Patient Information for the Medtronic CoreValve® U.S. Pivotal Trial

CAUTION- Investigational device. Limited by United States law to investigational use.

This booklet is provided to help you learn more about the Medtronic CoreValve® U.S. Pivotal Trial.
The purpose of the trial is to assess the safety and performance of a new approach to aortic valve replacement. The valve being studied has been developed for patients with severe aortic stenosis (AS). Please note as you read the different treatments for severe AS, that if you are interested in being part of the CoreValve trial, you are not guaranteed to receive the valve being studied. Discuss any questions you may have with your heart doctor. Only a doctor can decide if you are a good candidate for participation in this clinical trial.

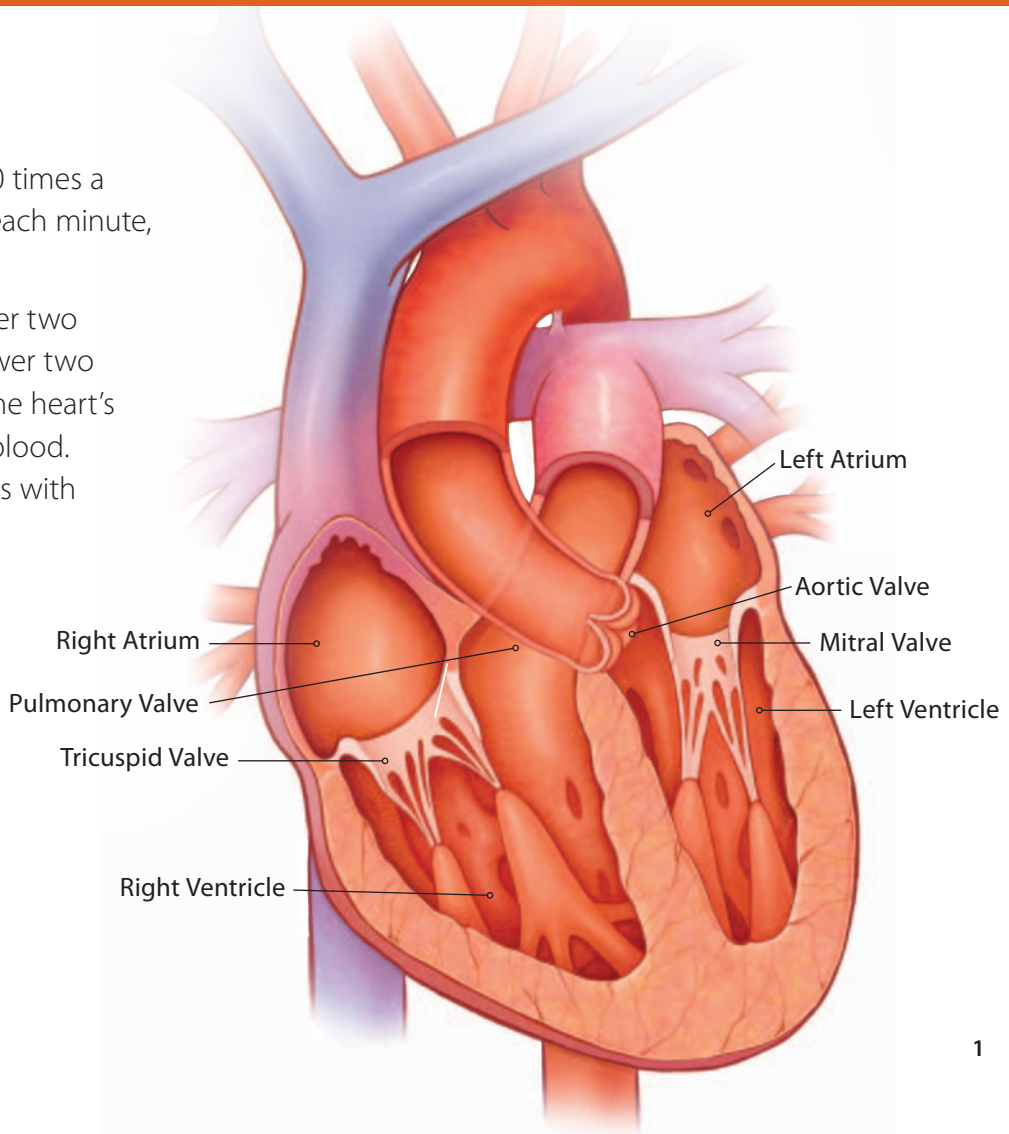
Table of Contents

About The Heart

How The Heart Works

A healthy heart beats approximately 100,000 times a day and pumps about five quarts of blood each minute, or 75 gallons (284 liters) every hour.

