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SYNERGY™ XD

MONORAIL™

Everolimus-Eluting Platinum Chromium Coronary Stent System

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℞ ONLY

Caution: Federal Law (USA) restricts this device to sale by or on the order of a physician.

This device is supplied in sterile condition. All materials inside the sterile barrier pouch (the delivery system and stent, as well as the carrier tube and pouch liner) are sterile. The external surface of the sterile barrier pouch, as well as the product carton, should not be considered sterile.

1 WARNING

Contents supplied STERILE using an ethylene oxide (EO) process. Do not use if sterile barrier is damaged. If damage is found, call your Boston Scientific representative.

For single use only. Do not reuse, reprocess or resterilize. Reuse, reprocessing or resterilization may compromise the structural integrity of the device and/or lead to device failure which, in turn, may result in patient injury, illness or death. Reuse, reprocessing or resterilization may also create a risk of contamination of the device and/or cause patient infection or cross-infection, including, but not limited to, the transmission of infectious disease(s) from one patient to another. Contamination of the device may lead to injury, illness or death of the patient.

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

2 DEVICE DESCRIPTION

The SYNERGY XD Everolimus-Eluting Platinum Chromium Coronary Stent System (SYNERGY XD Stent System) is a device/drug combination product consisting of a drug/polymer-coated balloon expandable stent, pre-mounted on a Monorail (MR) delivery catheter. The stent is made from a platinum chromium alloy (PtCr), which consists of platinum, chromium, iron, nickel, and molybdenum. The characteristics of the SYNERGY XD Stent System are described in Table 2.1. SYNERGY XD Stent System Product Description:

Table 2.1 SYNERGY™ XD Stent System Product Description

	SYNERGY XD Monorail™ Stent Delivery System
Drug Coated Stent	
Available Stent Lengths (mm)	8, 12, 16, 20, 24, 28, 32, 38, 48*
Available Stent Diameters (mm)	2.25, 2.50, 2.75, 3.00, 3.50, 4.00, 4.50** and 5.00**
Stent Material	Platinum Chromium Alloy (PtCr) (PtCr alloy components: platinum, chromium, iron, nickel, and molybdenum)
Stent Strut Thickness	2.25 mm - 2.75 mm: 0.0029 inches (0.074 mm) 3.00 mm - 3.50 mm: 0.0031 inches (0.079 mm) 4.00 mm - 5.00 mm: 0.0032 inches (0.081 mm)
Drug Product	An abluminal (outer surface of the stent in contact with the vessel wall) coating of a bioabsorbable polymer carrier PLGA [poly (DL-lactide-co-glycolide)] with approximately 1 µg of everolimus per mm² of total stent surface area with a maximum nominal drug content of 364 µg on the largest stent.
Delivery System	
Effective Length	144 cm
Delivery System Ports	Single access port to inflation lumen. Guidewire exit port is located approximately 23 cm from tip. Designed for guidewire ≤0.014 inches (0.36 mm).
Stent Delivery	A balloon, with two radiopaque balloon markers, nominally placed 0.4 mm (0.016 inches) beyond the stent at each end.
Balloon Inflation Pressure	Nominal Inflation Pressure for all Diameters: 11 atm (1117 kPa) Rated Burst Inflation Pressure: • Diameters 2.25 mm – 2.75 mm: 18 atm (1827 kPa) • Diameters 3.00 mm – 5.00 mm: 16 atm (1620 kPa)
Catheter Shaft Outer Diameter	Proximal: 2.0F (0.67 mm) Distal: 2.25 mm – 2.75 mm: 2.6F (0.89 mm) 3.00 mm: • 8 mm – 28 mm: 2.6F (0.89 mm) • 32 mm – 48 mm: 2.7F (0.92 mm) 3.50 mm: • 8 mm – 20 mm: 2.6F (0.89 mm) • 24 mm – 48 mm: 2.7F (0.92 mm) 4.00 mm - 5.00 mm: 2.7F (0.92 mm)
Guide Catheter Minimum Inner Diameter Requirement	2.25 mm - 4.00 mm: ≥5F (0.056 inches/1.42 mm) 4.50 mm - 5.00 mm: ≥6F (0.070 inches/1.78 mm)

* The 48 mm length is not available in 2.25 mm, 4.50 mm or 5.00 mm diameters.
** The 4.50 mm and 5.00 mm diameter is not available in 8 mm, 38 mm and 48 mm lengths.

2.1 User Information

Only Physicians who have received adequate training should perform implantation of the stent.

2.2 Non-Pyrogenic

SYNERGY XD Everolimus-Eluting Platinum Chromium Coronary Stent System is sterile, non-pyrogenic in unopened, undamaged packaging.

2.3 Device Component Description

The SYNERGY XD Stent System consists of a platinum chromium stent platform with an abluminal drug/polymer coating mounted onto Monorail Delivery System.

The SYNERGY XD Stent System is available in three stent models, each engineered for specific diameters to provide consistent stent-to-artery ratios across the range of reference vessel diameters indicated:

- Small Vessel (SV): 2.25 mm, 2.50 mm and 2.75 mm
- Workhorse (WH): 3.00 mm, 3.50 mm
- Large Vessel (LV): 4.00 mm, 4.50 mm and 5.00 mm

Contents for (1) SYNERGY XD Monorail Stent System

- One (1) SYNERGY XD Monorail Stent System
- One (1) Flushing needle with luer fitting

2.4 Drug Component Description

The stent component of the SYNERGY XD Stent System is a PtCr stent with a drug/polymer coating. The coating is comprised of a bioabsorbable polymer matrix that contains an active pharmaceutical ingredient (everolimus). This is the same active pharmaceutical ingredient as is used in PROMUS™ (XIENCE V™) and the existing SYNERGY matrix.

See Section 2.4.1 Everolimus and 2.4.2 Polymer Carrier sections for descriptions of drug and polymer, respectively.

