhibitor), which in turn inhibits the cell cycle controlling cyclin-dependent kinases (CDK) such as the CDK4 and CDK2.
- A typical target cell is the activated T-lymphocyte, which undergoes G1 to S phase progression in response to antigenic and cytokine T-cell growth-pro-moting stimulation (Interleukin IL-2, IL-4, IL-7 and IL-15). In parallel, sirolimus inhibits antibody production.
- Other target cells are the smooth muscle cells (SMC) and the endothelial cells. Sirolimus inhibits the proliferation and the migration of SMCs and shows an antiproliferative effect on endothelial cells. Sirolimus also inhibits several phases of the restenosis cascade such as inflammation, neointimal hyperplasia formation, total protein and collagen synthesis.

Pharmacokinetics

- A human PK sub-study of the GENOSS DES was not conducted.

Drug Interactions

- Drug interaction studies have not been performed. Sirolimus is metabolized by CYP3A4. Strong inhibitors of CYP3A4 (e.g. ketoconazole) may cause increased sirolimus exposure to levels associated with systemic effects, especially if multiple stents are deployed. Systemic exposure of sirolimus should also be taken into consideration if the patient is treated concomitantly with systemic immunosuppressive therapy.
- While no specific data are available, drugs like tacrolimus, which act through the same binding protein (FKBP) may interfere with the efficacy of sirolimus.

Metagenesis

- Sirolimus was not mutagenic in the in vitro bacterial reverse mutation assay with or without metabolic activation up to 5000 μg/plate, the Chinese hamster ovary cell chromosomal aberration assay with and without metabolic activation, the mouse lymphoma cell forward mutation assay with and without metabolic activation, or the in vivo mouse micronucleus assay.

Carcinogenicity

- Carcinogenicity studies were conducted in animals. In an 86-week female mouse study at sirolimus doses 30 to 120 times higher than the 2 mg daily clinical dose (adjusted for body surface area), there was a statistically significant increase in malignant lymphoma at all dose levels compared with controls. In a second mouse study at dosages that were approximately 3 to 16 times the clinical dose (adjusted for body surface area), hepatocellular adenoma and carcinoma in males were considered sirolimus-related. In a 104-week study in rats with 0, 0.05, 0.1, and 0.2 mg/kg/day dosages, there was an increased incidence of testicular interstitial cell adenoma in the 0.1 and 0.2 mg/kg/day groups. There were no significant findings for animals treated with equal or lower doses than the clinical dose of 2 mg/day (adjusted for body surface area). Although not directly measured in the study, it is conceivable that this increase may be related to altered luteinizing hormone levels secondary to decreased serum testosterone levels.
- As luteinizing hormone receptors are different in humans and rats and the age of onset of the tumors is also different, the increased incidence in rats may therefore be considered not predictive for humans.
- Carcinogenicity studies with sirolimus indicate that the intrinsic potential for carcinogenicity was secondary to that induced by the pharmacological action. The mechanism is non-genotoxic and it was stated that the involved receptor is different in human and animals. Moreover, the doses where the effects were detected were higher than the clinical human doses which are currently used.

Reproductive Toxicity

- The study of the effects of sirolimus on the different stages of the reproductive process were conducted in rats. Male rats showed decreased fertility and testicular atrophy (giant cells and hypospermia in the testes and epididymides). The fertility of female rats was not affected, but a reduced size of ovaries and uteri were observed. Sirolimus was associated with embryo and fetal toxicity in rats, but no teratogenic effects were observed.

Pregnancy and Lactation

- Sirolimus belongs to the FDA Pregnancy Category C. There are no adequate and well-controlled studies available for use in pregnant or lactating women. During pregnancy, the stent should be considered only if the potential benefit outweighs the potential risk to the embryo/fetus. Effective contraception must be initiated before stent implantation and for 12 months after the procedure.
- It is not known whether sirolimus is excreted into breast milk. A decision to discontinue breastfeeding during the mother's exposure to sirolimus may be needed.