A normal heart has four chambers. The upper two chambers are the right and left atria. The lower two chambers are the right and left ventricles. The heart's job is to supply the body with oxygen-rich blood. Blood is pumped through the four chambers with the help of four heart valves—the tricuspid, pulmonary, mitral and aortic valves.

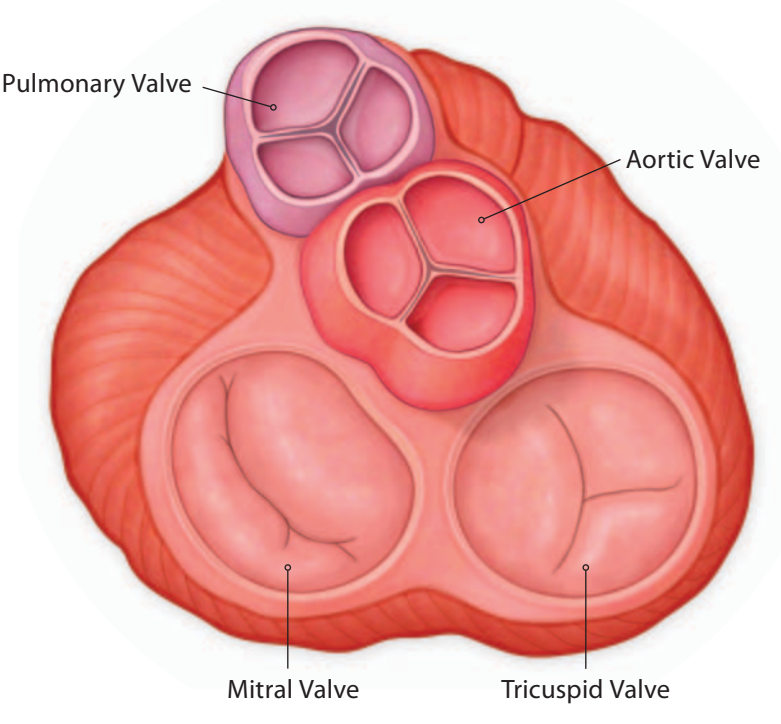


About The Heart *(continued)*

What Heart Valves Do

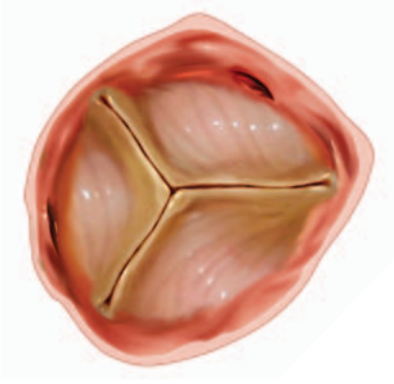
Heart valves open when the heart pumps to allow blood to flow forward, and close quickly between heartbeats to make sure blood does not flow backward. Any disruption in this normal flow will make it difficult for the heart to effectively pump the blood where it needs to go.

- The **tricuspid valve** sits between the right atrium (upper chamber) and right ventricle (lower chamber). The tricuspid valve directs blood flow from the right atrium to the right ventricle.
- The **pulmonary valve** directs blood flow from the right ventricle into the pulmonary artery, which splits into two arteries so that the blood from the body can get to both lungs.
- The **mitral valve** sits between the left atrium (upper chamber) and left ventricle (lower pumping chamber). The mitral valve directs blood flow from the left atrium into the left ventricle.
- The **aortic valve** directs blood from the left ventricle into the aorta. The aorta is the major blood vessel that leads from the left ventricle out to the rest of the body.

