INSTRUCTION FOR USE

BioMatrix Flex™ Drug Eluting Coronary Stent System

English

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CE 0344

1. DEVICE DESCRIPTION

The BioMatrix Flex™ Drug Eluting Coronary Stent System (BioMatrix Flex™ DES) is a Drug Eluting Stent (DES) System for coronary use with a biodegradable polymer coating. The DES is a combination product comprised of two key components: the stent (which includes the active pharmaceutical ingredient BA9™ (Biolimus A9™) incorporated into a polymer coating), and the delivery system.

1.1. Device Component Description

- A balloon expandable intra-coronary 316L stainless steel stent with a biodegradable polymer coating Poly-lactic Acid containing the BA9™ drug pre-mounted onto a semi-compliant rapid exchange balloon delivery system.
- The delivery system has two radiopaque markers, which fluoroscopically mark the ends of the stent to facilitate proper stent placement.
- At the proximal end of the delivery system is a female luer lock connector hub. This hub connects to the balloon inflation lumen.
- The guidewire enters the distal tip of the catheter and exits 23±0.5 cm proximal to the tip of the delivery system.

Table 1: Device Description

Stent Pattern:	6-crown model	9-crown model
Stent Diameters (mm):	2.25 – 3.0	3.5 – 4.0
Stent Lengths (mm):	8, 11, 14, 18, 24, 28, 33*, 36*	
Stent Material / Coating:	316L stainless steel stent / Poly-lactic Acid (PLA) and BA9™ drug	
Delivery Catheter Working Length:	142 cm	
Stent Delivery Balloon:	Polyamide Elastomer	
Balloon Inflation:		
Nominal Inflation Pressure:	6 atm / 608 kPa	6 atm / 608 kPa
Rated Burst Pressure:	16 atm / 1621 kPa	14 atm /1418 kPa

*** BioMatrix Flex™ with a length of 33 and 36 mm is only available for diameters from 2.5 to 3.5mm.**

1.2. Drug Component Description

- The BA9™ (Biolimus A9™) drug, a proprietary formulation of umirolimus, is a semi-synthetic sirolimus derivative with enhanced pharmacokinetic properties. The BA9™ drug, as provided on the BioMatrix Flex™ DES, inhibits smooth muscle cell proliferation within the stent proximity.
- Poly-lactic acid (PLA) is combined with the BA9™ drug and acts as the carrier to control the release of the drug from the stent.

Table 2: Nominal BA9™ Drug Dosage

Product Code	Nominal Expanded Inner Diameter (mm)	Nominal Unexpanded Stent Length (mm)	Nominal Dose of BA9™ drug (µg)
BMX-2208	2.25	8	133
BMX-2211	2.25	11	178
BMX-2214	2.25	14	225
BMX-2218	2.25	18	292
BMX-2224	2.25	24	384
BMX-2228	2.25	28	453
BMX-2508	2.5	8	133
BMX-2511	2.5	11	178
BMX-2514	2.5	14	225
BMX-2518	2.5	18	292
BMX-2524	2.5	24	384
BMX-2528	2.5	28	453
BMX-2533	2.5	33	521
BMX-2536	2.5	36	566
BMX-2708	2.75	8	133
BMX-2711	2.75	11	178
BMX-2714	2.75	14	225
BMX-2718	2.75	18	292
BMX-2724	2.75	24	384
BMX-2728	2.75	28	453
BMX-2733	2.75	33	521
BMX-2736	2.75	36	566
BMX-2733	2.75	33	521
BMX-2736	2.75	36	566
BMX-3008	3.0	8	133
BMX-3011	3.0	11	178
BMX-3014	3.0	14	225
BMX-3018	3.0	18	292
BMX-3024	3.0	24	384
BMX-3028	3.0	28	453
BMX-3033	3.0	33	521