2.4.1 Everolimus

The active pharmaceutical ingredient in the SYNERGY XD Stent is everolimus. The everolimus chemical name is 40-O-(2-hydroxyethyl)-rapamycin and its chemical structure is provided in Figure 2.1.

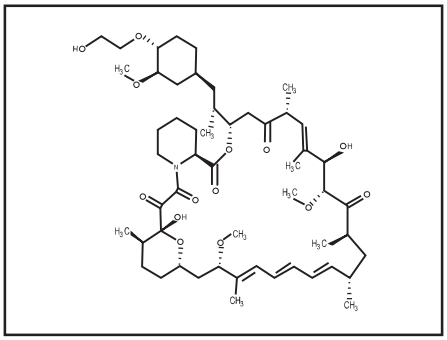

Figure 2.1 The Chemical Structure of Everolimus

2.4.2 Polymer Carrier

The SYNERGY XD Stent is coated on the abluminal stent surface (surface in contact with vessel wall) with a bioabsorbable drug matrix. The bioabsorbable drug matrix is composed of PLGA [poly (DL-lactide-co-glycolide)] mixed with everolimus. The chemical structure of PLGA is shown below in Figure 2.2. In vivo studies support that the polymer degradation is essentially complete by 4 months.

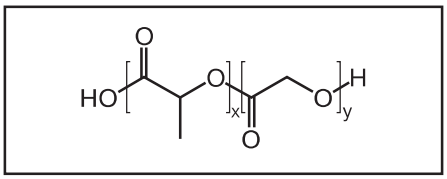

Figure 2.2 The Chemical Structure of PLGA

2.4.3 Product Matrix and Everolimus Content

Table 2.2 SYNERGY XD Stent System Product Matrix and Everolimus Content

Product Code	Nominal Expanded Stent Inner Diameter (mm)	Nominal Unexpanded Stent Length (mm)	Nominal Everolimus Content (µg)
H7493941808220	2.25	8	38.9
H7493941808250	2.50	8	38.9
H7493941808270	2.75	8	38.9
H7493941808300	3.00	8	46.5
H7493941808350	3.50	8	46.5
H7493941808400	4.00	8	67.5
H7493941812220	2.25	12	58.3
H7493941812250	2.50	12	58.3
H7493941812270	2.75	12	58.3
H7493941812300	3.00	12	66.3
H7493941812350	3.50	12	66.3
H7493941812400	4.00	12	96.2
H7493941812450	4.50	12	96.2
H7493941812500	5.00	12	96.2
H7493941816220	2.25	16	77.6
H7493941816250	2.50	16	77.6
H7493941816270	2.75	16	77.6
H7493941816300	3.00	16	92.7
H7493941816350	3.50	16	92.7
H7493941816400	4.00	16	124.8
H7493941816450	4.50	16	124.8
H7493941816500	5.00	16	124.8
H7493941820220	2.25	20	96.9
H7493941820250	2.50	20	96.9
H7493941820270	2.75	20	96.9
H7493941820300	3.00	20	112.5
H7493941820350	3.50	20	112.5
H7493941820400	4.00	20	153.5
H7493941820450	4.50	20	153.5
H7493941820500	5.00	20	153.5
H7493941824220	2.25	24	121.1
H7493941824250	2.50	24	121.1
H7493941824270	2.75	24	121.1
H7493941824300	3.00	24	132.3
H7493941824350	3.50	24	132.3
H7493941824400	4.00	24	182.2
H7493941824450	4.50	24	182.2
H7493941824500	5.00	24	182.2
H7493941828220	2.25	28	140.5
H7493941828250	2.50	28	140.5
H7493941828270	2.75	28	140.5
H7493941828300	3.00	28	158.7
H7493941828350	3.50	28	158.7
H7493941828400	4.00	28	210.8
H7493941828450	4.50	28	210.8

Product Code	Nominal Expanded Stent Inner Diameter (mm)	Nominal Unexpanded Stent Length (mm)	Nominal Everolimus Content (µg)
H7493941828500	5.00	28	210.8
H7493941832220	2.25	32	159.8
H7493941832250	2.50	32	159.8
H7493941832270	2.75	32	159.8
H7493941832300	3.00	32	178.5
H7493941832350	3.50	32	178.5
H7493941832400	4.00	32	239.5
H7493941832450	4.50	32	239.5
H7493941832500	5.00	32	239.5
H7493941838220	2.25	38	188.9
H7493941838250	2.50	38	188.9
H7493941838270	2.75	38	188.9
H7493941838300	3.00	38	211.6
H7493941838350	3.50	38	211.6
H7493941838400	4.00	38	287.2
H7493941848250	2.50	48	237.2
H7493941848270	2.75	48	237.2
H7493941848300	3.00	48	271.0
H7493941848350	3.50	48	271.0
H7493941848400	4.00	48	363.6

3 INTENDED USE/INDICATIONS FOR USE

The SYNERGY™ XD Everolimus-Eluting Platinum Chromium Coronary Stent System is indicated for improving luminal diameter in patients, including those with diabetes mellitus, with symptomatic heart disease, stable angina, unstable angina, non-ST elevation MI or documented silent ischemia due to atherosclerotic lesions in native coronary arteries ≥2.25 mm to ≤5.00 mm in diameter in lesions ≤44 mm in length.

4 CONTRAINDICATIONS

Use of the SYNERGY XD Everolimus-Eluting Platinum Chromium Coronary Stent System is contraindicated in patients with known hypersensitivity to:

- 316L stainless steel, platinum, chromium, iron, nickel or molybdenum
- Everolimus or structurally-related compounds
- The polymer or their individual components (see Section 2.4.2 Polymer Carrier)

Coronary Artery Stenting is contraindicated for use in:

- Patients judged to have a lesion that prevents complete inflation of an angioplasty balloon or proper placement of the stent or delivery device.
- Patients with uncorrected bleeding disorders or patients who cannot receive anticoagulation or antiplatelet aggregation therapy (see Section 6.2, Pre- and Post-Procedure Antiplatelet Regimen for more information).