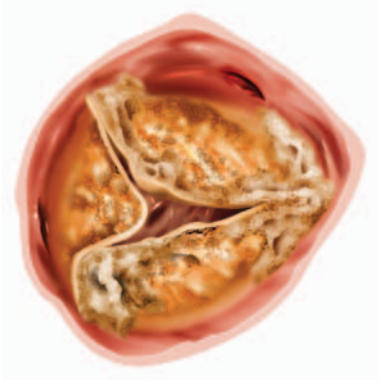


Severe Aortic Stenosis

Severe AS occurs when the aortic valve doesn't open properly. This forces your heart to work harder to pump blood throughout your body. Over time, the heart muscle weakens. This affects your overall health and keeps you from participating in normal daily activities. Left untreated, severe AS is a very serious, life-threatening condition, leading to heart failure and increased risk for sudden cardiac death.



Normal Valve



Stenotic Valve

Causes

Severe AS is often not preventable and may be related to age; buildup of calcium deposits on the aortic valve (stenosis), which causes narrowing; radiation therapy; medications; a history of rheumatic fever or high cholesterol.

Symptoms of Severe AS

Signs and symptoms of severe AS can include:

- Chest pain or tightness
- Feeling faint or fainting with activity
- Dizziness
- Fatigue
- Shortness of breath
- Heart palpitations
- Heart murmur

CoreValve® U.S. Pivotal Trial Overview

CoreValve® Trial Overview

CoreValve is considered an investigational device, which means that clinical studies are required to determine if it is safe and effective in Transcatheter Aortic Valve Implantation (TAVI), a minimally invasive treatment option for people with severe AS.

The CoreValve clinical study involves over 1,300 patients at up to 40 hospitals in the United States. Prior to participation in the CoreValve clinical study, you will need to sign a consent form.

Depending on your condition, you may be put in a treatment group that will be randomized. The two treatment options in this study are open-heart surgical aortic valve replacement and CoreValve TAVI.

Current Treatments for Severe AS

Medical Management

Medicines for severe AS focus on treating problems that can occur as a result of your diseased aortic heart valve. For example, patients with severe AS may take medicines that help control irregular heartbeats or prevent blood clots. These medicines may help control your symptoms for a period of time; however, without aortic valve replacement, severe AS could worsen to a more serious condition.

In addition to medications and if your physician determines appropriate, a procedure called Balloon Valvuloplasty can be performed to relieve symptoms. It is a non-surgical procedure that is performed by placing a balloon into the aortic valve and inflating the balloon. A thin flexible tube (catheter) is first inserted through an artery in the groin or arm and threaded into the heart. Once the tube reaches the narrowed aortic valve, a balloon located on the tip of the catheter is quickly inflated. The balloon presses against the narrowed valve leaflets, which separates and stretches the valve opening and allows more blood to flow through the heart. This procedure does not require open-heart surgery.

Risks

Because risks will vary depending on your medical management, talk about adverse risk events with your doctor.

Current Treatments for Severe AS

Open-Heart, Surgical Aortic Valve Replacement

Aortic valve replacement surgery is an effective, life-saving treatment option for people with severe AS. Depending on your risk factors, such as health, diagnosis, and age, your health care providers will be able to recommend the appropriate valve replacement for you.

A traditional aortic valve replacement surgery often requires a median sternotomy, where the sternum is split down the middle (some are performed without splitting the sternum). The chest is then opened with special retractors. This provides the surgeon with necessary access to the heart and chest cavity, in order to replace your aortic valve.

Because each patient has his or her unique medical history, this information cannot replace discussions with your doctor.

During the Procedure

The operation varies from patient to patient, lasting a minimum of two hours and often longer. During this time, you are asleep under general anesthesia. During the operation, the surgeon will remove any tissue and calcium deposits that are interfering with the normal function of the valve. Your damaged valve may be completely removed. Then, the new valve will be sewn into the space where your own valve used to be. After the surgeon makes sure your valve is working properly, blood flow will be restored to your heart and the incisions will be closed.

Your surgery is performed while the function of your heart is taken over by a heart-lung machine (called CPB, for cardiopulmonary bypass).

