Patient Care Brochure

Fistula Dysfunction & the LUTONIX® 035 Drug Coated Balloon PTA Catheter

LUTONIX® 035

Drug Coated Balloon PTA Catheter

BD

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Contents

End-Stage Kidney Disease (ESKD) Background

Your kidneys work hard getting rid of waste and extra water from your body. But if your kidneys can't continue supporting your body's needs, then you may be at risk for Chronic Kidney Disease (CKD).

End-Stage Kidney Disease (ESKD), sometimes called End-Stage Renal Disease (ESRD), is the final stage of chronic kidney disease. The word "renal" means kidney, and renal and kidney can be used interchangeably. When you have ESKD, your kidneys can no longer keep up your body's needs anymore. As a result, your body is in great danger because extra waste and water aren't getting removed. ESKD can occur long after chronic kidney disease begins, sometimes as long as 10-20 years later. ESKD is also commonly known as kidney failure.

Renal Replacement Therapy, Hemodialysis, and Arteriovenous (AV) Fistulae

Once kidney function goes below 10-15% of normal function, dialysis treatments or a kidney transplant are necessary to sustain life. There are two types of dialysis: hemodialysis and peritoneal dialysis. Both dialysis treatments are able to replace the kidneys' function of cleaning the blood of toxins and removing extra fluids for people with kidney failure.

During hemodialysis, your blood is removed from your body and "cleaned" in an external machine before being returned to you.

An "access" to the blood stream is required in order to perform hemodialysis. Most commonly, this is an arteriovenous (AV) fistula. The creation of a fistula allows for high blood flow so that needles can be inserted to remove the blood for dialysis.

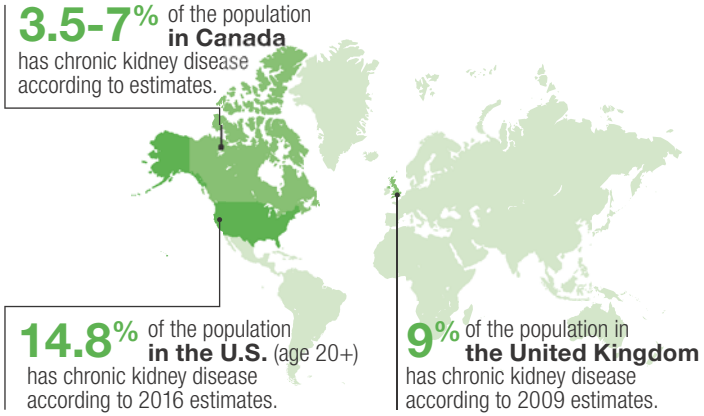
Fistulae are a natural option that offer patients a longer life and fewer complications than other access types. A working fistula is considered the preferred access type.

QUICK FACTS:
CHRONIC KIDNEY DISEASE AND END-STAGE KIDNEY DISEASE

End-Stage Kidney Disease (ESKD) is the final stage of Chronic Kidney Disease (CKD). The word "renal" means kidney, and renal and kidney can be used interchangeably. When you have ESKD, your kidneys can no longer keep up with your body's needs anymore. As a result, your body is in great danger because extra waste and water aren't getting removed.

+33 MILLION

Over **33 million Americans** have chronic kidney disease.



Fistula Dysfunction

Globally, there are more than 2 million patients on hemodialysis with the majority depending on a fistula as their lifeline for renal replacement therapy. Sometimes, even when you are very careful, your fistula may stop working as well as it once did. The most common dialysis access problem is when a narrowed area in your fistula develops, causing the blood flow to slow down and reduce the effectiveness of your dialysis.

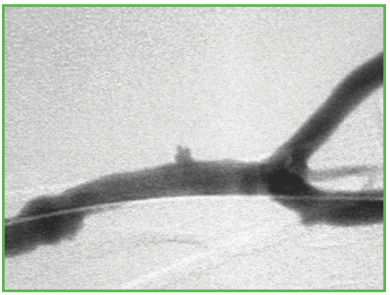
How to Diagnose Fistula Dysfunction Caused by Narrowing

Once your doctor has confirmed fistula dysfunction caused by narrowing, they will determine whether a ***minimally invasive endovascular procedure*** or a surgical procedure is the best treatment to re-establish flow to your fistula.