Product Code	Nominal Expanded Inner Diameter (mm)	Nominal Unexpanded Stent Length (mm)	Nominal Dose of BA9™ drug (µg)
BMX-3036	3.0	36	566
BMX-3508	3.5	8	133
BMX-3511	3.5	11	178
BMX-3514	3.5	14	225
BMX-3518	3.5	18	292
BMX-3524	3.5	24	384
BMX-3528	3.5	28	453
BMX-3533	3.5	33	521
BMX-3536	3.5	36	566
BMX-4008	4.0	8	133
BMX-4011	4.0	11	178
BMX-4014	4.0	14	225
BMX-4018	4.0	18	292
BMX-4024	4.0	24	384
BMX-4028	4.0	28	453

2. INDICATIONS

The BioMatrix Flex™ DES is indicated for improving coronary luminal diameter for the treatment of de novo lesions in native coronary arteries with a reference diameter ranging between 2.25 mm and 4.0 mm. Stents with length 33mm and 36mm are only available for artery diameters ranging between 2.5mm and 3.5mm.

The BioMatrix Flex™ DES with stent length up to 28mm is also indicated for use in patients with:

- ST Elevated Myocardial Infarction (STEMI)
- Acute Coronary Syndromes (ACS) including ACS-STEMI, ACS-NSTEMI and Unstable Angina
- Diabetes Mellitus

3. CONTRAINDICATIONS

The BioMatrix Flex™ DES is contraindicated for use in:

- Patients in whom anti-platelet and/or anti-coagulant therapy is contraindicated.
- Patients with lesion(s) that prevent complete inflation of an angioplasty balloon.
- Patients with known sensitivity to the BA9™ drug or its derivatives.
- Patients with a known allergy to stainless steel, nickel or other metal ions found in 316L.
- Patients with known sensitivity to contrast agents that cannot be controlled prophylactically prior to BioMatrix Flex™ stent implantation.
- Off-label use (i.e. outside of the approved indications for use). Patient outcomes may not be the same as the results observed in clinical trials.

4. ANTIPLATELET REGIMEN

Administration of appropriate anticoagulant, antiplatelet and coronary vasodilator therapy is critical for a successful long term result implantation.

An antiplatelet regimen of clopidogrel or ticlopidine administered pre-procedure and for at least 3 months post-procedure was used during clinical trials with the BA9™ DES. Clopidogrel is required for **a minimum of 6 months** and strongly recommended for 12 months in patients who are not at high risk of bleeding per the ACC/AHA/SCAI 2005 Guideline Update for Percutaneous Coronary Intervention. Acetylsalicylic acid is to be administered indefinitely to reduce the risk of thrombosis.

5. WARNINGS

For 33 and 36 mm stent lengths of the BioMatrix Flex™ DES, the indication for use in patients with STEMI, ACS or Diabetes Mellitus has not been established (refer to section 2. INDICATIONS).

Judicious selection of patients is necessary since the use of this device carries the associated risk of thrombosis, vascular complications and/or bleeding events. Hence patients should be maintained on clinically adequate post-procedural antiplatelet therapy (acetylsalicylic acid, clopidogrel or ticlopidine).

Only physicians who have received appropriate training should perform implantation of the stent.

Stent placement should only be performed at hospitals where emergency coronary artery bypass graft surgery can be readily performed.

Subsequent restenosis may require repeat dilatation of the arterial segment containing the stent. The long-term outcome following repeat dilatation of endothelialized stents is unknown at present.

Ensure that the inner packaging has not been damaged or opened as this may indicate a breach of the sterile barrier.

This stent deployment device must not be reused in another procedure. The performance characteristics of the balloon are degraded during use.

When multiple tandem stents are required, stent materials should be of similar composition to avoid dissimilar metal corrosion.

Direct stenting has been performed in the studies using this device. However, as direct stenting was no study endpoint it is not recommended.

Stent occlusion may require repeat dilations of the target lesion. The long-term outcome following repeat dilations of the target lesion is presently unknown.

This product is not intended or approved for use in peripheral applications.