After the Surgery

Immediately after the operation, you'll probably be drowsy. You will spend the next few hours, or possibly the night, in the intensive care unit. When intensive care monitoring is no longer needed, you will be moved to a step-down unit and eventually to a routine-care hospital floor. A typical hospital stay is 5-10 days. After you're released from the hospital, you will need to see your doctor periodically for follow-up visits.

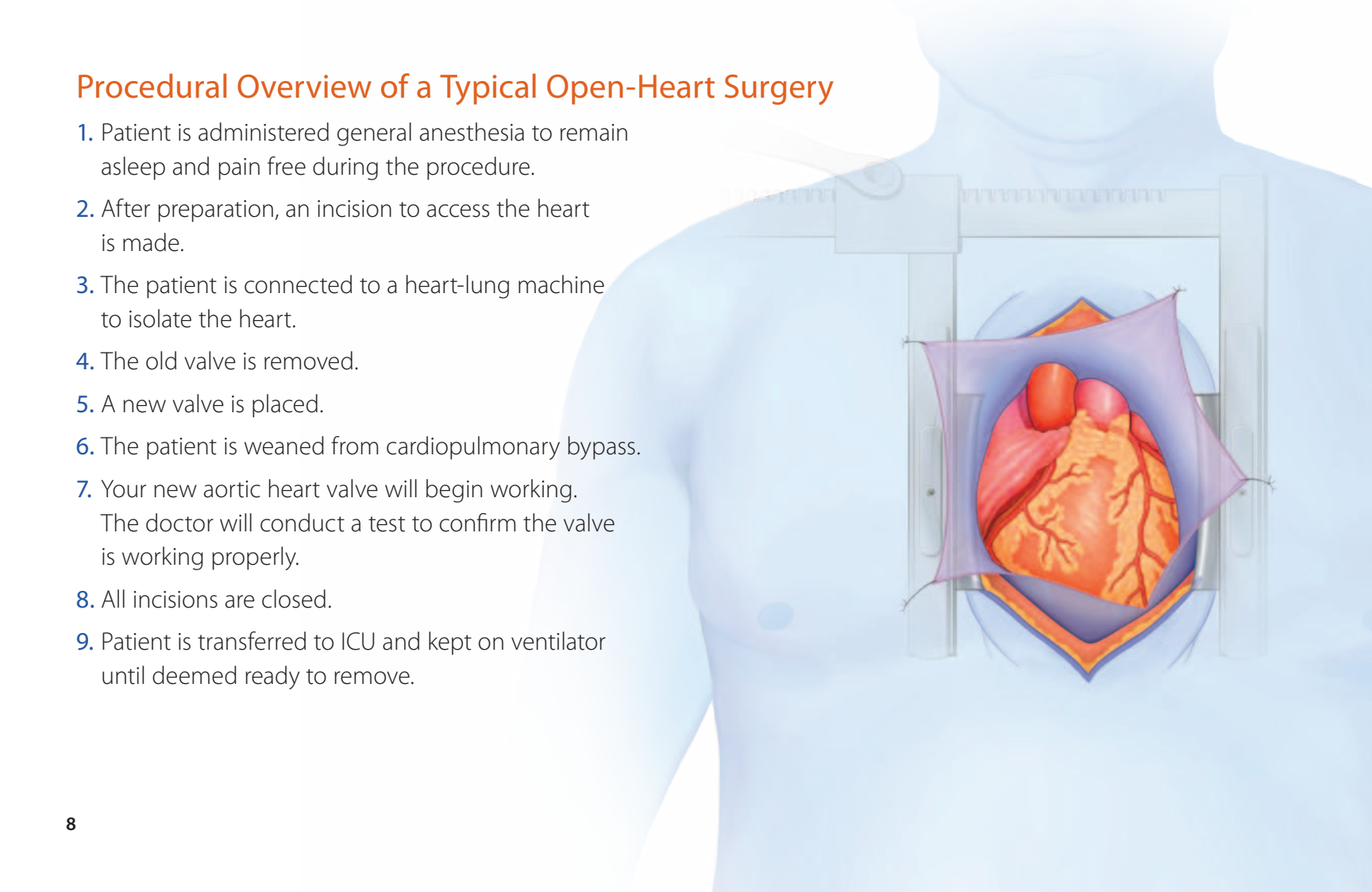
Summary of Open-Heart Surgical Aortic Valve Replacement

