

Orsiro[®]

Sirolimus-eluting Cobalt Chromium (CoCr) Coronary
Stent

Patient Information Guide

Understanding Coronary Artery Disease and Drug-Eluting Stents

TABLE OF CONTENTS

1. Understanding Your Heart and Coronary Artery Disease	3
1.1. Your Heart – The Engine of Life.....	3
1.2. Coronary Artery Disease	3
1.3. What Causes CAD?	3
1.4. How do I recognize CAD?	4
1.5. What are the Risk Factors for Coronary Artery Disease?.....	4
1.6. How Is Coronary Artery Disease Diagnosed?	4
2. Coronary Angiography	4
2.1. Before the procedure.....	4
3. Treatment Options	4
3.1. Medications.....	4
3.2. Surgery	4
3.3. Balloon Angioplasty.....	4
4. Treatment with a Coronary Artery Stent	5
5. Orsiro [®] Drug-eluting Stent	5
6. Polymer Coating	5
7. Drug Release	5
8. Potential Adverse Events	5
9. Clinical Data Summary	6
10. Medications.....	6
11. After the Procedure	6
12. Activity.....	6
13. Frequently Asked Questions	6
14. More Information	7



Patient Information Guide

This guide explains the possible risks associated with having a stent implanted along with medication recommendations and answers to questions you may have about coronary stents.

your arteries.

1. Understanding Your Heart and Coronary Artery Disease

1.1. Your Heart – The Engine of Life

The circulatory system carries vital oxygen, water, nutrients and hormones through our bodies. Your “engine” – the heart – keeps this system running. In the span of one minute, the heart muscle pumps all of our blood through the entire body with rhythmic contractions. Over one’s lifetime, the heart beats three billion times and transports 66 million gallons of blood – an astonishing performance that no other engine can compete with. Coronary arteries are blood vessels that carry oxygen and nutrient-rich blood to the heart muscle, so it can function properly.

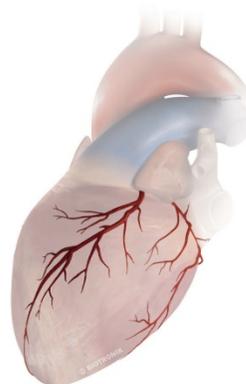


Figure 1. Picture of the your heart and coronary arteries (in red)

1.2. Coronary Artery Disease

Coronary artery disease (CAD) is caused by narrowing of the arteries in the heart. This narrowing is also called a stenosis. Coronary arteries are blood vessels that carry oxygen and nutrient-rich blood to the heart muscle. Arteries are normally smooth and unobstructed on the inside, but they can become blocked if a sticky substance called plaque builds up in the walls of

1.3. What Causes CAD?

Plaque is usually caused by a build-up of fat or calcium deposits. As more plaque builds up, your arteries can narrow and stiffen through a process called atherosclerosis (hardening of the arteries) which can result in blocked arteries. When this happens, your heart muscle may not receive the oxygen it needs to work effectively as a pump due to blood flow reduction in one or more of the coronary arteries.



Figure 2. Inside a healthy coronary artery

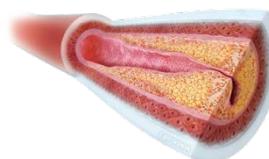


Figure 3. Inside a diseased coronary artery (atherosclerosis or plaque)



1.4. How do I recognize CAD?

Since arteries narrow and harden gradually over the years, it can take decades before patients experience discomfort. The first symptoms usually appear when the heart is under stress, for example during exercise. Symptoms vary and may also occur at rest or during sleep. The lack of blood flow resulting from CAD can result in chest pain, shortness of breath and possibly a heart attack.