5 WARNINGS

- To maintain sterility, the package should not be opened or damaged prior to use.
- The use of this product carries the risks associated with coronary artery stenting, including stent thrombosis, vascular complications, and/or bleeding events.
- This product should not be used in patients who are not likely to comply with recommended antiplatelet therapy.

6 PRECAUTIONS

6.1 General Precautions

- Only physicians who have received adequate training should perform implantation of the stent.
- Stent placement should only be performed at hospitals where emergency coronary artery bypass graft surgery is readily available.
- Subsequent stent blockage may require repeat dilation of the arterial segment containing the stent. The long-term outcome following repeat dilation of endothelialized stents is not well characterized.
- Careful consideration should be given to the risks and benefits of use in patients with history of severe reaction to contrast agents.
- Do not expose the delivery system to organic solvents such as alcohol or detergents.
- Care should be taken to control the position of the guide catheter tip during stent delivery, deployment and balloon withdrawal. Ensure balloon is fully deflated before delivery system withdrawal. Larger and longer balloons will take more time to deflate than smaller and shorter balloons. Allow adequate time, at least 30 seconds, for balloon deflation. Before withdrawing the stent delivery system, visually confirm complete balloon deflation under fluoroscopy. Failure to do so may cause increased SDS withdrawal forces and result in guide catheter movement into the vessel and subsequent arterial damage.
- Stent thrombosis is a rare event and is frequently associated with myocardial infarction (MI) or death. In the clinical trials analyzed to date, differences in the incidence of stent thrombosis have not been associated with an increased risk of cardiac death, MI, or all-cause mortality.
- When DES are used outside the specified Indications for Use, patient outcomes may differ from the results observed during the EVOLVE clinical trials.
- Compared to use within the specified Indications for Use, the use of DES in patients and lesions outside of the labeled indications may have an increased risk of adverse events, including stent thrombosis, stent embolization, MI or death. When treating such patients, physicians should be aware of this increased risk and consider available data and the limitations of such data.
- Orally-administered everolimus combined with cyclosporine is associated with increased serum cholesterol and triglyceride levels.

SYNERGY XD leverages the clinical data from the EVOLVE Clinical Trial Program. Therefore, the statements below regarding SYNERGY also apply to SYNERGY XD.

6.2 Pre- and Post-Procedure Antiplatelet Regimen

In the EVOLVE II Trial, a $P2Y_{12}$ inhibitor was administered pre-procedure and for a period of 6 months post procedure and for 12 months in patients who were not at high risk of bleeding. Aspirin was administered concomitantly with the $P2Y_{12}$ inhibitor and was required to be continued indefinitely to reduce the risk of thrombosis.

The optimal duration of antiplatelet therapy, specifically $P2Y_{12}$ inhibitor therapy, is unknown and DES thrombosis may still occur despite continuation of therapy beyond current professional society guidelines. Data from several studies suggest that a longer duration of antiplatelet therapy than was recommended post-procedurally in DES pivotal clinical trials may be beneficial. Provided herein are recommendations for post-procedural antiplatelet therapy from the 2016 ACC/AHA/SCAI Guideline Focused Update on Duration of Dual Antiplatelet Therapy in Patients with Coronary Artery Disease; see Section 6.2.1, Oral Antiplatelet Therapy.

6.2.1 Oral Antiplatelet Therapy

Continuation of combination treatment with aspirin and a $P2Y_{12}$ inhibitor after PCI appears to reduce major adverse cardiac events. On the basis of randomized clinical trials and the 2016 ACC/AHA guidelines recommend aspirin 81 mg daily be given indefinitely after PCI. In patients who are not at high risk of bleeding, a $P2Y_{12}$ inhibitor should be given daily for at least 6 months in stable ischemic heart disease patients and for at least 12 months in acute coronary syndrome (ACS) patients.

Full guidelines are provided at the following website:

http://www.onlinejacc.org

Consistent with the 2016 ACC/AHA guidelines,[1] and the DAPT Study,[2] longer duration of DAPT may be considered in patients who have tolerated DAPT without a bleeding complication and who are not at high bleeding risk. In patients who are at a high risk of bleeding or who develop significant bleeding during DAPT treatment, these guidelines suggest that a shorter DAPT duration may be reasonable. However, definitive evidence supporting the safety of short DAPT duration has not been established in prospective clinical studies.

Decisions about duration of DAPT are best made on an individual basis and should integrate clinical judgment, ischemic and bleeding risks, and patient preference.

It is very important that the patient is compliant with the post-procedural antiplatelet recommendations. Premature discontinuation of prescribed antiplatelet medication could result in a higher risk of thrombosis, MI or death. Prior to PCI, if a surgical or dental procedure is anticipated that requires early discontinuation of antiplatelet therapy, the interventional cardiologist and patient should carefully consider whether a DES and its associated recommended antiplatelet therapy is the appropriate PCI choice. Following PCI, should a surgical or dental procedure be recommended that requires suspension of antiplatelet therapy, the risks and benefits of the procedure should be weighed against the possible risk associated with premature discontinuation of antiplatelet therapy. Generally, it is recommended to postpone elective surgery for one year and among those patients for whom surgery cannot be deferred, ASA should be considered during the perioperative period in high risk DES patients.

Patients who require premature discontinuation of antiplatelet therapy secondary to significant active 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.

[1] Levine GN, Bates ER, Bittl JA 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;68:1082 -1115.

[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.

6.3 Longitudinal Stent Deformation

Longitudinal stent deformation is a recognized potential failure mode of thin strut coronary stents.[3] Crossing a newly deployed stent with a second device, such as a balloon catheter, stent system or IVUS catheter, can lead to the second device transmitting force to the implanted stent. In this situation, if the second device is advanced or retracted, longitudinal stent deformation (i.e., longitudinal compression or elongation) of the implanted stent may occur. Although a rare event, longitudinal stent deformation may result in adverse clinical events and/or the need for additional treatment including repeat dilation of the implanted stent, placement of a second stent, and/or surgical intervention.