- General anesthesia
- Patient on heart-lung bypass machine
- Chest open, 7-inch incision (often, but alternatives exist)
- Valve replaced during 2-4 hour procedure (typical)
- 5-10 day hospital stay (typical)
- Approximately 6-8 week recovery period

Current Treatments for Severe AS

Procedural Overview of a Typical Open-Heart Surgery

1. Patient is administered general anesthesia to remain asleep and pain free during the procedure.
2. After preparation, an incision to access the heart is made.
3. The patient is connected to a heart-lung machine to isolate the heart.
4. The old valve is removed.
5. A new valve is placed.
6. The patient is weaned from cardiopulmonary bypass.
7. Your new aortic heart valve will begin working. The doctor will conduct a test to confirm the valve is working properly.
8. All incisions are closed.
9. Patient is transferred to ICU and kept on ventilator until deemed ready to remove.



Potential Risks for Surgical Aortic Valve Replacement

Valve replacement can include the following risks:

- Death.
- Blood clots that develop in the heart or on the replacement valve. These clots may break loose and travel through the bloodstream (thromboembolism). This problem may cause a stroke or heart attack.
- Obstruction of blood circulation to the heart resulting in damage to the heart tissue (myocardial infarction).
- Angina.
- Abnormal heart beat (cardiac arrhythmia and dysrhythmia).
- Heart failure.
- Damage to red blood cells (hemolysis) that can result in anemia.
- Blood leaking around the outside of the prosthetic valve (paravalvular leak) or any problem with the valve that causes leaking of blood after the valve has closed (transvalvular leak).
- Any problem with the prosthetic valve that causes narrowing of the valve opening (stenosis).
- Failure of the valve to open and close properly.
- Inflammation of the lining of the heart (endocarditis).

The potential risks are shown in the order of severity, from most severe to least severe. This list is not inclusive of all risks. Talk to your physician regarding more information about aortic valve replacement surgery.

Investigational Treatment for Severe AS

CoreValve® Transcatheter Aortic Valve Implantation (TAVI)

CoreValve is an investigational device only available through the clinical trial. The CoreValve aortic heart valve is made of natural tissue obtained from the heart of a pig. The leaflets that control the flow of blood in the CoreValve heart valve are secured to a flexible, self-expanding frame for support.

With CoreValve TAVI, an incision is made and a new aortic valve is delivered via a catheter. It is a less invasive treatment option than open-heart valve surgery.

During the Procedure

Patients may be sedated during the 1-3 hour procedure. You may first have a test that uses sound waves to take a closer look at the inside structures of the heart. With CoreValve TAVI, a catheter (thin, hollow tube) holding a specially designed heart valve is guided to the heart. Special imaging equipment is used to guide position and placement of the CoreValve aortic heart valve.

After the Procedure

Following CoreValve TAVI, you will be moved to an intensive care unit or cardiac care unit. Patients typically are able to be up and walking within 24-48 hours after their procedure. Your doctor will determine when you are ready to move to a standard hospital room. The typical hospital stay for CoreValve TAVI is 3-5 days.

Summary of CoreValve TAVI

- Local or general anesthesia
- Heart pumps normally
- Catheter delivers valve to heart
- Valve replaced during 1-3 hour procedure (typical)
- 3-5 day hospital stay (typical)
- Approximately 1-week recovery period