Physical Exam: Your doctor may use their hands to feel the blood flow in your fistula.

Angiogram/Venogram: Your doctor may perform a contrast angiogram, which is a medical procedure that takes pictures of your blood vessels so the doctor can observe any narrowing or blockage.

1. Angiogram image of a fistula with a narrowing that is causing access dysfunction and reduced blood flow.



2. Angiogram after angioplasty (see page 6) showing the narrowing now open and faster blood flow resumed.

Warning Signs of Fistula Dysfunction Due to Narrowing:

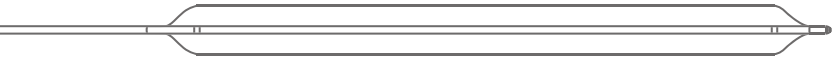
- Absence of the vibration (thrill) or sound (bruit) at your fistula site
- Swelling of your arm
- A decrease in your delivered dose of dialysis (Kt/V or URR)
- Changes in other lab values
- Difficult cannulation
- Increased bleeding after needle removal

How to Treat Fistula Dysfunction Caused by Narrowing

Minimally Invasive Endovascular Procedures

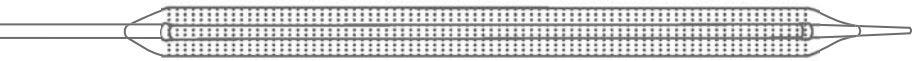
Conventional Balloon Angioplasty

A balloon that is placed in a narrowed fistula and then inflated to open the narrowing; the balloon is then removed.



Drug Coated Balloon Angioplasty

A balloon that is coated with a drug is used to open a narrowed fistula. The balloon delivers a therapeutic dose of drug intended to keep the vessel open longer than conventional angioplasty.



Note: Dots superimposed over balloon are used to indicate paclitaxel formulation

Stent

A stent is a small wire mesh tube that is placed in the fistula and remains in the body after the procedure to help keep the fistula open.

Stent Graft

A stent graft is a small wire mesh tube that is covered with fabric that is placed in the fistula and remains in the body after the procedure to help keep the fistula open.

Surgical Procedure

Surgical Revision

A surgical procedure where your doctor reroutes or bypasses the blood flow above and below the blockage.

LUTONIX® 035 Drug Coated Balloon (DCB)

Indications for Use: The LUTONIX® Catheter is indicated for percutaneous transluminal angioplasty (PTA), after pre-dilatation, for treatment of stenotic lesions of dysfunctional native arteriovenous dialysis fistulae that are 4 mm to 12 mm in diameter and up to 80 mm in length.

What is the LUTONIX® 035 Drug Coated Balloon?

LUTONIX® 035 Drug Coated Balloon (DCB) is a balloon catheter with the drug paclitaxel applied to the balloon. With exception of the drug coating, the LUTONIX® 035 Drug Coated Balloon is similar to other conventional balloon catheters. A clinical study has demonstrated that the LUTONIX® 035 DCB is safe and effective in delaying re-narrowing of the fistula compared to conventional balloon angioplasty for treatment of patients with fistula dysfunction due to narrowing.

What is paclitaxel?

Paclitaxel is the active drug component of the LUTONIX® 035 DCB. Paclitaxel is often known for its use in cancer treatments where it is used systemically (in the blood flow) in much larger doses than the dose on drug coated balloons.

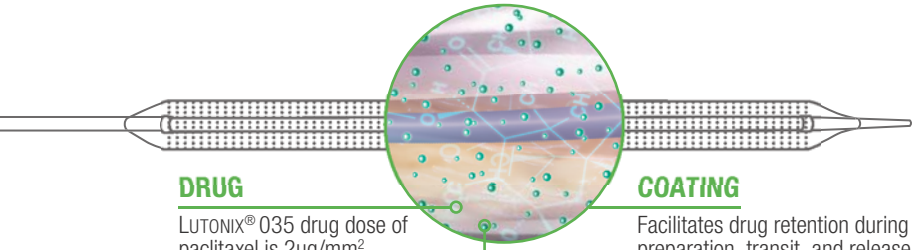
The LUTONIX® 035 DCB uses a very small amount of paclitaxel (around 2% of a single cancer treatment) and the drug is applied directly to the narrowed vessel wall. After the drug is delivered to the area of narrowing, it is processed in the liver and the kidneys and removed from the body within hours.