1.5. What are the Risk Factors for Coronary Artery Disease?

- Age (over 45 for men, over 55 for women)
- A family history of heart and vascular disease
- Diabetes
- Smoking
- Hypertension (high blood pressure)
- High level of blood cholesterol (LDL, sometimes called "bad" cholesterol) and triglyceride levels (a type of fat found in blood)
- Low level of "good" cholesterol (HDL)
- Being overweight or obese
- Sedentary lifestyle
- Emotional stress

1.6. How Is Coronary Artery Disease Diagnosed?

These tests may be used to confirm coronary artery disease:

- Electrocardiography (ECG or EKG): records the electrical activity of the heart.
- Echocardiogram (ECHO): uses an ultrasound to detect how the heart is working.
- Stress test: a heart can function normally while at rest, so it is important to repeat tests while the heart is under physical or pharmacological stress.
- Catheterization of the heart (also called Coronary Angiography): a test done in a catheterization laboratory ("cath lab") in which a cardiologist injects contrast dye into the vascular system. X-ray images of the heart then show where the coronary vessels are narrowed.
- Intravascular ultrasound (IVUS): performed in the cath lab using high-frequency ultrasound waves to show the inside of a vessel.
- Magnetic resonance imaging (MRI): a non-invasive method to show lesions in the arteries.
- Computer tomography (CT): an X-ray scan showing the arteries at different angles.
- Blood tests: to check blood fat levels in the blood. Certain parameters can indicate damaged heart muscle cells

2. Coronary Angiography

2.1. Before the procedure

You may have been told you need an angiogram. The angiogram will look at your vessels through X-ray images so that the doctor can determine if you need balloon treatment (angioplasty) and/or stent placement to open the vessel.

A mild sedative may be given to you before your doctor begins the procedure. You will lie on your back on a table, which may be tilted during the procedure in order to take images of your heart from different angles. Cameras may move around and over you.

Several devices will be used to monitor your body, such as electrodes placed on your chest to monitor your heart, and a blood pressure cuff to monitor your blood pressure.

A small incision is made, so that a long, thin, flexible tube called a

catheter can be inserted into your artery.

Figure 4. Heart angiogram being performed in a catheterization laboratory



The catheter is carefully guided to your coronary arteries in your heart. A type of dye is injected into the blood vessels of your heart, which is visible on the X-ray. You may feel a warm sensation temporarily, but you should tell your health care team if you feel pain or discomfort.

This procedure will help your doctor visualize whether there are any blockages in your coronary arteries and decide what type of treatment would be best for you. Your doctor may recommend balloon angioplasty or stent placement, both of which begin with the same coronary angiography procedure.

3. Treatment Options

Treatment for CAD can include lifestyle changes, medications, and minimally invasive or surgical procedures.

3.1. Medications

Your doctor may recommend medications that help to increase the flow of blood to your heart by expanding the coronary arteries, relieve your chest pain, lower cholesterol and/or reduce blood pressure.

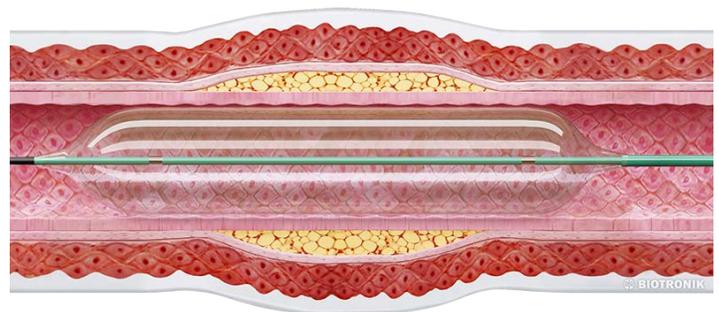
3.2. Surgery

Coronary Artery Bypass Surgery (CABG), which involves implanting a segment of a healthy vessel from another part of the patient's body to the coronary artery beyond the blockage site, provides a new route for the blood to flow around a blocked artery.

3.3. Balloon Angioplasty

In an angioplasty, your doctor inserts a long, thin, flexible tube called a catheter into a small puncture in an artery. The catheter is guided through your arteries to the blocked area. Once in place, a special balloon attached to the catheter is inflated and deflated. The balloon pushes the plaque in your artery against your artery walls, widening the artery. There are then several additional treatment options. A commonly selected option is to treat with a coronary artery stent.