6. PRECAUTIONS

6.1 Drug Interactions

Consideration should be given to the potential for drug interactions when deciding to place a BioMatrix Flex™ stent in a patient who is taking a drug that could interact with the BA9™ drug or when deciding to initiate therapy with such a drug in a patient who has recently received a BioMatrix Flex™ stent. The effect of BioMatrix Flex™ DES drug interactions on safety or efficacy has not been determined.

There is no specific clinical data available for the interactions of the BA9™ drug with other drugs. However, drugs like Tacrolimus that may act through the same binding proteins (FKBP) may interfere with the efficacy of the BA9™ drug. Drug interaction studies have not been performed. The BA9™ drug is metabolized by CYP3A4. Strong inhibitors of CYP3A4 (e.g. ketoconazol) might cause increased BA9™ drug exposure to levels associated with systemic effects, especially if multiple stents are deployed. Systemic exposure of the BA9™ drug should be taken into consideration if the patient is treated concomitantly with systemic immunosuppressive therapy.

Patient's exposure to the BA9™ drug is directly related to the length of the BioMatrix Flex™ stent or stents implanted.

6.2. Stent Handling – Precautions

For single use only. Do not resterilize or reuse.

Do not use a product that has reached or exceeded its labeled expiration date.

Do not use if packaging has been damaged or opened. **The sterility and stability of the BioMatrix Flex™ DES cannot be guaranteed once the pouch has been opened** and hence the device MUST be used promptly. Un-used devices should be discarded or returned to Biosensors International and should not be re-stocked.

Do not use if stent coating is subjected to abrasions beyond those of normal insertion and delivery.

Do not use if stent is exposed to abnormal rubbing or contact with objects other than the guide catheter or opened hemostasis valve prior to implantation.

DO NOT RUB OR SCRAPE THE STENT COATING.

Do not remove stent from its delivery catheter as removal may damage the stent and/or lead to stent embolization. BioMatrix Flex™ stent is intended to perform as a system.

The delivery system should not be used in conjunction with other stents.

Special care must be taken not to handle or in any way disrupt the stent on the balloon.

Do not "roll" the mounted stent with your fingers as this action may loosen the stent from the balloon and cause subsequent dislodgement, or cause some loss of drug coating.

Use only the appropriate balloon inflation media. Do not use air or any gaseous medium to inflate the balloon as this may cause uneven expansion and difficulty in deployment of the stent.

Do not attempt to straighten the proximal shaft (hypotube) as it may cause the catheter to break if it is accidentally bent.

Exposing the stent to fluids before implantation is not recommended. Exposure to fluids prior to implantation may result in premature release of drug.

IN THE EVENT THAT THE STENT IS NOT SUCCESSFULLY DEPLOYED, THE STENT AND DELIVERY SYSTEM SHOULD BE RETURNED TO BIOSENSORS INTERNATIONAL.

6.3. Stent Placement – Precautions

Do not prepare, introduce negative pressure, or pre-inflate the delivery system prior to stent deployment other than as directed. Use balloon purging technique described in 9.4. Delivery System Preparation.

The labeled stent diameter refers to the expanded stent inner diameter.

Implanting a stent may lead to dissection of the vessel distal and/or proximal to the stent and may cause acute closure of the vessel requiring additional intervention (CABG, further dilatation, placement of additional stents, or other).

When treating multiple lesions, distal lesions should be stented first followed by proximal lesion stenting. 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.

Use of Multiple Stents: The extent of the patient's exposure to drug and polymer is directly related to the number of stents implanted.

Do not expand the stent if it is not properly positioned in the vessel. (See 6.4. Stent / System Removal – Precautions)

Placement of a stent has the potential to compromise side branch patency.

Do not exceed rated burst pressure as indicated on product label. Use of pressures higher than specified on the product label may result in a ruptured balloon with possible intimal damage and dissection.

Do not attempt to pull an unexpanded stent back through the guiding catheter, as dislodgement of the stent from the balloon may occur. Remove as a single unit as described in 6.4. Stent / System Removal – Precautions.

Stent retrieval methods (use of additional wires, snares and/or forceps) may result in additional trauma to the coronary vasculature and/or the vascular access site. Complications may include bleeding, hematoma or pseudoaneurysm.