An analysis of complaint reports suggests that coronary artery calcification, vessel tortuosity, and stent malapposition in conjunction with crossing a newly deployed stent with an ancillary device may be associated with an increased risk of longitudinal stent deformation. Implantation techniques that may reduce the likelihood of procedure related complications, including stent deformation, are described in the appropriate sections of this DFU (see Sections 14.3.4 Delivery Procedure, 14.3.5 Deployment Procedure, 14.3.6 Removal Procedure and Post-Deployment Dilation of Stented Segment).

[3] Hanratty CG, Walsh SJ. Longitudinal Compression: A "new" Complication with Modern Coronary Stent Platforms - Time to Think Beyond Deliverability? Eurointervention 2011;7:872-877.

6.4 Use of Multiple Stents

In the EVOLVE Clinical Program, the protocols specified that lesions were to be treated with no more than one stent, except in situations involving bailout stenting. The use of multiple DES will expose the patient to larger amounts of drug and polymer. When more than one stent is required, resulting in stent-to-stent contact, stent materials should be of similar composition to avoid the possibility of corrosion due to the presence of dissimilar metals in a conducting medium. Potential interactions of the SYNERGY Stent with other drug-eluting or coated stents have not been evaluated and should be avoided whenever possible.

6.5 Brachytherapy

The safety and effectiveness of the SYNERGY Stent in patients with prior brachytherapy of the target lesion have not been established. The safety and effectiveness of the use of brachytherapy to treat in-stent restenosis in a SYNERGY Stent have not been established. Both vascular brachytherapy and the SYNERGY Stent alter arterial remodeling. The interaction between these two treatments has not been determined.

6.6 Use in Conjunction with Other Procedures

The safety and effectiveness of using mechanical atherectomy devices or laser angioplasty catheters in conjunction with an implanted SYNERGY Stent have not been established.

6.7 Use in Special Populations

6.7.1 Pregnancy

Pregnancy "Category C". See Section 7.5, Pregnancy. The SYNERGY Stent has not been tested in pregnant women or in men intending to father children. Effects on the developing fetus have not been studied. Effective contraception should be initiated before implanting a SYNERGY Stent and continued for one year after implantation. While there is no contraindication, the risks and reproductive effects are unknown at this time. There are also potential risks to the fetus due to the ionizing radiation required for visualization during PCI procedures.

Subjects who are pregnant or with known intention to procreate within 12 months after the index procedure are excluded from the study. Women of child-bearing potential who are sexually active must agree to use a reliable method of contraception from the time of screening through 12 months after the index procedure.

6.7.2 Lactation

See Section 7.6, Lactation. A decision should be made whether to discontinue nursing prior to stent implantation considering the importance of the stent for the mother.

6.7.3 Gender

See Clinical Information – Section 10, Clinical Studies. The EVOLVE II randomized controlled clinical study was not powered to study safety or effectiveness of the SYNERGY™ Stent in sex-specific subgroups, however exploratory analyses were performed.

6.7.4 Ethnicity

See Clinical Information – Section 10, Clinical Studies. Clinical studies of the SYNERGY Stent did not include sufficient numbers of patients to assess for differences in safety and effectiveness due to ethnicity, either by individual category or when grouped by Caucasian and non-Caucasian.

6.7.5 Pediatric Use

The safety and effectiveness of the SYNERGY Stent in pediatric patients have not been established.

6.7.6 Geriatric Use

Clinical studies of the SYNERGY Stent did not have an upper age limit. Among the 846/1684 patients treated with the SYNERGY Stent in the EVOLVE II Randomized controlled study, 407 patients were age 65 or older and 46 patients were age 80 or older. A post hoc analysis of patients treated with the SYNERGY Stent showed no significant differences in 12 month clinical outcomes (primary endpoint of target lesion failure) between patients under age 65 and those age 65 or older.

6.8 Lesion/Vessel Characteristics

The safety and effectiveness of the SYNERGY Stent have not been established in the cerebral, carotid, or peripheral vasculature or in the following patient populations:

- Patients with vessel thrombus at the lesion site.
- Patients with coronary artery reference vessel diameters <2.25 mm or >5.00 mm.
- Patients with coronary artery lesions longer than 44 mm or requiring more than one SYNERGY Stent.
- Patients with lesions located in saphenous vein grafts, in the left main coronary artery, ostial location, or complex bifurcation (e.g. bifurcation lesion requiring treatment with more than one stent).
- Patients with diffuse disease or reduced blood flow distal to the identified lesions.
- Patients with a recent acute ST elevation myocardial infarction where there is evidence of thrombus or poor flow.
- Patients with in-stent restenosis.
- Patients with a chronic total occlusion.
- Patients with 3 vessel disease.

6.9 Drug Interactions

See Section 7.3, Drug Interactions. Several drugs are known to affect everolimus metabolism, and other drug interactions may also occur. Everolimus is known to be a substrate for both P4503A4 (CYP3A4) and P-glycoprotein. Everolimus absorption and subsequent elimination may be influenced by drugs that affect these pathways. Everolimus has also been shown to reduce the clearance of some prescription medications when administered orally along with cyclosporine (CsA). Formal drug interaction studies have not been performed with the SYNERGY Stent because of limited systemic exposure to everolimus eluted from SYNERGY Stent used in the EVOLVE clinical trials (see Section 7.2, Pharmacokinetics). Therefore, due consideration should be given to the potential for both systemic and local drug interactions in the vessel wall when deciding to place a SYNERGY XD Stent in a patient taking a drug with known interaction with everolimus, or when deciding to initiate therapy with such a drug in a patient who has recently received a SYNERGY XD Stent.