The safety of the LUTONIX® Drug Coated Balloon use was evaluated in the Lutonix AV Clinical Trial and found to be comparable to using a conventional balloon angioplasty.

LUTONIX® 035 Drug Coated Balloon

Who should not receive a LUTONIX® 035 DCB?

- Women who are breastfeeding, pregnant or are intending to become pregnant or men intending to father children over the next 2 years. It is unknown whether paclitaxel will be excreted in human milk and there is potential for adverse reaction in nursing infants from paclitaxel exposure.
- Patients judged to have a lesion that prevents complete inflation of an angioplasty balloon or proper placement of the delivery system.



DRUG

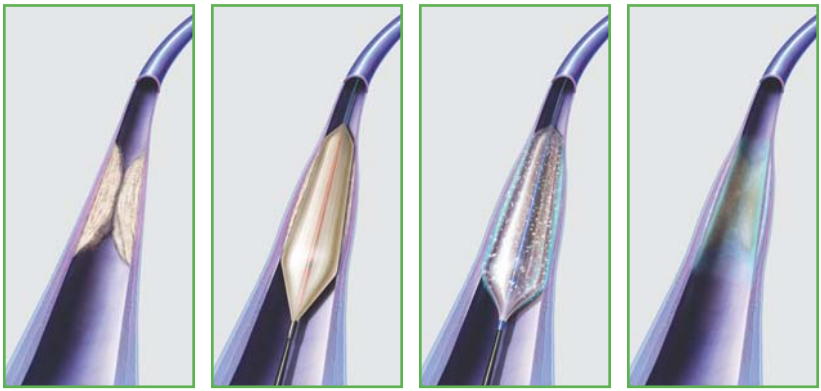
LUTONIX® 035 drug dose of paclitaxel is 2µg/mm^2

CARRIER

Polysorbate and sorbitol

COATING

Facilitates drug retention during preparation, transit, and release of a therapeutic drug dose at the treatment site



Narrowed Vessel | Pre-Dilatation | Drug Coated Balloon | Treated Vessel

Adverse Events

What are the potential adverse events associated with the LUTONIX® 035 DCB?

A study published in December 2018 in the Journal of the American Heart Association reported an increased risk of death starting at 2 years and up to 5 years after treatment with paclitaxel-coated devices in the upper leg compared to treatment with uncoated devices. The U.S. Food and Drug Administration also observed this increased risk of death associated with paclitaxel-coated devices that are approved in the U.S. Additional studies are being conducted to better understand this risk.

This device is a paclitaxel-coated device used in dialysis fistula. The risk for this device is unknown. However, this is important information for you to have when making a decision about treatment options. Your doctor can explain the risks and benefits of paclitaxel-coated devices that are specific to you.

Potential adverse events which may be associated with a PTA balloon dilatation procedure include, but are not limited to, the following:

- Additional intervention
- Allergic reaction to drugs or contrast medium
- Aneurysm or pseudoaneurysm
- Arrhythmias
- Embolization
- Hematoma
- Hemorrhage, including bleeding at the puncture site
- Hypotension/hypertension
- Inflammation
- Loss of permanent access
- Occlusion
- Pain or tenderness
- Sepsis/infection
- Shock
- Steal Syndrome
- Stroke
- Thrombosis
- Vessel dissection, perforation, rupture, or spasm

Adverse Events

Potential adverse events, not described in the above source, which may be unique to the paclitaxel drug coating include, but are not limited to, the following:

- Allergic/immunologic reaction to the drug coating (paclitaxel)
- Alopecia
- Anemia
- Blood product transfusion
- Gastrointestinal symptoms
- Hematologic dyscrasia (including leukopenia, neutropenia, thrombocytopenia)
- Hepatic enzyme changes
- Histologic changes in vessel wall, including inflammation, cellular damage, or necrosis
- Myalgia/Arthralgia
- Myelosuppression
- Peripheral neuropathy