6.4 Stent / System Removal – Precautions

Should unusual resistance be felt at any time during either lesion access or removal of the stent delivery system prior to the stent being implanted, the entire system should be removed as a single unit.

When removing the stent delivery system as a single unit:

- Do not attempt to retract an unexpanded stent into the guiding catheter while engaged in the coronary arteries.
- Stent damage or dislodgement may occur. Advance the guidewire into the coronary anatomy as far distally as safely possible.
- Position the proximal balloon marker just distal to the tip of the guiding catheter.

NOTE: If it is necessary to maintain guidewire position, the guidewire must either be converted to an exchange wire length or a second guidewire must be inserted.

- Tighten the rotating hemostatic valve to secure the delivery system to the guiding catheter. Remove the guiding catheter and stent delivery system as a **single unit**.

Do not attempt to pull the guiding catheter and delivery system through the femoral sheath. When the distal tip of the guiding catheter reaches the distal end of the femoral sheath, remove sheath, guiding catheter, and delivery system as a single unit and replace sheath per hospital protocol.

Failure to follow these steps and/or applying excessive force to the stent delivery system can potentially result in stent dislodgement or damage to the stent and/or delivery system components.

6.5. Post Implant – Precautions

Care must be exercised when crossing a newly deployed stent with a coronary guidewire, IVUS catheter, balloon or another stent delivery system to avoid disrupting the stent geometry.

6.6 Magnetic Resonance Imaging (MRI)

Non-clinical testing has demonstrated that the BioMatrix Flex™ DES is MR Conditional. A patient with a BioMatrix Flex™ stent can be scanned safely, immediately after placement of this implant, under the following conditions:

- Static magnetic field of 3-Tesla or less
- Spatial gradient field of 720-Gauss/cm or less
- Maximum MR system reported whole-body-averaged specific absorption rate (SAR) of 3-W/kg for 15 minutes of scanning.

In non-clinical testing, the BioMatrix Flex™ DES (single and two stents overlapping) produced a temperature rise of less than or equal to 2.1°C at a maximum MR system reported whole body averaged specific absorption rate (SAR) of 3-W/kg for 15-minutes of MR scanning in a 3-Tesla, 128 MHz MR system (Excite, Software G3.0-052B, General Electric Healthcare, Milwaukee, WI). The effect of performing MRI procedures using higher levels of RF energy on the BioMatrix Flex™ stent has not been determined. The effect of heating in the MRI environment on more than two overlapping stents is unknown.

MR image quality may be compromised if the area of interest is in the same area or relatively close to the position of the BioMatrix Flex™ DES.

7. INDIVIDUALIZATION OF TREATMENT

The risks and benefits of drug-eluting stents should be considered for each patient before use of the BioMatrix Flex™ stent. Physicians are responsible for assessing patient appropriateness for stent implantation prior to procedure.

8. USE IN SPECIAL POPULATIONS

The safety and effectiveness of the BioMatrix Flex™ DES has not been established in the following patient populations:

- Pregnancy: There are no data available for use of the BioMatrix Flex™ stent in pregnant women.
- During Lactation: The effects of the BA9™ drug during lactation have not been evaluated.
- Pediatric use: The safety and efficacy of the BioMatrix Flex™ stent has not been established.

Carefully consider whether it is appropriate to use in the above patient populations

The safety and effectiveness beyond two years, or of using mechanical atherectomy devices (directional atherectomy catheters, rotational atherectomy catheters) or laser angioplasty catheters to treat in-stent stenosis has not been established.

9. OPERATOR'S MANUAL

9.1. Inspection Prior to Use

1. Inspect the stent delivery system package for damage to the sterile barrier.
2. Carefully remove the system from the package and inspect the delivery catheter for bends, kinks, and other damage.
3. Carefully remove the stent guard covering the stent /balloon. The pre-attached stylet is automatically removed.
4. Inspect the stent to ensure that it has not been damaged or displaced from its original position on the balloon. Verify that the stent is positioned between the proximal and distal balloon markers.
5. Note the position of the stent relative to the proximal and distal marker bands for use as reference under fluoroscopy.