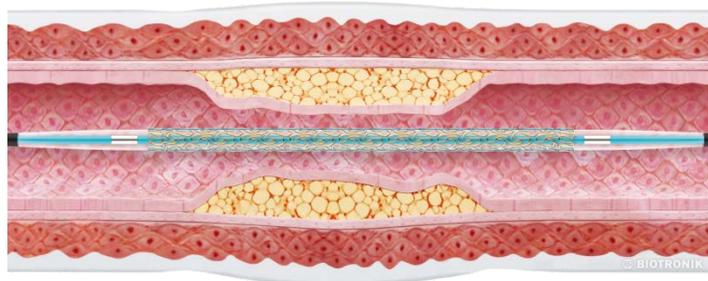
Figure 5. Inflated balloon in a coronary artery for balloon angioplasty



4. Treatment with a Coronary Artery Stent

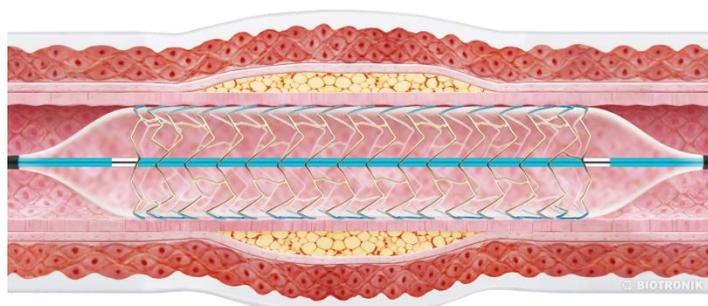
Your physician may have informed you that one or more of your coronary arteries that supply blood to your heart has significantly narrowed and that you may be suitable for treatment with a stent. A stent is a tiny metal mesh-like tube used to hold the artery walls open and allow blood to flow through. The stent is delivered into your coronary arteries on a catheter delivery system.

Figure 6. A permanent metallic stent is inserted into the affected artery.



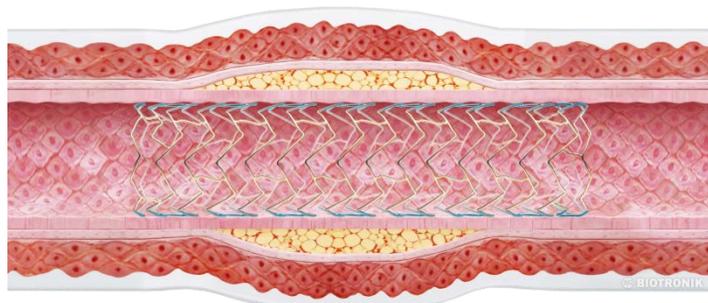
Once positioned within the stenosis (the narrowed section of an artery), the stent is expanded by inflating the balloon (of the delivery system). The stent and balloon push the plaque in your coronary artery against the artery walls and widens the artery.

Figure 7. The metallic stent is opened within the artery by inflating the balloon.



The balloon and delivery system are removed from the body. The stent is then left in the artery to keep it open and help prevent further narrowing of the coronary artery. Over time, the artery wall will heal around the stent as it continues to support the artery.

Figure 8. The metallic stent remains permanently in the treated vessel.



5. Orsiro® Drug-eluting Stent

The Orsiro® stent (hereinafter Orsiro) is intended as a permanent implant. It is made from a cobalt chromium (CoCr) alloy which consists of cobalt, chromium, tungsten and nickel. The stent is coated with a

special bioabsorbable drug matrix (drug and polymer) to help reduce the chance of the artery becoming blocked again. The drug is called sirolimus and it is released from the stent over a period of time during which re-blockage is most likely to occur. The stent is designed to be very flexible, allowing it to fit the shape of your artery.

The Orsiro stent is delivered to the artery using a balloon catheter delivery system. Together, the Orsiro stent and the delivery system make up the Orsiro Sirolimus-eluting Coronary Stent System.