6.10 Immune Suppression Potential

Everolimus, the active drug component of the SYNERGY XD Stent, is an immunosuppressive agent. Immune suppression as a result of everolimus exposure was not observed in the EVOLVE Clinical Program. However, for patients who receive several SYNERGY XD Stents simultaneously, it may be possible for everolimus systemic concentrations to approach immunosuppressive levels temporarily, especially in patients who also have hepatic insufficiency or who are taking drugs that inhibit CYP3A4 or P-glycoprotein. Therefore, consideration should be given to patients taking other immunosuppressive agents or who are at risk for immune suppression.

6.11 Lipid Elevation Potential

Oral everolimus use in renal transplant patients was associated with increased serum cholesterol and triglycerides that in some cases required treatment. The effect was seen with both low- and high-dose prolonged oral therapy in a dose-related manner. When used according to the indications for use, exposure to systemic everolimus concentrations from the SYNERGY XD Stent is expected to be significantly lower than concentrations usually obtained in transplant patients.

6.12 Magnetic Resonance Imaging (MRI) Safety Information

Non-clinical testing has demonstrated that the SYNERGY XD Stent is MR Conditional for single and overlapped conditions up to 94 mm. A patient with this device can be safely scanned in a Magnetic Resonance system meeting the following conditions:

- Static magnetic field of 3.0 and 1.5 Tesla only
- Maximum spatial gradient magnetic field of 2300 gauss/cm (23 T/m)
- Maximum Magnetic Resonance system reported, whole body averaged specific absorption rate (SAR) of ≤2 W/kg (Normal Operating Mode)

Under the scan conditions defined above, the SYNERGY XD Stent is expected to produce a maximum temperature rise of 5 °C or less after 15 minutes of continuous scanning.

MR Image quality may be compromised if the area of interest is within the lumen or relatively near the stent. Therefore, it may be necessary to optimize MR imaging parameters for the presence of the stent. The image artifact extends approximately 1 cm from the stent when scanned in non-clinical MR testing specified in ASTM F2119-07. The artifact does obscure the device lumen. Image artifact was minimized using the spin echo sequence versus gradient echo.

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.

MR Magnetic Resonance Conditional

6.13 Stent Handling (also see Section 14, Operational Instructions)

- For single use only. Do not resterilize or reuse this product. Note product "Use By" date. (see Section 1, Warning)
- The premounted SYNERGY XD Stent and its delivery system are designed for use as a unit. The stent is not to be removed from its delivery balloon. The stent is not designed to be crimped onto another balloon. Removing the stent from its delivery balloon may damage the stent and coating and/or lead to stent embolization.
- Special care must be taken not to handle or in any way disrupt the stent position on the delivery balloon. This is most important during catheter removal from packaging, placement over guidewire, and advancement through hemostasis valve adapter and guide catheter hub.
- Excessive manipulation or handling may cause coating damage, contamination, or dislodgment of the stent from the delivery balloon.
- Use only the appropriate balloon inflation media (see Section 14.3.3, Balloon Preparation). Do not use air or any gas medium to inflate the balloon.
- In the event the SYNERGY XD Stent is deployed or damaged, do not use the product and contact your local Boston Scientific Representative for return information.

6.14 Stent Placement

Preparation

- Do not prepare or pre-inflate balloon prior to stent deployment other than as directed. Use the balloon purging technique described in Section 14.3.3, Balloon Preparation.
- The vessel should be pre-dilated with an appropriate sized balloon. Failure to do so may increase the risk of placement difficulty and procedural complications.
- If unusual resistance is felt at any time during lesion access before stent implantation, see Section 6.15, Stent Delivery System Removal.
- 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 guide catheter as stent or coating damage or stent dislodgment from the balloon may occur.

Placement

- Do not expand the stent if it is not properly positioned in the vessel (see Section 6.15, Stent Delivery System Removal).
- Balloon pressures should be monitored during inflation. Do not exceed rated burst pressure as indicated on product label (see Section 14.4, In Vitro Information, Table 14.1, Typical SYNERGY XD Stent System Compliance). Use of pressures higher than specified on product label may result in a ruptured balloon and intimal damage and dissection.
- The stent inner diameter should approximate 1.1 times the reference diameter of the vessel.
- Stent placement may potentially compromise side branch patency.
- Implanting a 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, repeat dilation, placement of additional stents, or other).
- When treating multiple lesions, the distal lesion should generally be stented first, followed by stenting of the more proximal lesion(s). Stenting in this order alleviates the need to cross the proximal stent in placement of the distal stent and reduces the chances of dislodging or damaging the proximal stent.

6.15 Stent Delivery System Removal

- Following stent placement, confirm complete balloon deflation. Ensure balloon is fully deflated before delivery system withdrawal. Larger and longer balloons will take more time to deflate than smaller and shorter balloons. Allow adequate time, at least 30 seconds, for balloon deflation. Before withdrawing the stent delivery system visually confirm complete balloon deflation under fluoroscopy.
- If unusual resistance is felt at any time during lesion access before stent implantation, the stent delivery system and the guide catheter should be removed as a single unit.
- Retraction of an unexpanded stent back into the guide catheter could result in stent or coating damage or stent dislodgment from the balloon. If retraction of the unexpanded stent back into the guide catheter is required, ensure that the guide catheter is coaxially aligned with the stent system and cautiously withdraw the stent system into the guide catheter under direct fluoroscopic visualization.
- Stent retrieval methods (use of additional wires, snares and/or forceps) may result in additional trauma to the vascular access site. Complications can include bleeding, hematoma, or pseudoaneurysm.

Note: When removing the entire stent delivery system and guide catheter as a single unit, the following steps should be executed under direct fluoroscopic visualization.