J Potential Adverse Events/Complications

Possible adverse events associated with PTCA and stent placement include, but are not limited to:

- Cardiac events: Myocardial infarction or ischemia, abrupt closure of coronary artery, restenosis of treated artery (greater than 50% obstruction), cardiogenic shock, angina, tamponade, perforation or dissection of coronary artery or aorta, cardiac perforation, emergency cardiac surgery, pericardial effusion, aneurysm formation.

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- Arrhythmic events: Ventricular tachycardia, ventricular fibrillation, atrial fibrillation, bradycardia.
- Stent system events: Failure to deliver stent to intended site, stent dislodgement from the delivery system, stent misplacement, stent deformation, stent embolization, stent thrombosis or occlusion, stent fracture, stent migration, inadequate apposition or compression of stent/s, inflation difficulties, rupture or pinhole of the delivery system balloon, deflation difficulties, withdrawal difficulties, embolization of catheter material.
- Respiratory events: Acute pulmonary edema, congestive heart failure, respiratory insufficiency or failure.
- Vascular events: Access site hematoma, hypotension/hypertension, pseudoaneurysm, arteriovenous fistula formation, retroperitomeal hematoma, vessel dissection or perforation, restenosis, thrombosis or occlusion, vasospasm, peripheral ischemia, dissection, distal embolization (air, tissue debris, thrombus).
- Neurologic events: Permanent (stroke) or reversible (TIA) neurologic event, femoral I nerve injury, peripheral nerve injury.
- Bleeding events: Access site bleeding or hemorrhage, hemorrhage requiring transfusion or other treatment.
- Allergic reactions to contrast media, antiplatelets, anticoagulants, L-605 cobalt chromium alloy, PLGA polymer, PLA polymer matrix, Sirolimus or Sirolimus derivatives.
- Death

Potential Adverse Events related to Sirolimus(Following Oral Aministration include but not limited to :
- Abnormal liver function tests
- Anemia
- Diarrhea
- Hypercholesterolemia
- Hypersensitivity, including anaphylactic/ anaphylactoid type reactions
- Hypertriglyceridemia
- Hypokalemia
- Infections
- Interstitial lung disease
- Leukopenia
- Lymphoma and other malignancies
- Thrombocytopenia

K Patient Selection. Individualization of Treatment

Judicious selection of patients according to the intended use is necessary since the use of this device carries the associated risks of complications listed in Potential Adverse Events/Complications section. The risks and benefit should be considered for each patient before use of the GENOSS DES Sirolimus Eluting Coronary Stent System.
Patient selection factors to be assessed should include a judgment regarding risk of long term antiplatelet therapy. Special consideration should be given to those patients with recently active gastritis or peptic ulcer disease and patients with high risk of bleeding in which anticoagulation therapy would be contraindicated. Antiplatelet drugs should be used in combination with GENOSS DES Sirolimus Eluting Coronary Stent System. Physician should use the information from the current drug eluting stent literature and specific antiplatelet/anticoagulation regime to be used for their patients in general practice.
It is very important that the patient is compliant with the post procedure antiplatelet recommendation. Premature discontinuation of prescribed antiplatelet medication could result in a higher risk of thrombosis, myocardial infarction or death. Prior to PCI, if a surgical or dental procedure is anticipated that requires early discontinuation of antiplatelet therapy, the interventionalist and patient should carefully consider whether a Drug Eluting Stent and its associated recommended antiplatelet therapy is the appropriate PCI choice. Following PCI, should a surgical or dental procedure be recommended, the risk and benefits of the procedure should be weighed against the possible risk associated with premature discontinuation of antiplatelet therapy.
Patients who require premature discontinuation of antiplatelet therapy secondary to significant bleeding, should be monitored carefully for cardiac events and, once stabilized, have their antiplatelet therapy restarted as soon as possible per the discretion of their treating physicians.
Premorbid conditions that increase the risk of poor initial result or the risk of emergency referral for bypass surgery (diabetes, renal failure, and severe obesity) should be reviewed, a review of the vessel location, reference vessel size, lesion length, qualitative target lesion characteristics, and the amount of myocardium in jeopardy from acute or subacute thrombosis must also be considered.
Thrombosis following stent implantation is affected by several baseline angiographic and procedural factors. These include vessel diameter less than 3mm, intra-procedural thrombus and dissection following stent implantation. In patients who have undergone coronary stenting, the persistence of thrombus or dissection should be considered a marker for subsequent thrombotic occlusion. Following PCI, the patients should be monitored very carefully during the first month after stent implantation.