Investigational Treatment for Severe AS

Procedural Overview of a Typical CoreValve® Transcatheter Procedure

1. Patients are normally sedated during the approximately 1-3 hour procedure. Because each patient is different, your doctor may determine whether or not you should be fully asleep for the procedure.
2. The interventional cardiologist or cardiac surgeon will make an incision and guide a sheath (long, hollow tube) into your heart.
3. Using special imaging equipment to look at your arteries, a catheter with a balloon on the tip is threaded through the sheath and into your heart. If you're not fully sedated, you may have a "fluttering" feeling in your chest. This is caused by extra heartbeats occurring once the catheter is in your heart.
4. When the end of the balloon is in your aortic valve, the balloon will be inflated and will force your narrowed aortic valve open to prepare it for your CoreValve aortic heart valve.
5. Again, using the special imaging equipment, your doctor will place the CoreValve aortic heart valve in position over your own diseased aortic valve.
6. Your new aortic heart valve will begin working. The doctor will conduct a test to confirm the valve is working properly.
7. The catheter will be removed, the incision will be closed, and the procedure will be complete.

Potential Risks for CoreValve® Implantation

Implantation of the CoreValve Transcatheter Valve may include, but are not limited to, the following:

- Death
- Acute myocardial infarction—heart attack; decrease blood flow to the heart causing death of an area of the heart muscle
- Stroke—decreased blood flow to the brain causing death of the brain cells
- Urgent need for surgery:
  - Coronary artery bypass—surgery where the chest is opened to place new vessels around the existing blocked vessels of the heart to improve blood supply to the heart
  - Heart valve replacement—replacing the existing heart valve with a new heart valve
  - Valve explant—the removal of the existing valve
- Urgent need for balloon valvuloplasty (balloon valvuloplasty during the TAVI procedure is expected)—a procedure through the vessels inside the body and heart in which a narrowed heart valve is stretched open
- Urgent need for Percutaneous Coronary Intervention (PCI)—a procedure through the vessels inside the body and heart used to treat or open narrowed vessels of the heart
- Cardiogenic shock—failure of the heart to pump enough blood to the body organs
- Perforation of the myocardium or vessel—a hole in the heart muscle or a blood vessel
- Cardiac Tamponade—the constriction or inability of the heart to pump due to build up of blood or fluid around the lining of the heart
- Ascending aorta trauma—injury to the large blood vessel leading blood away from the heart
- Myocardial ischemia—reduced blood supply to the heart
- Acute coronary artery occlusion—blockage or closure of an artery that supplies the heart with blood

The potential risks are shown in the order of severity from most severe to least severe. This list is not inclusive of all risks. For a complete listing of possible risks and discomforts, see your informed consent information form, or talk with your doctor.

(continued on next page)

Potential Risks for CoreValve® Implantation *(continued)*

- Disturbances in the electrical system of the heart that may result in the permanent placement of a device (pacemaker) that delivers electrical impulses to the heart to help your heart beat normally.
  - Atrio-ventricular node block—a block in the electrical path from the top part of the heart (atria) to the bottom part of the heart (ventricle)
  - Bundle branch block—a delay or block in the electrical path in the bottom part of the heart (ventricle)
  - Asystole—when the heart stops beating
- Ventricular arrhythmias—abnormal fast or slow heart beats in the lower part of the heart (ventricles)
- Valve or Distal Embolism—an abnormal particle (air, blood clots) floating in the blood stream or attached to an object, including in the valve
- Thrombosis (including valve thrombosis)—blood clot, including a blood clot on the valve
- Hemorrhage requiring transfusion—bleeding requiring blood to be put back into the body
- Arteriovenous fistula—abnormal connection between an artery vessel that takes blood away from the heart and a vein vessel that takes blood to the heart
- Vessel dissection or spasm—the separation of the walls of a vessel or a sudden narrowing of the vessel
- Valve migration—upward or downward movement of the device from where it was originally placed
- Valve dysfunctions of the CoreValve including but not limited to:
  - Fracture (break) in the valve frame
  - Bending (out-of-round configuration) of the valve frame
  - The valve frame does not open (expand) all the way
  - Calcification (build up of calcium on the valve)
  - Pannus—the formation of scar tissue that may cover or block the valve from functioning normally
  - Wear, tear or movement forward (prolapse) or backward (retraction) from the normal position of the valve leaflets
  - The valve leaflets do not close together
  - A break in the stitches (sutures) of the valve frame or leaflets
  - Leakage through or around the valve or valve frame