- If greater than usual resistance is felt during delivery system withdrawal, pay particular attention to guide catheter position. In some cases it may be necessary to pull back slightly on the guide catheter in order to prevent deep seating (unplanned advancement) of the guide catheter and subsequent vessel damage. In cases where unplanned guide catheter movement has occurred, angiographic assessment of the coronary tree should be undertaken to ensure that there is no damage to the coronary vasculature.
- Following stent placement, confirm complete balloon deflation. Deflate the balloon by pulling negative pressure on the inflation device. Allow adequate time, at least 30 seconds, for balloon deflation. Larger and longer balloons may require more time for deflation. Before withdrawing the stent delivery system visually confirm complete balloon deflation under fluoroscopy.
- Maintain guidewire placement across the lesion during the entire removal process. Carefully pull back the stent delivery system until the proximal balloon marker of the stent delivery system is just distal to the guide catheter distal tip.
- The stent delivery system and the guide catheter should be pulled back until the tip of the guide catheter is just distal to the arterial sheath, allowing the guide catheter to straighten. Carefully retract the stent delivery system into the guide catheter and remove the stent delivery system and the guide catheter from the patient as a single unit while leaving the guidewire across the lesion.

Failure to follow these steps, and/or applying excessive force to the stent delivery system, can potentially result in stent or coating damage, stent dislodgment from the balloon, and/or damage to the delivery system.

6.16 Post-Procedure

- Care must be exercised when crossing a newly deployed stent with any wire, catheter or ancillary device to avoid disrupting the stent placement, apposition, geometry, and/or coating.

subgroups, so these analyses were performed *post hoc* and are considered hypothesis-generating.

In the EVOLVE 48 study, of the 100 patients enrolled, 60 patients were male (60.0%) and 40 patients were female (40.0%). Gender based data is available in Table 10.5.4.

Table 10.5.4 EVOLVE 48 Primary Endpoint Results by Gender, Male and Female Patients (N=100)

	Male Patients (N=60)	Female Patients (N=40)
12 Month TLF	6.8% (4/59)	0.0% (0/39)
Numbers are % (count/sample/size)		

Note: Subjects with respective event or sufficient follow up are included in the denominator, two subjects without TLF event and without sufficient follow-up 335 days were excluded from denominator.

Real World Evidence

The SYNERGY™ 48 mm stent has been commercialized in Sweden since February 2017, and data from the Swedish Coronary Angiography and Angioplasty Registry (SCAAR) provides real world evidence on the outcomes in an unselected population. The registry provides extensive data from all 29 centers in Sweden that perform PCI. A 500-patient cohort of patients treated with the SYNERGY 48 mm stent, and no other non-SYNERGY stents, who had follow-up through 1-year was identified. The group was predominately male (78%), had an average age of 69.4 years, and 25% were medically treated diabetics. Outcomes at 1-year included all-cause death (6.8%), myocardial infarction (3.0%), and target lesion revascularizations 4.4% and a derived target lesion failure rate of 11.2% (defined as the composite of all deaths, all myocardial infarctions, and all target lesion revascularizations). Stent thrombosis occurred in two SYNERGY 48 mm stents (0.4%). The data from SCAAR demonstrates positive real-world evidence on the SYNERGY 48 mm stent.

11 INDIVIDUALIZATION OF TREATMENT

See Section 6.7, Use in Special Populations and Section 6.8, Lesion/Vessel Characteristics.

The risks and benefits should be carefully considered for each patient before use of the SYNERGY XD Stent System. Patient selection factors to be assessed should include a judgment regarding risk of prolonged antiplatelet therapy. On the basis of randomized clinical trial protocols, a $P2Y_{12}$ inhibitor should be given for at least 6 months after everolimus-eluting stent (EES) implantation and ideally up to 12 months. Aspirin should be administered concomitantly with the $P2Y_{12}$ inhibitor and then continued indefinitely. Stenting is generally avoided in those patients at heightened risk of bleeding (e.g., those patients with recently active gastritis or peptic ulcer disease) in whom antiplatelet therapy would be contraindicated.

Premorbid conditions that increase the risk of poor initial results or the risks of emergency referral for bypass surgery (diabetes mellitus, renal failure and severe obesity) should be reviewed.

12 PATIENT COUNSELING INFORMATION

Physicians should consider the following in counseling patients 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 term.

The following patient materials are available for this product:

- A Patient Information Guide (included in the package and available on-line) which includes both product information and a stent implant card.
- An Angioplasty and Stent Education Guide (available on-line or by request) which includes information on coronary artery disease, the implant procedure and frequently asked questions.

13 HOW SUPPLIED

STERILE: This product is sterilized with ethylene oxide gas. It is intended for single use only. Do not resterilize.

The SYNERGY XD Everolimus-Eluting Platinum Chromium Coronary Stent System is sterile, non-pyrogenic in unopened, undamaged packaging.

Do not use if package is opened or damaged.

Do not use if labeling is incomplete or illegible.

HANDLING and STORAGE:

Keep dry and protect from light. Recommended storage at 25 °C (77 °F); excursions permitted to 15 °C – 30 °C (59 °F – 86 °F).

Store product in outer carton.

DO NOT REMOVE FROM FOIL POUCH UNTIL READY FOR USE.

Do not store devices where they are directly exposed to organic solvents or ionizing radiation.

The foil pouch contains nitrogen gas (N_2) and desiccant as a storage medium.

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

14 OPERATIONAL INSTRUCTIONS

14.1 Inspection Prior to Use

Check foil pouch for "Use By" date. Do not use the product after the "Use By" date. Carefully inspect the foil pouch before opening. If the integrity of the foil pouch has been compromised prior to the product "Use By" date (e.g., damage of the package), contact your local Boston Scientific representative for return information. Do not use if any defects are noted.

Note: At any time during use of the SYNERGY XD Monorail™ Stent Delivery System, if the proximal shaft (hypotube) has been bent or kinked, do not continue to use the catheter.