6. Polymer Coating

The bioabsorbable polymer carries and protects the drug before and during the procedure. Once the stent is implanted, it helps control the drug release into the coronary artery wall. The polymer coating has been designed to be reabsorbed by your body over time.

7. Drug Release

The combination of the sirolimus drug and the polymer has been designed to allow a consistent and controlled rate of drug release from the stent surface into the artery walls. Both the amount of drug and the drug release rate have been selected so that healing can occur while minimizing the processes leading to restenosis (recurrent blockage of the artery), thus reducing the likelihood that additional treatment in the stented area will be needed in the future.

8. Potential Adverse Events

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

- Heart events: heart attack or reduced blood flow to your heart, abrupt closure of an artery, re-closing or re-narrowing of the treated artery (greater than 50% blockage) due to re-growth of tissue, cardiogenic shock (damage to your heart where it cannot supply enough blood to the rest of your body), chest pain, fluid build-up in the lining around the heart causing pressure which may result in a decreased blood flow and pumping, hole or tear in an artery or in your heart muscle, need for emergency heart surgery, widening/expansion of an artery in your heart or enlarged heart muscle.
- Abnormal heart rates or rhythms, such as a rapid heart rate, slow heart rate or an irregular heart rate that can cause a quivering sensation in your chest, shortness of breath, dizziness, fatigue or weakness.
- Stent system events: stent placed in a different part of the vessel or unplanned location, stent falling off the balloon catheter, stent deformation (bending or twisting), stent embolization, stent thrombosis (blood clot) or occlusion (closed artery), stent fracture (break), stent movement, stent is not fully against the vessel wall, inflation difficulties, rupture or pinhole of the balloon, balloon deflation difficulties, difficulty removing the balloon catheter, embolization of balloon catheter material (may enter the blood stream and cause damage or clotting).
- Breathing or lung events: build-up of fluid around your lungs, heart failure (disease that may cause heart muscle weakness), difficulty breathing or inability to breathe.
- Blood vessel system events: access site bruising and/or pooling of blood under the skin, hypotension/hypertension, pooling of blood that forms as the result of a leaking hole in an artery, arteriovenous fistula formation (an abnormal connection between an artery and a vein), retroperitoneal bruising and/or pooling of blood under the skin, vessel dissection or perforation (hole or tear in a blood vessel wall), re-narrowing of blood vessels, blood clot formation or closure of a vessel, closure or narrowing of vessels connected to the artery, spasm or injury of a blood vessel, deficient blood distribution in the limbs due to narrowing or closed arteries, tear in a vessel, distal embolization (air, tissue, debris or blood clot may enter the blood stream and cause damage or clotting).
- Neurological/Nervous system events: stroke, transient ischemic

attack (TIA), nerve damage or pain.

- o Bleeding events: bleeding from the site where the stent system was inserted into the skin, requiring special medication or blood transfusions (severe bleeding).
- o Allergic reaction to the contrast media, antiplatelet medications or anticoagulants (drugs used to thin the blood) during the procedure, or stent material.
- o Death.
- o Infection and sepsis (life-threatening complication of an infection).

The potential adverse events related to the oral administration of sirolimus is provided for information only. The amount of sirolimus circulated in your bloodstream will be significantly lower for stent implants than when obtained in oral doses. They include, but are not limited to:

- o Abnormal liver function tests.
- o Allergic reaction to the drug which can include an itchy rash or a more severe reaction of difficulty breathing, throat swelling and low blood pressure.
- o Anemia (low red blood cell count).
- o Cancer of the lymph nodes or other types of cancer.
- o Diarrhea.
- o Diseases that affect the tissues and space around the air sacs of the lungs.
- o Increased levels of cholesterol and triglycerides (fat or lipids) in the blood.
- o Joint pain.
- o Low level of potassium in the blood.
- o Low platelet count in the blood.
- o Low white cell count in the blood.
- o Inform and discuss the stent procedure with your doctor if you're:
 - o Taking immunosuppressive medications.
 - o Pregnant (as there is also potential harm to the fetus).
 - o There may be other potential adverse events that are unforeseen at this time.