The LUTONIX® 035 Procedure

Background

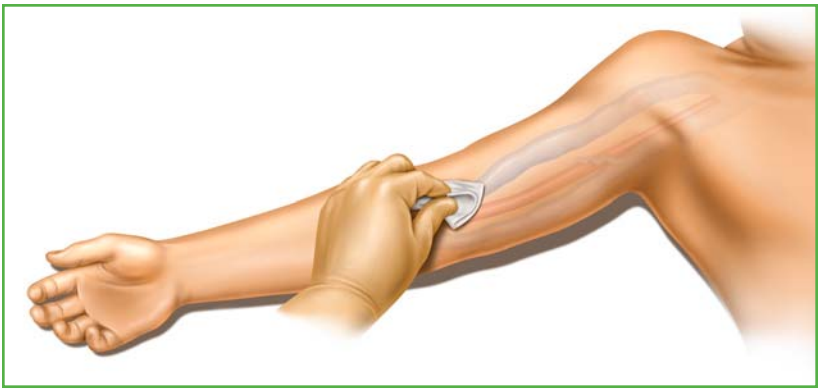
An angiogram is performed when there is dysfunction in the fistula that is interrupting hemodialysis. The procedure is typically performed in a hospital or a free-standing clinic by a physician trained in these procedures. Most commonly it will be an Interventional Nephrologist, Interventional Radiologist, or Vascular Surgeon.

Before the Procedure

You may be asked to avoid eating or drinking anything after midnight the night before the procedure. You may also be asked to take aspirin or other medication for a few days prior to the procedure to thin your blood and prevent clots from forming. Upon arrival to the procedure room, you will lie on an x-ray table and be given medication to help you relax.

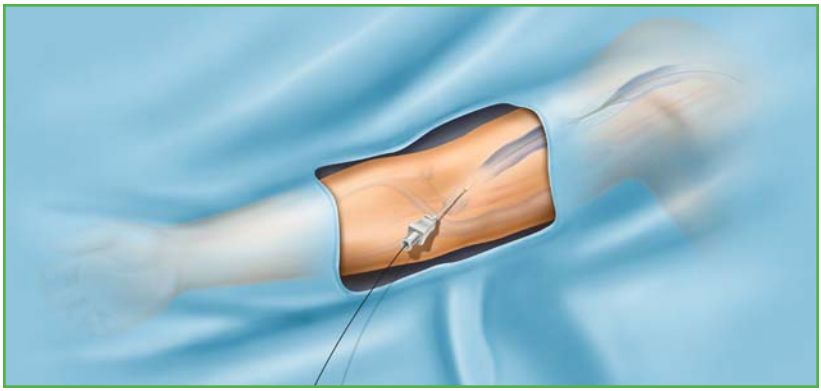
Steps to the Procedure

1. Your doctor will be accessing your fistula through your arm. Your skin will be scrubbed with antiseptic and then you will be injected with lidocaine/ numbing medicine.

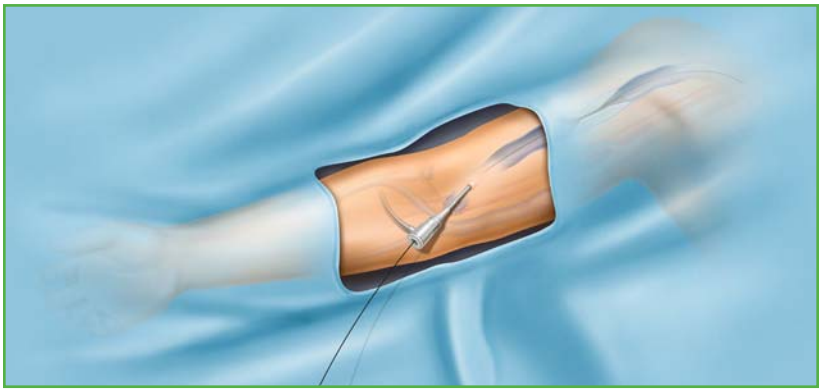


The LUTONIX® 035 Procedure

2. A tapered needle with a hollow middle will be inserted into your fistula. A small wire will be inserted through the needle and travel through your fistula to the location that contains the blockage.