L Use in Special Populations

The safety and effectiveness of the GENOSS DES Sirolimus Eluting Coronary Stent System has not yet been established in the following patient population:
- Patients with unresolved thrombus at the lesion site.
- Patients with unprotected lesions located in the left main coronary artery.
- Patients with tortuous vessels that may impair stent placement in the region of the obstruction or proximal to the lesion.
- Patients with recent acute myocardial infarction where there is evidence of thrombus or poor flow.
- Patients with brachytherapy treatment of the target lesion.
- Pregnant patients: There are no adequate and well controlled studies in pregnant women or men intending to father children. Effective contraception should be initiated before implanting a GENOSS DES Sirolimus Eluting Coronary Stent System and for 12 weeks after implantation. The GENOSS DES Sirolimus Eluting Coronary Stent System should be used during pregnancy only of the benefit outweighs the risk to the embryo or fetus.
- Pediatric use: the safety and efficacy in pediatric patients below the age of 18 years have not been established with GENOSS DES Sirolimus Eluting Coronary Stent System.

M Magnetic Resonance Imaging (MRI) Safety Information

Non-Clinical testing has demonstrated that the GENOSS DES Sirolimus Eluting Coronary Stent is MR Conditional for single and overlapped conditions up to 71mm. A patient with this device can be scanned in a Magnetic Resonance system meeting the following conditions:
- Static magnetic field of 1.5T MRI, only
- Maximum spatial gradient magnetic field of 3,000 Guass/cm(extrapolated) or less
- Maximum MR system reported, whole body averaged specific absorption rate(SAR) or 2 W/k

Under the scan conditions defined above, GENOSS DES Sirolimus Eluting Coronary Stent rises maximum 2.7 °C for 15 min of continuous scanning.

Image Artifact Information
Under T1 SE and GRE pulse sequence, GENOSS DES Sirolimus Eluting Coronary Stent extended maximum 5 mm artifact size compared to its original shape.

Medical Registration
It is recommended that patients register the conditions under which the implant can be scanned safely with the MedicAlert Foundation (www.medicalert.org) or equivalent organization.

N Directions for Use

Patient preparation and stent system selection
1. Prepare the patient and vascular access site for a PCI procedure according to the institution's standard clinical practice. Prepare lesion site according to standard practice.
2. Pre-dilatation of the lesion is mandatory. Pre-dilatation is recommended to be performed with a balloon diameter 0.5mm smaller than the reference vessel diameter and balloon length equal to or shorter than the target lesion length. Select the stent inner diameter according to the reference vessel diameter of the target lesion. Stent length must be equal or longer than the lesion length.

Stent system preparation
1. Before opening, carefully inspect outer and inner package. DO NOT use if there is any damage to the packaging and/or any information provided upon is obscured.
2. Exercise care during handling. Remove the protection ring containing the stent system from the sterile package and place it onto a sterile field.
3. Gently pull out the stent system from the protection ring.
4. Pull at the distal end of the protector and carefully remove the balloon /stent protector.
5. Visually check the stent crimping for uniformity, no protruding struts, and centering on the balloon and verify that the stent is positioned between the proximal and distal balloon markers. DO NOT use if any defects are noted.

Pre-flush guidewire lumen
1. Connect a syringe containing heparinized normal saline to an appropriately sized "flushing needle". Carefully apply the needle to the distal tip of the delivery system and flush the guidewire lumen until fluid exits the guidewire exit port.
2. Remove the syringe and the "flushing needle."
3. Leave the prepared stent system at ambient pressure.