9. Clinical Data Summary

The principal safety and effectiveness information for the Orsiro stent system is derived from the BIOFLOW-V clinical trial. The BIOFLOW-V randomized controlled trial compared the Orsiro stent to the FDA approved Xience¹ stent in 1334 patients with a planned five-year clinical follow-up. Safety and effectiveness for Orsiro was established by combining these trial results with the results from two additional BIOFLOW clinical trials which were previously conducted outside the US (BIOFLOW II and BIOFLOW IV), for a total of 2282 patients studied.

The BIOFLOW-V study principal ('primary endpoint') results showed that at one year following Orsiro stent deployment, the combined occurrence of heart-related death, heart attack, bypass surgery and repeat treatment in the lesion where the stent was placed was 6.3 % for the Orsiro stent as compared to 8.9% for the FDA approved Xience stent.

Additional analyses conducted on the BIOFLOW-V study results also support the safety and effectiveness of the Orsiro stent when used in the treatment diabetic patients.

In summary, the BIOFLOW-V clinical trial results showed that the Orsiro stent system is safe and effective when used to treat coronary blockages.

10. Medications

Your doctor has prescribed a number of medications to thin the blood and prevent blood clots from forming and adhering to the surface of the stent. These medications ('antiplatelet drugs') may include aspirin and other blood-thinning drugs such as clopidogrel (Plavix[®]), ticlopidine (Ticlid[®]), prasugrel (Effient[®]) or ticagrelor (Brilinta[®]). Your doctor will tell you how long you should continue taking the antiplatelet drugs. It is extremely important to follow your medication regimen exactly as prescribed by your doctor. If you stop taking these medications before being instructed by your doctor, there are increased chances of blood clot formation on the stent, subsequent heart attack or even death..

Report side effects from medications immediately. These may include headaches, nausea, vomiting or rash.

¹Xience is a registered trademark of Abbott Cardiovascular Systems Inc.

Do not stop taking your medications unless you are asked to stop by the doctor who implanted your stent.

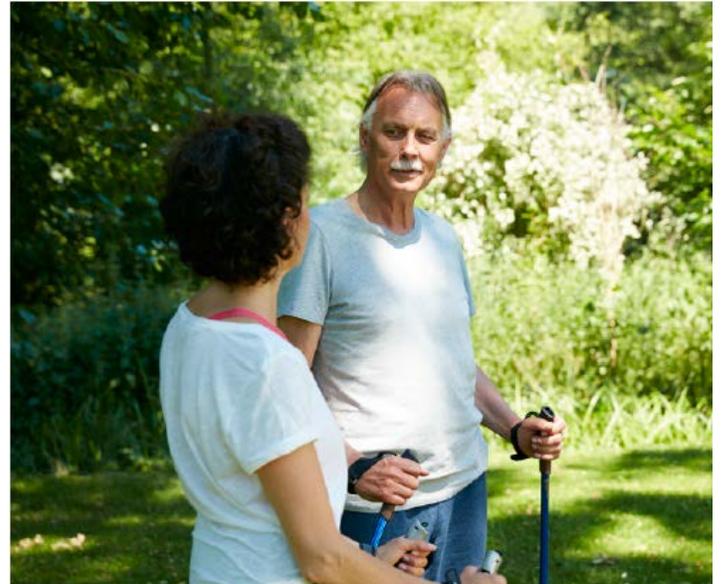
If surgery or dental work is recommended that would require you to stop taking these medications prematurely, you and your doctors should carefully consider the risks and benefits of this additional surgery or dental work versus the possible risks from early discontinuation of these medications.

If you do require premature discontinuation of these medications because of significant bleeding, then your doctor will be carefully monitoring you for possible complications. Once your condition stabilizes, your doctor will probably put you back on these medications.