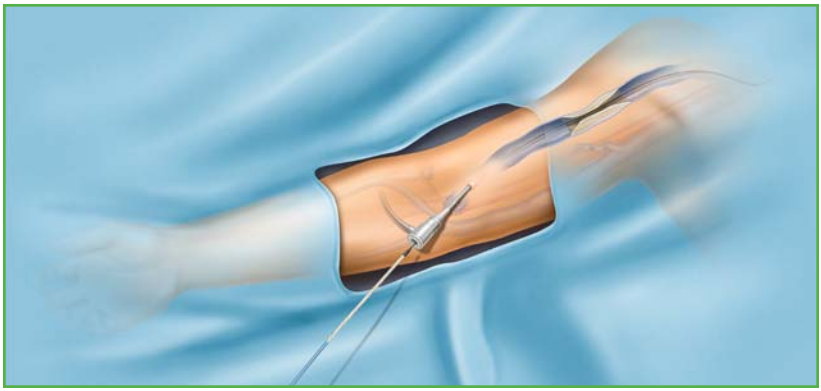
3. The needle will be removed and an introducer sheath will replace it.



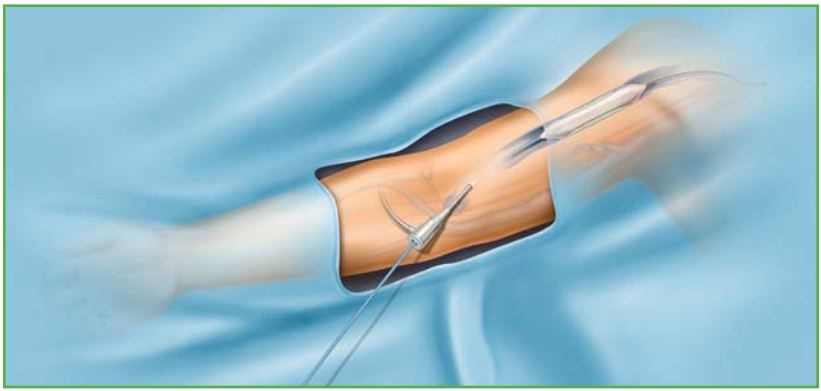
4. A series of x-rays (angiogram) will then be performed for visualization of your fistula to diagnose the area of the blockage.

The LUTONIX® 035 Procedure

5. If it is determined that your fistula dysfunction is caused by narrowing, an angioplasty balloon will be inserted into your fistula over the wire.



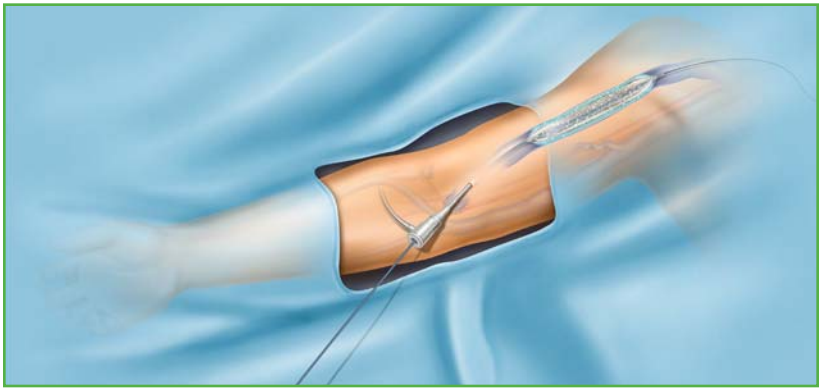
6. The balloon is inflated and deflated at the area of narrowing, and then removed (angioplasty procedure).