- Incorrect size of the valve implanted
- Incorrect position or placement of the valve, either too high or too low
- Regurgitation—backward flow of blood through the valve
- Stenosis—narrowing of the opening of the valve

- Mitral valve regurgitation—a leaking valve between the left upper (left atrium) and left lower (left ventricle) parts of the heart where blood flows backward through the valve
- Hypotension or hypertension—low or high blood pressure
- Acute renal injury—failure of the kidneys to work correctly
- Allergic reaction (unfavorable reaction by the body) to:
  - antiplatelet agents—drugs that keep blood clots from forming
  - contrast medium—a substance used to increase the visualization of body structures such as x-ray dye
- Infection, including infection of the heart or heart valves (endocarditis),—an abnormal growth of germs in the body or body part
- Bowel ischemia—decrease blood supply to the intestines
- Complications at the area where the doctor opened the skin or relating to opening the skin, including but not limited to:
  - pain
  - bleeding
  - hematoma—blood collecting under the skin
  - pseudoaneurysm—blood collecting on the outside of a vessel wall causing a balloon-like widening
  - irreversible nerve damage—permanent damage to nerves
  - compartment syndrome—squeezing of nerves and muscles in a closed space that could cause muscle or nerve damage
  - stenosis—narrowing of a vessel (artery)

The potential risks are shown in the order of severity from most severe to least severe. This list is not inclusive of all risks. For a complete listing of possible risks and discomforts, see your informed consent information form, or talk with your doctor.

Clinical Trial Follow-up / Online Resources

Follow-up Care

As part of this clinical trial, you will be expected to participate in follow-up evaluations. Follow-up visits are at 30 days, 6 months, and annually for 5 years. These visits are needed to check your heart valve function and will take place at your doctor's office. Ask your heart doctor or nurse about your follow-up appointment schedule or any other questions you have.

As a precaution, you'll want to inform your dentist and other doctors about your heart valve before any dental or medical procedure.

If you require a magnetic resonance imaging (MRI) scan, tell the doctor or MRI technician that you have had a heart valve procedure.

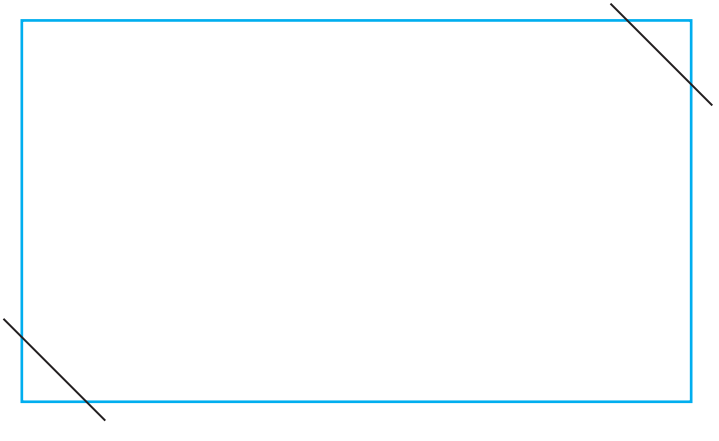
Online Resources

For more information on aortic stenosis, visit the following web sites:

- American Heart Association, **www.americanheart.org**
- Mayo Clinic, **www.mayoclinic.com**
- WebMD, **www.webmd.com**
- Clinical Trials, **www.clinicaltrials.gov**
- Aortic Stenosis Trial, **www.AorticStenosisTrial.com**

CAUTION- Investigational device.
Limited by United States law to investigational use.

CoreValve is a registered trademark of Medtronic CV Luxembourg S.a.r.l.



www.medtronic.com

World Headquarters
Medtronic, Inc.
710 Medtronic Parkway
Minneapolis, MN 55432-5604
USA
Tel: (763) 514-4000
Fax: (763) 514-4879

Medtronic USA, Inc.
Toll-free: 1 (800) 328-2518
(24-hour technical support for
physicians and medical professionals)

LifeLine
CardioVascular Technical Support
Tel: (877) 526-7890
Tel: (763) 526-7890
Fax: (763) 526-7888
E-mail: rs.cstechsupport@medtronic.com

UC201005966 EN