11. After the Procedure

After the stent is implanted, you will rest in a unit where nurses and doctors can monitor you closely as you begin to recover. You may be asked to stay in bed for several hours. You may have some bruising and soreness at the area where the catheter was inserted, which is normal. If you received a sedative, you may feel sleepy or forgetful. You will gradually begin to feel normal. Pressure may be applied to the area of the incision to promote healing and prevent bleeding. It may be one or more days before you are discharged from the hospital.

12. Activity



- o Follow your doctor's guidelines.
- o Return to normal activities gradually. Pace yourself with resuming activities as you feel better. Ask your doctor about specific exercise or strenuous activities.
- o Let your doctor know about any changes in lifestyle you make during your recovery period.
- o Keep up with all follow-up appointments, including any laboratory blood tests.
- o Carry your Patient Implant Card at all times and show it to any medical professional who treats you, e.g. for dental work, medical care or when reporting to an emergency center.
- o Register the stent and the conditions under which it can be scanned safely with the MedicAlert Foundation (www.medicalert.org) or equivalent organization.

13. Frequently Asked Questions

Can the stent move?

No, the stent cannot move because it is firmly implanted into the artery. Over time, the stent will be covered by the artery lining and becomes embedded in the artery wall so it cannot move.

Can the stent rust?

The stent is made of a rust-resistant material, meaning it will not rust



inside your body.

Can I walk through metal detectors or security with a stent?

Yes, you may walk through metal detectors or security with a stent without any fear of setting them off.

How soon can I go back to work?

Please ask your doctor about when you can return to work. The majority of people return to work within about a week following the procedure.

What if I still have pain?

If you experience pain, immediately inform your doctor or the center where the procedure was performed.

Can I undergo an X-ray, MRI or scanner tests with a stent?

An X-Ray or CT Scan can be performed at any time. For MRI, inform your doctor or MR technician that you have a Orsiro stent prior to undergoing an MRI scan and show your Patient Implant Card for the scanning conditions (MRI safety tests have demonstrated that the Orsiro stent is 'MR conditional').

Can I exercise or play sports?

Your doctor will tell you what types of exercise and sports you can play and when you can start them.

What should I change in my diet?

Your doctor may prescribe a low-fat, low-cholesterol diet to help reduce the levels of fat in your blood to reduce your coronary risk. Ask your doctor if you have questions about your diet.

Does Sirolimus (the drug delivered by the Orsiro stent) have any drug interactions that I should be concerned about?

Sirolimus is delivered to the wall of your coronary artery from the stent placed in your coronary artery. It is estimated that the sirolimus drug will be released into the surrounding arterial tissue following stent implantation. It is expected that the levels of sirolimus in your blood may be measurable for about one week. It is not expected that the drug will have effects anywhere other than in your heart. The dose of sirolimus that you would receive from the Orsiro stent is less than the recommended daily dose of sirolimus that an organ transplant patient would be prescribed. Formal drug interaction studies with sirolimus-based stents have not been conducted. Since some sirolimus could remain on the stent, drug interactions at the location of the stent itself (affecting the performance of the drug) cannot be ruled out. Be sure to discuss with your doctor any drugs you are taking or are planning to take.

What if I have taken sirolimus (the drug delivered by the Orsiro stent) before for cancer treatment and had a reaction to it?

Be sure to let your doctor know if you have had a previous allergic reaction to sirolimus.

Where does the bioabsorbable polymer go once it's absorbed?

The bioabsorbable polymer is eliminated from the body as carbon dioxide and water through natural metabolic processes.

14. More Information

For more information about the Orsiro stent, please visit our website (www.biotronik.com) or call our 24-hour Support at (800) 547-0394.



CAUTION: Federal (U.S.A.) law restricts these products to sale by or on the order of a physician.

Indications, contraindications, warnings and the directions for use can be found in the product's Instructions For Use manual.

Orsiro Sirolimus-eluting Coronary Stent System is a product of BIOTRONIK.

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