14.2 Materials Required (not included in Stent Delivery System package)

Quantity	Material
1	Appropriate guide catheter (see Table 2.1, SYNERGY XD Stent System Product Description)
2 – 3	20 ml (cc) syringe
1000 u/500 cc	Normal heparinized sterile saline
1	≤0.014 in (0.36 mm) guidewire
1	Hemostatic valve
1	Diluted contrast medium 1:1 with normal heparinized sterile saline
1	Inflation Device
1	Torque Device
1	Pre-deployment dilation catheter
1	Three-way stopcock
1	Appropriate arterial sheath

14.3 Preparation

14.3.1 Packaging Removal

Step Action

1. Open the outer box to reveal the foil pouch and carefully inspect the foil pouch for damage.
2. Carefully peel open the foil pouch using aseptic techniques and extract the stent delivery system.
3. Carefully remove the delivery system from its protective tubing for preparation of the delivery system. Do not bend or kink the device during removal.
4. Remove the product mandrel and stent protector by grasping the catheter just proximal to the stent protector, and with the other hand, grasp the distal end of the stent protector and gently remove.

   Note: If unusual resistance is felt during product mandrel and stent protector removal, do not use the product and replace with another.
5. Examine the device for any damage. If it is suspected that the sterility or performance of the device has been compromised, the device should not be used.

14.3.2 Guidewire Lumen Flush

Step Action

1. Flush the stent delivery system guidewire lumen with normal heparinized saline using the flushing needle supplied for the Monorail delivery system at the distal end.
2. Verify that the stent is positioned between the proximal and distal balloon markers. Check for bends, kinks and other damage. Do not use if any defects are noted.

   Note: Avoid manipulation of the stent during flushing of the guidewire lumen, as this may disrupt the placement of the stent on the balloon.

   Note: Use caution while flushing guidewire lumen with flushing needle to avoid damage to catheter tip.

14.3.3 Balloon Preparation

Step Action

1. Stent contact with any fluid is not recommended, as there is a possibility of initiating drug release. However, if it is absolutely necessary to flush the stent with saline, contact time should be limited (1 minute maximum).
2. Prepare inflation device/syringe with diluted contrast medium.
3. Attach inflation device/syringe to stopcock; attach to inflation port. Do not bend the proximal shaft when connecting to inflation device/syringe.
4. With tip down, orient stent delivery system vertically.
5. Open stopcock to stent delivery system; pull negative for 15 seconds; release to neutral for contrast fill.
6. Close stopcock to stent delivery system; purge inflation device/syringe of all air.
7. Repeat steps 4 through 6 until all air is expelled. If bubbles persist, do not use product.
8. If a syringe was used, attach a prepared inflation device to stopcock.
9. Open stopcock to stent delivery system.
10. Leave on neutral.

14.3.4 Delivery Procedure

Step Action

1. Obtain vascular access according to standard PTCA practice. Select a guide catheter that provides adequate support and coaxial alignment with the coronary ostium to deliver interventional equipment.
2. Pre-dilate the lesion/vessel with appropriate diameter balloon.
3. Maintain neutral pressure on inflation device attached to stent delivery system.
4. Backload stent delivery system onto proximal portion of guidewire while maintaining guidewire position across target lesion.
5. Fully open hemostatic valve to allow for easy passage of the stent and prevent damage to the stent.
6. Carefully advance the stent delivery system into the hub of the guide catheter. Be sure to keep the proximal shaft straight. Ensure guide catheter stability before advancing the stent delivery system into the coronary artery.

   Note: If unusual resistance is felt before the stent exits the guide catheter, do not force passage. Resistance may indicate a problem, and use of excessive force may result in stent damage or stent dislodgment from the balloon. Maintain guidewire placement across the lesion, and remove the stent delivery system and guide catheter as a single unit.
7. Advance the stent delivery system over the guidewire to target lesion under direct fluoroscopic visualization. Utilize the proximal and distal radiopaque balloon markers as a reference point. If the position of the stent is not optimal, it should be carefully repositioned or removed (See also Precautions – Section 6.15, Stent Delivery System Removal). The inside edges of the marker bands indicate both the stent edges and balloon shoulders. Expansion of the stent should not be undertaken if the stent is not properly positioned in the target lesion segment of the vessel.

   Note: If unusual resistance is felt at any time during lesion access before stent implantation, the stent delivery system and the guide catheter should be removed as a single unit. (See also Precautions – Section 6.15, Stent Delivery System Removal). Once the stent delivery system has been removed do not re-use.
8. Sufficiently tighten the hemostatic valve. The stent is now ready to be deployed.

14.3.5 Deployment Procedure

Step Action

1. Inflate the delivery system expanding the stent to a minimum pressure of 11 atm (1117 kPa). Higher pressure may be necessary to optimize stent apposition to the arterial wall. Accepted practice generally targets an initial deployment pressure that would achieve a stent inner diameter of about 1.1 times the reference vessel diameter (see Table 14.1). Balloon pressure must not exceed rated burst pressure of 18 atm (1827 kPa) for the 2.25 mm – 2.75 mm diameter stents and 16 atm (1620 kPa) for the 3.00 mm – 5.00 mm diameter stent sizes (see Table 14.1).
2. Maintain inflation pressure for 15 seconds – 30 seconds for full expansion of the stent.
3. Deflate balloon by pulling negative pressure on inflation device until balloon is fully deflated. Ensure balloon is fully deflated before delivery system withdrawal. Larger and longer balloons will take more time to deflate than smaller and shorter balloons. Allow adequate time, at least 30 seconds, for balloon deflation. Before withdrawing the stent delivery system visually confirm complete balloon deflation under fluoroscopy.
4. Confirm stent position and deployment using standard angiographic techniques. For optimal results, the entire stenosed arterial segment should be covered by the stent. Fluoroscopic visualization during stent expansion should be used in order to properly judge the optimum expanded stent diameter as compared to the proximal and distal coronary artery diameter(s). Optimal expansion requires that the stent be in full contact with the artery wall. Stent wall contact should be verified through angiography or intravascular ultrasound (IVUS).
5. If stent sizing/apposition requires optimization, re-advance the stent delivery system balloon, or another high-pressure, balloon catheter of the appropriate size, to the stented area using standard angioplasty techniques.
6. Inflate the balloon to the desired pressure while observing under fluoroscopy (refer to product labeling and/or Table 14.1 for balloon compliance chart). Deflate the balloon. Ensure balloon is fully deflated before delivery system withdrawal. Larger and longer balloons will take more time to deflate than smaller and shorter balloons. Allow adequate time, at least 30 seconds, for balloon deflation. Before withdrawing the stent delivery system visually confirm complete balloon deflation under fluoroscopy.
7. If more than one SYNERGY™ XD Stent is needed to cover the lesion and balloon treated area, it is suggested that, to avoid the potential for gap restenosis, the stents be adequately overlapped. To ensure that there are no gaps between stents, the balloon marker bands of the second SYNERGY XD Stent should be positioned inside of the deployed stent prior to expansion.
8. Reconfirm stent position and angiographic result. Repeat inflations until optimal stent deployment is achieved, or remove stent delivery system for larger post-dilation balloon catheter.