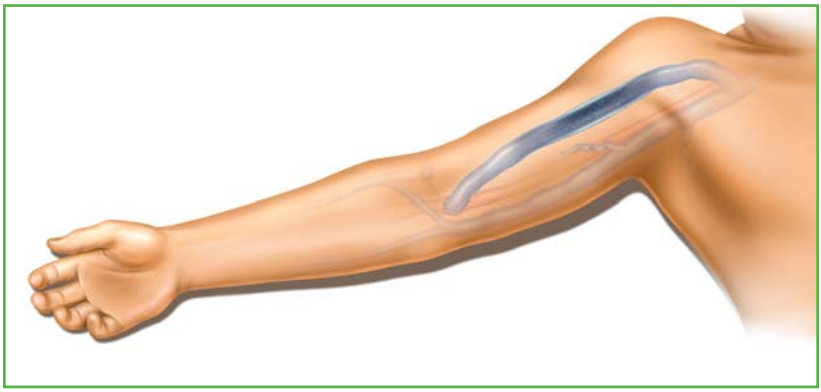


7. An additional angiogram will be performed to help the doctor determine when the narrowing has improved.

The LUTONIX® 035 Procedure

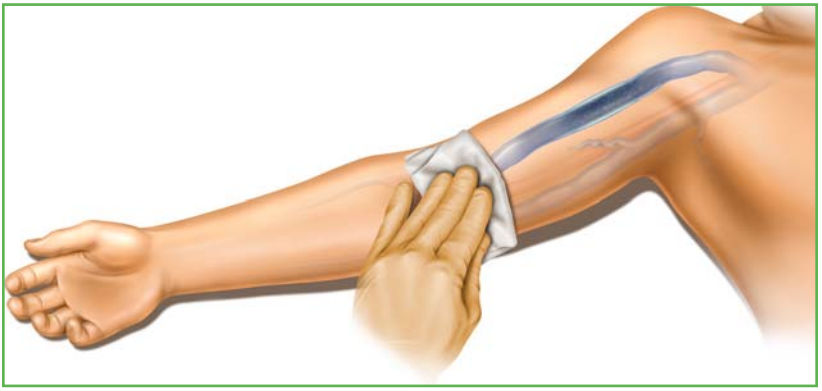
8. The LUTONIX® 035 DCB Catheter will then be advanced over the wire and through the sheath to the same location as the previous balloon. The drug, paclitaxel, is delivered to the target site when the balloon is inflated. The balloon is then deflated and removed with the wire and the sheath. A therapeutic dose of the drug remains on the vessel wall.





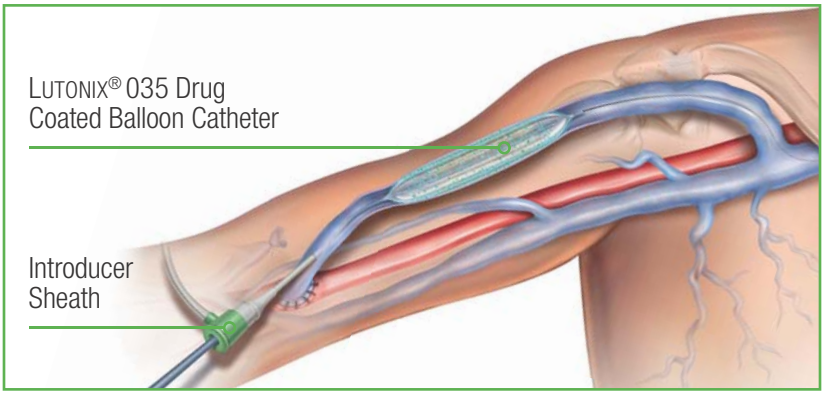
The LUTONIX® 035 Procedure

9. Your doctor or nurse will put light pressure on the small hole where the needle was inserted until bleeding has stopped.



After the Procedure

After your procedure is finished, you will be moved to a recovery area. Your doctor will determine when you are allowed to go home based on your recovery and the standard protocol of the facility where your procedure was performed.



Upper arm fistula with an inflated LUTONIX® 035 Drug Coated Balloon Catheter. After balloon has been inflated for a few minutes and the therapeutic dose of drug is delivered to the vessel wall, it will be deflated and removed from the fistula through the sheath.

Summary of Clinical Information

The LUTONIX® 035 Drug Coated Balloon was evaluated in the LUTONIX® AV Clinical Trial, which enrolled 285 patients. Through 12 months, it was determined that the procedure was successful in most patients and that the LUTONIX® 035 Drug Coated Balloon was successful in delaying re-narrowing of the fistula as compared to conventional balloon catheters. The safety of using a LUTONIX® 035 Drug Coated Balloon was comparable to using a conventional balloon catheter.

The results of this study showed that the LUTONIX® 035 Drug Coated Balloon is safe and effective for treating stenotic lesions in dysfunctional fistulae and may lengthen the time to restenosis compared to standard angioplasty. Your doctor can explain the risks and benefits that are specific to you.

Taking Care of Your Fistula

Keeping your fistula working well will help you get the most from hemodialysis, and help you feel your best. The following are recommended care procedures for fistulae.