Do not use if any defects are noted.

9.2. Materials Required

1	A guiding catheter with a minimum inner diameter of 0.056" for the 6-crown model (2.25-3.0 mm diameter) and 0.070" for the 9-crown model (3.5-4.0 mm diameter)
1	Pre-dilatation balloon catheter
1	10-20 cc syringe

1000 IU	Heparin per 500 cc Normal Saline (HepNS)
1	0.014 inch guidewire ≥ 175 cm
1	Rotating hemostatic valve
N/A	Contrast diluted 1 : 1 with normal saline
1	Inflation device
1	Three-way stopcock

9.3. Delivery System Preparation

1. Prepare inflation device/syringe with diluted contrast medium.
2. Attach inflation device to the three-way stopcock; attach to balloon inflation port hub.

   NOTE: DO NOT apply negative or positive pressure to the balloon at this time as it can cause premature dislodgement of the stent.
3. Open stopcock to stent delivery system.
4. Leave on neutral.

9.4. Stent Delivery Procedure

1. Prepare vascular access site according to standard PTCA practice.
2. Pre-dilate lesion with a balloon diameter 0.5 mm smaller than the stent, and a balloon length equal to or shorter than the target lesion length, and shorter than the length of the stent to be implanted.
3. Immediately prior to backloading the stent delivery catheter onto the guidewire, flush the guidewire lumen with HepNS according to hospital protocol. Avoid contact with the stent.

   NOTE: Stent contact with fluid has the possibility of initiating drug release. Fluid contact time should be limited to immediately prior to loading the delivery catheter on the guidewire. When flushing the delivery catheter, ensure that damage to the stent does not occur.
4. Backload stent delivery system onto the proximal portion of the guidewire while maintaining guidewire position across target lesion.
5. Open rotating hemostatic valve on the guiding catheter hub as widely as possible, and close when the stent has been advanced safely inside the guide catheter.
6. Advance the stent delivery system over the guidewire to the target lesion under fluoroscopic guidance. Utilize the radiopaque balloon markers to position the stent across the lesion. Perform angiography to confirm stent position.

   NOTE: If resistance is felt, DO NOT FORCE PASSAGE. Resistance may indicate a problem and may result in damage to the vessel or stent, or in stent dislodgement if it is forced. Remove the stent delivery system and the guiding catheter as a single unit (see 6.4. Stent / System Removal - Precautions).

9.5. Deployment Procedure

1. Consult the balloon compliance chart on the compliance card or at the back of the product box in order to determine the balloon inflation pressure appropriate for the target vessel diameter.

   CAUTION: Different compliance charts apply for different stent lengths.
2. Before deployment, reconfirm the correct position of the stent relative to the target lesion via the balloon markers.
3. Ensure that the three-way stopcock on the stent delivery system is open to the inflation device and apply negative pressure to purge the balloon of air.
4. Turn the three-way stopcock on the stent delivery catheter off to the balloon port and purge the inflation device of air. Open the side port of the three-way stopcock to the delivery system.
5. Under fluoroscopic visualization, inflate the balloon to at least 6 atm to deploy the stent, but do not exceed the labeled rated burst pressure (RBP). Optimal expansion requires the stent to be in full contact with the artery wall with the stent internal diameter matching the size of the reference vessel diameter. ENSURE THAT THE STENT IS NOT UNDERDILATED.
6. Deflate the balloon by pulling a vacuum with the inflation device for up to 15 seconds. Make sure the balloon is fully deflated before attempting any movement of the system.
7. Confirm adequate stent expansion and balloon deflation by angiographic injection through the guiding catheter.
8. If more than one BioMatrix Flex™ stent is needed to cover the lesion and balloon treated area, adequately overlap the stents (at least 2 mm) to avoid potential gap stenosis.