Insertion and stent positioning
1. Attach a rotating haemostatic valve to the Luer-port of the guiding catheter positioned within the vasculature.
2. Position the guidewire under fluoroscopy in accordance with PCI techniques.
3. Backload the distal tip of the delivery system onto the proximal portion of the guidewire while maintaining the guidewire position across the target lesion.
4. Open the rotating haemostatic valve completely to allow for easy passage of the stent.
5. Carefully insert the stent system through the rotating haemostatic valve.
6. Advance the stent system through the guiding catheter using fluoroscopic guidance to determine when the delivery system tip approaches the distal tip of the guiding catheter.
   Note: The shaft exit markers on the hypotube may be used to approximate when the stent system has reached the distal end of the guiding catheter.
7. Carefully advance the stent system into the coronary artery over the guidewire while maintaining stable guiding catheter seating and stable guidewire placement across the target lesion.
8. Position the stent within the lesion using the balloon radiopaque markers as reference points.

⚠ **Caution:** DO NOT apply excessive force whilst accessing or crossing the target lesion. If any resistance is felt, DO NOT force the passage. If the stent system is unable to reach or cross the lesion easily, the procedure should be aborted. See "Removal of an Unexpanded stent" section.

9. Verify the stent position via high resolution fluoroscopy to assure an adequate coverage of the lesion including the proximal and distal margins. If the position of the stent is not optimal, it should be carefully repositioned or removed (Refer to the section "Removal of an unexpanded stent") Expansion of the stent should not be undertaken if the stent is not properly positioned within the target lesion segment of the vessel.
10. Sufficiently tighten the rotating haemostatic valve.

Remove air from the delivery system
1. Connect a three-way stopcock to the Luer-Lock of the catheter.
2. Prepare and remove air from a 20ml capacity inflation/deflation device according to manufacturer's recommendations and instructions.
3. Attach the inflation/deflation device containing 3ml of balloon inflation medium to the stopcock.
4. Open the stopcock so that an open fluid path between the catheter and the inflation/deflation device is established.
5. Pull the plunger of the inflation/deflation device and aspirate air from the catheter for at least 30 seconds. Release the plunger to neutral for contrast fill.
6. Close the stopcock so that the fluid path to the catheter is closed and evacuate all air from the inflation/deflation device through the stop cock.
7. Repeat steps 25-27 if necessary, to ensure air contained in the balloon and inflation lumen are removed and prevent uneven stent expansion. Release the inflation/deflation barrel to normal pressure.
8. Open the stopcock. Set the system on neural aside for use.

Stent deployment
1. Prior to stent expansion, reconfirm the correct position of the stent relative to the target lesion. Utilize high-resolution fluoroscopy to verify the stent has not been damaged or shifted during positioning. Inflate the dilatation balloon gradually to expand the stent to the calculated diameter in accordance with the compliance chart. Hold that pressure for 15-30 seconds.
   Note: Diameter values listed on the compliance chart were assessed in non- clinical testing with no lesion-resistance during inflation. Clinical conditions might differ.

⚠ **Warning:** DO NOT exceed the labeled rated burst pressure.

2. Use multiple fluoroscopy views to ensure that the stent has been completely expanded.
3. If necessary, the delivery system balloon may be dilated once more or further dilated in order to achieve complete apposition of the stent to the artery wall.

⚠ **Caution:** DO NOT post-dilate the stent to more than the maximum expandable diameter recommended in the table "Available sizes"

4. If the stent is still not completely apposed to the vessel wall, the stent can be re-crossed and further expanded with a larger balloon. Deployed stents should not be left under-dilated. Stent wall apposition should be verified through routine angiography or intravascular ultrasound.

Balloon deflation and delivery system removal
1. Deflate the balloon in accordance with standard PCI procedures. Apply negative pressure to the balloon for at least 20 seconds. Deflation of the balloon should be confirmed by absence of contrast within the balloon.
2. Open the rotating haemostatic valve to allow removal of the delivery system.
3. Maintain position of guide catheter and guidewire to prevent them from being drawn into the vessel. Under fluoroscopic control, and maintaining negative pressure. Carefully pull the completely deflated delivery system out of the target vessel into the guiding catheter.
   Note: If the deflated balloon cannot be easily withdrawn from the wall-apposed stent, slightly advance and retract the delivery system carefully. If resistance is still felt, repeat the operation until it is possible to gently pull the balloon out of the stent.