- Make sure your dialysis care team checks your access often.
- Do not let anyone measure your blood pressure on your access arm, or take blood from your access arm when you are not getting dialysis. Your other arm should be used to measure blood pressure and do blood tests.
- Do not be afraid to ask your dialysis care team to rotate needle sites.
- Track your important test results, such as your Kt/V and your URR.
- Ask your dialysis care team if you have questions about your access or any other aspects of your hemodialysis care.
- Check the blood flow several times each day by feeling for vibration, also called pulse or thrill, as well as for sound, also called bruit. If either is absent or there is a change, call your doctor or dialysis center.
- Do not wear tight clothes or jewelry on your access arm.
- Do not carry anything heavy or do anything that would put pressure on the access.
- Do not sleep with your head on the arm that has your access.
- Apply only gentle pressure to the access site after the needle is removed. Too much pressure will stop the flow of blood through the access.

Glossary

Access: A method of gaining entry to the bloodstream to allow dialysis. Access methods used for hemodialysis include a catheter, fistula or graft.

Anastomosis: The site(s) of surgical connection between an AV access graft or artery (fistula) and venous structures.

Angiogram: A type of X-ray that allows physicians to visualize the inside of a blood vessel.

Angioplasty: The use of a balloon catheter to stretch/open the narrowing in a blood vessel.

Arteriovenous (AV) Fistula: Surgically-created connections between the artery and vein in an extremity. These direct connections are called arteriovenous fistulae (AVFs).

Arteriovenous (AV) Graft: A natural or synthetic tube structure used for AV access.

Balloon Catheter: See angioplasty.

Bruit: The sound of the blood flow in a fistula or graft.

Cannulation: The method of accessing a fistula or graft for hemodialysis with two dialysis needles so that blood can flow from the body to the dialysis machine to be cleaned and then back into the body again.

Catheter: A flexible plastic tube used to enter the interior of the body. A catheter is one of the access options for patients on hemodialysis. For patients on peritoneal dialysis, a catheter allows dialysis fluid to be put into, and removed, from the peritoneal cavity.

Conventional Balloon Angioplasty: See angioplasty.

DCB: Drug Coated Balloon; see LUTONIX®.

Dysfunctional Fistula: A fistula that is not able to support adequate dialysis function. Common signs of dysfunction include decreased blood flow or dialysis dose, prolonged bleeding, difficult puncture, pulling clots, arm swelling, and elevated venous pressures.

Fistula: An enlarged vein, usually at the wrist or elbow, that gives access to the bloodstream for hemodialysis. The fistula is created by a surgeon in a small operation. It is created by joining a vein to an artery. This increases the flow of blood through the vein and causes it to enlarge, making it suitable for hemodialysis needles.

Introducer Sheath: A hollow tube that is placed in a blood vessel prior to medical devices being inserted.

KT/V: A measure of dialysis adequacy. The calculation is rather complicated, but it measures the amount of dialysis given and corrects for body size.

LUTONIX® 035 Drug Coated Balloon: Balloon catheter with the drug paclitaxel applied to the balloon. With the exception of the drug coating, the LUTONIX® 035 Drug Coated Balloon is similar to other conventional balloon catheters.

PTA: Percutaneous Transluminal Angioplasty. See angioplasty.

Stenosis: Narrowing of the blood vessel. Percent (%) stenosis or residual stenosis is measured in comparison to the reference vessel diameter.

Stent: A small wire mesh tube that is placed into a blood vessel after angioplasty and remains in the body after the procedure to help keep the blood vessel open and helps prevent further narrowing of the vessel.

Stent Graft: A small wire mesh tube that is covered with fabric, placed in a blood vessel after angioplasty and remains in the body after the procedure to help keep the blood vessel open and help prevent further narrowing of the vessel.

Thrill: The vibration or tremble of blood flow in a graft or fistula.

URR (Urea Reduction Ratio): A measure of dialysis adequacy. It is the fall in blood urea levels over a session of hemodialysis, expressed as a percentage.

Notes

For more information on End-Stage Kidney Disease (ESKD) , the following websites are designed for further patient education:

www.CRBard.com/en-US/Patients-Caregivers/End-Stage-Renal-Disease

www.Kidney.org/Patients

www.DPCEDCenter.org

www.NIDDK.NIH.gov/health-information/Kidney-Disease

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Please consult package inserts for more detailed safety information and instructions for use. Rx_{Only}

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