9.6. Removal Procedure

1. Ensure that the balloon is fully deflated.
2. Fully open the rotating hemostatic valve.
3. While maintaining guidewire position and negative pressure on inflation device, withdraw the delivery system.
4. Tighten rotating hemostatic valve.
5. Repeat angiography to assess the stented area.

9.7. Further Dilatation of Stent Segments

1. If an adequate expansion has not been obtained, re-advance the stent delivery system or exchange for another balloon catheter of appropriate balloon diameter to achieve proper stent apposition to the vessel wall.

   NOTE: Post-dilatation should be performed within the stented segment. DO NOT dilate beyond the stent edges.
2. Reconfirm stent position and angiographic result. Repeat inflations until optimal stent deployment is achieved. Final stent diameter should match reference vessel.

10. POTENTIAL ADVERSE EVENTS

Adverse events that may be associated with the use of a stent in native coronary arteries include but not limited to:

- Abrupt stent closure or failure to expand the stent.
- Abrupt vessel closure or spasm
- Acute myocardial infarction
- Allergic reaction to anti-coagulation and/or anti-thrombotic therapy, contrast material, or stent and/or delivery system materials
- Aneurysm, pseudoaneurysm or arteriovenous fistula
- Arrhythmias, including ventricular fibrillation and ventricular tachycardia
- Cardiac tamponade
- Cardiogenic shock
- Death
- Dissection, perforation, or rupture of the artery
- Emboli, distal (air, tissue or thrombotic emboli)
- Emergency coronary artery bypass grafting (CABG) as a result of damage to the stent or injury to the vessel
- Fever
- Hematoma at insertion site
- Hemorrhage requiring transfusion
- Hypotension/hypertension
- Infection and/or pain at insertion site
- Late stent thrombosis/stent thrombosis/occlusion
- Perforation or rupture of the artery
- Peripheral ischemia or peripheral nerve injury
- Stroke or transient ischemic attack
- Renal failure
- Restenosis of stented segment
- Stent migration or stent embolization
- Total occlusion of coronary artery
- Unstable angina

Adverse events that may be associated with BA9™ drug coating.

NOTE: BA9™ drug administration is limited to intra-coronary stent delivery. The adverse effects of using this drug have not been fully characterized and may have additional side effects / complications associated with the use of the BA9™ drug at significantly higher doses than what would be delivered via the BioMatrix Flex™ DES. They include the following:

• Nausea

• Lymphadenopathy

• Mouth ulcers

• Chest heaviness

• Dizziness

11. HOW SUPPLIED

STERILE, NON-PYROGENIC. This device is sterilized via e-beam sterilization.

CONTENTS: One Biosensors BioMatrix Flex™ Drug Eluting Coronary Stent System.

STORAGE: Store in a cool dark dry place. Do not store above 25°C.

DISPOSAL: Dispose device in accordance with local regulations.

12. SYMBOLS USED IN LABELING

INSTRUCTION FOR USE

BioMatrix Flex™ Drug Eluting Coronary Stent System

	**Legal Manufacturer**
	**Date of Manufacture**
	**Catalog number**
	**Batch code**
	**Caution, consult accompanying documents**
	**Consult Instruction For Use**
	**Do not re-sterilize**
	**Do not re-use**
	**This product has been sterilized using irradiation**
	**Use by date** **Do not use this product after the indicated date (Year-month-day)**
	**Do not store above 25°C**
	**Keep dry**
	**Keep away from sunlight or heat**
	**MR conditional**
	**Do not use if package is damaged or open**

	**Stent Length**
	**Stent Diameter**
	**Maximum Guidewire Outer Diameter (O.D.)**
	**Minimum Guiding Catheter Inner Diameter (I.D.)**
NP	**Nominal Pressure**
RBP	**Rated Burst Pressure**

13. WARRANTY

Biosensors warrants that its products are manufactured to the specifications set forth on its packaging, instructions for use and related literature.

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. Biosensors neither assumes, nor authorizes any other person to assume for it, any other or additional liability or responsibility in connection with this product.

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