⚠ **Caution:** If resistance to pull the delivery system into the guiding catheter is felt, remove the delivery system and the guiding catheter as a single unit (proceed as directed.)

4. After removal of the delivery system, tighten the rotating haemostatic valve.
5. Inspect the device immediately upon removal from the patient for any signs of breakage or fragmentation.
6. Observation of the patient and angiographic evaluation should be performed periodically in the 15minutes after the stent implantation.
7. After use dispose the product and packaging in accordance with hospital, administrative and/or local government policy.

Removal of an unexpanded stent
1. If removal of stent system is required prior to deployment, ensure that the guide 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.
2. 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 to pull the stent system into the guiding catheter is felt, remove the stent system and the guiding catheter as a single unit (proceed as directed).

3. The lesion must be pre-dilated again or otherwise prepared before a second attempt at stenting is undertaken.

Removal of the stent system/delivery system and the guiding catheter as a single unit
1. DO NOT retract the stent system/delivery system into the guiding catheter. Maintain guidewire placement across the lesion and carefully pullback the stent system/delivery system. Position the proximal balloon marker just distal to the tip of the guiding catheter.
2. Advance the guide wire into the artery as distally as safely possible.
3. Tighten the rotating haemostatic valve to secure the stent system/delivery system to the guiding catheter.
4. Remove the guiding catheter and the stent system/delivery system as a single unit.

O Warranty/Liability

The product and each component of its system (hereinafter "the product") have been designed, manufactured, tested and packaged with all reasonable care. However, GENOSS has no control over the conditions under which the product is used and a disturbance of the intended function of the product may occur for various reasons. In this respect, the warnings in this product publication/instruction for use are expressly to be considered as an integral part of this Disclaimer and provide more detailed information. For this reason, GENOSS disclaims all warranties, expressed or implied regarding the product, including but not limited to, any warranty of merchantability or fitness for a particular purpose of the product. Product descriptions or user guidelines in publications do not constitute any expressed representation or any expressed or implied warranty. GENOSS is not liable for any direct, incidental or consequential damages or medical expenses caused by any use, defect, failure or malfunction of the product whether the claim is based on contract, warranty, tort or otherwise. This does not apply in the case of intention or in the case of gross negligence of legal representatives or executive staff of GENOSS. In commercial transactions relating to merchants, the liability is limited to the compensation of typical damages; compensation for any untypical or incidental damage is excluded.
These limitations of liability and warranty are not intended to contravene any mandatory provisions of law applicable in the respective country.
If any clause of the Disclaimer is considered by a competent court to be invalid or to be in conflict with the applicable law, the remaining part of it shall not be affected and remain in full force and effect. The invalid clause shall be substituted by a valid clause which best reflects GENOSS's legitimate interest in limiting its liability or warranty without infringing any mandatory provisions of applicable law. No person has any authority to bind GENOSS to any warranty or liability regarding the product.

P Available sizes

	Stent Inner Diameter(mm)							
Stent Length(mm)	2.25	2.50	2.75	3.00	3.25	3.50	3.75	4.00
8	X	X	X	X	X	X	X	X
13	X	X	X	X	X	X	X	X
15	X	X	X	X	X	X	X	X
18	X	X	X	X	X	X	X	X
20	X	X	X	X	X	X	X	X
23	X	X	X	X	X	X	X	X
28	X	X	X	X	X	X	X	X
33	X	X	X	X	X	X	X	X
38	X	X	X	X	X	X	X	X

Note : If post-dilation is required, DO NOT post-dilate more than the maximum expandable diameter.

Q Symbols

	Manufacturer		Keep away from sunlight
	Date of manufacture		Keep dry
	Use by date	15°C 30°C	Temperature limit
LOT	Batch code		Do not re-use
REF	Catalogue number		Consult instructions for use
STERILE EO	Sterilized using ethylene oxide		Caution
	Do not resterilize	MD	Medical device
	Do not use if package is damaged	EU REP	Authorized representative in the European Union
	Single Sterile barrier system with protective packaging outside		Contains a medicinal substance

MS-P314/IFU-S0501(Rev.12,2512)

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