14.3.6 Removal Procedure

Step Action

1. Deflate balloon by pulling negative pressure on inflation device until balloon is fully deflated. Ensure balloon is fully deflated before delivery system withdrawal. Larger and longer balloons will take more time to deflate than smaller and shorter balloons. Allow adequate time, at least 30 seconds. Before withdrawing the stent delivery system visually confirm complete balloon deflation under fluoroscopy.
2. Fully open hemostatic valve.
3. While maintaining guidewire position and negative pressure on inflation device, withdraw delivery system.
4. Repeat angiography to assess the stented area. If an adequate expansion has not been obtained, exchange back to the original stent delivery catheter or exchange to another balloon catheter of appropriate balloon diameter to achieve proper stent apposition to the vessel wall.

Post-Deployment Dilation of Stented Segments

Precaution: Do not dilate the stent beyond the limits tabulated below.

Nominal Stent Diameter (ID)	Dilation Limits (ID)*
2.25 mm, 2.50 mm, 2.75 mm	3.50 mm
3.00 mm, 3.50 mm	4.25 mm
4.00 mm, 4.50 mm, 5.00 mm	5.75 mm

*Max Stent Inner Diameter

All efforts should be taken to assure that the stent is not under-dilated. 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 post dilation balloon catheter may be used to expand the stent. The stent may be expanded using a low profile and high pressure balloon catheter. If this is required, the stented segment should be re-crossed carefully with a prolapsed guidewire to avoid dislodging the stent. The balloon should be centered within the stent and should not extend outside of the stented region.

Note: In line with Section 6.16, Post-Procedure: Care must be exercised when crossing a newly deployed stent with any wire, catheter or ancillary device to avoid disrupting the stent placement, apposition, geometry, and/or coating.

5. Complete angiographic confirmation, remove devices, and close vascular access site according to standard practice.

14.4 In Vitro Information

Table 14.1 Typical SYNERGY XD Stent System Compliance

Pressure atm (kPa)	Stent Inner Diameters (mm)							
	2.25 mm	2.50 mm	2.75 mm	3.00 mm	3.50 mm	4.00 mm	4.50 mm	5.00 mm
6 (607)						3.55		
7 (710)				2.72	3.19	3.68		
8 (814)	2.09			2.81	3.31	3.81	4.11	4.62
9 (910)	2.14	2.40	2.63	2.89	3.40	3.90	4.24	4.73
10 (1014)	2.19	2.46	2.70	2.96	3.47	3.99	4.35	4.85
11 Nominal (1117)	2.25	2.52	2.76	3.02	3.55	4.06	4.46	4.95
12 (1213)	2.29	2.57	2.82	3.06	3.60	4.12	4.54	5.03
13 (1317)	2.32	2.61	2.87	3.11	3.66	4.18	4.61	5.11
14 (1420)	2.36	2.65	2.90	3.15	3.70	4.22	4.68	5.17
15 (1517)	2.38	2.68	2.94	3.18	3.74	4.27	4.73	5.22
16*(1620)	2.41	2.71	2.97	3.21	3.78	4.32	4.78	5.28
17 (1724)	2.43	2.74	3.00	3.25	3.82	4.37	4.83	5.34
18* (1827)	2.46	2.77	3.03	3.29	3.88	4.44	4.89	5.39
19 (1924)	2.48	2.80	3.06	3.34	3.94	4.52	4.96	5.45
20 (2027)		2.83	3.10	3.39	4.01		5.04	5.50

* RATED BURST PRESSURE. DO NOT EXCEED.
Note: The Stent I.D. values listed are actual average stent inner diameters at the specific balloon inflation pressures obtained during in vitro testing at 37 °C. Balloon pressure must not exceed rated burst pressure of 18 atm (1827 kPa) for the 2.25 mm – 2.75 mm diameter stents and 16 atm (1620 kPa) for the 3.00 mm – 5.00 mm diameter stent sizes.

15 WARRANTY STATEMENT

Boston Scientific Corporation (BSC) warrants that reasonable care has been used in the design and manufacture of this instrument. **This warranty is in lieu of and excludes all other warranties not expressly set forth herein, whether express or implied by operation of law or otherwise, including, but not limited to, any implied warranties of merchantability or fitness for a particular purpose.** Handling, storage, cleaning and sterilization of this instrument as well as other factors relating to the patient, diagnosis, treatment, surgical procedures and other matters beyond BSC's control directly affect the instrument and the results obtained from its use. BSC's obligation under this warranty is limited to the repair or replacement of this instrument and BSC shall not be liable for any incidental or consequential loss, damage or expense directly or indirectly arising from the use of this instrument. BSC neither assumes, nor authorizes any other person to assume for it, any other or additional liability or responsibility in connection with this instrument. **BSC assumes no liability with respect to instruments reused, reprocessed or resterilized and makes no warranties, express or implied, including but not limited to merchantability or fitness for a particular purpose, with respect to such instruments.**

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