



# Edwards SAPIEN Transcatheter Heart Valve with the RetroFlex 3 Delivery System

## Instructions for Use

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

### Transfemoral Retrograde Approach

Implantation of the transcatheter heart valve should be performed only by physicians who have received Edwards Lifesciences training. The implanting physician should be experienced in balloon aortic valvuloplasty.

Please verify that you have the latest version of the instructions for use prior to using the device by visiting <http://THVIFU.edwards.com> or by calling 1.800.822.9837. In order to access the instructions for use, an IFU Code will be required.

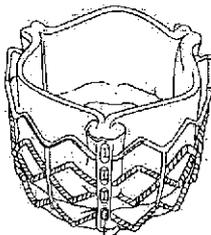
**STERILE:** The bioprosthesis is supplied sterilized with glutaraldehyde solution. The delivery system is supplied sterilized with ethylene oxide gas.

### 1.0 Device Description

- Edwards SAPIEN Transcatheter Heart Valve – Model 900TFX (Figure 1)

The Edwards SAPIEN transcatheter heart valve (bioprosthesis) is comprised of a balloon-expandable, radiopaque, stainless steel (316 L) frame, three bovine pericardial tissue leaflets, and a polyethylene terephthalate (PET) fabric. The bioprosthesis is treated according to the Carpentier-Edwards ThermaFix process, packaged, and terminally sterilized in glutaraldehyde.

Figure 1. Edwards SAPIEN Transcatheter Heart Valve



Bioprosthesis Diameter	Frame Height (Profile)
23 mm	14.3 mm
26 mm	16.1 mm.

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The following table identifies the bioprosthesis size that should be used based on native valve annulus size, as measured by transesophageal echocardiography (TEE).

Native Valve Annulus Size (Tissue Annulus Diameter)	Bioprosthesis Diameter
18-22 mm	23 mm
21-25 mm	26 mm

- RetroFlex 3 Delivery System – Model 9120FS23 for 23 mm valve procedure and 9120FS26 for 26 mm valve procedure (Figure 2)

The RetroFlex 3 delivery system includes a rotating wheel within the handle for articulation of flex catheter, a tapered tip at the distal end of the delivery system to facilitate crossing the native valve, a balloon for deployment of the bioprosthesis, and radiopaque marker as indicated in Figure 2.

Figure 2. RetroFlex 3 Delivery System



Black dots indicate position of radiopaque markers.

Nominal Balloon Diameter	RBP
23 mm	7 ATM (709 kPa)
26 mm	7 ATM (709 kPa)

The following table identifies the access vessel diameters that should be used for delivery system access.

Ilio-Femoral Vessel Diameter	Delivery System
≥ 7 mm	23 mm
≥ 8 mm	26 mm

## 2.0 Indications

The Edwards SAPIEN Transcatheter Heart Valve, model 9000TFX, sizes 23 mm and 26 mm, is indicated for transfemoral delivery in patients with severe symptomatic native aortic valve stenosis who have been determined by a cardiac surgeon to be inoperable for open aortic valve replacement and in whom existing co-morbidities would not preclude the expected benefit from correction of the aortic stenosis.

The RetroFlex 3 Delivery System is indicated for the transfemoral delivery of the Edwards SAPIEN Transcatheter Heart Valve.

## 3.0 Contraindications

The bioprosthesis and delivery system are contraindicated in patients who cannot tolerate an anticoagulation/antiplatelet regimen or who have active bacterial endocarditis or other active infections.

## 4.0 Warnings

- Observation of the pacing lead throughout the procedure is essential to avoid the potential risk of pacing lead perforation. There is an increased risk of stroke in transcatheter aortic valve replacement procedures, as compared to balloon aortic valvuloplasty or other standard treatments.
- The devices are designed, intended, and distributed for single use only. **Do not re-sterilize or reuse the devices.** There are no data to support the sterility, non-pyrogenicity, and functionality of the devices after reprocessing.
- Incorrect sizing of the bioprosthesis may lead to paravalvular leak, migration, embolization and/or annular rupture.
- Accelerated deterioration of the bioprosthesis may occur in patients with an altered calcium metabolism. Bioprosthesis must remain hydrated at all times and cannot be exposed to solutions other than its shipping storage solution and sterile physiologic rinsing solution. Bioprosthesis leaflets mishandled or damaged during any part of the procedure will require replacement of the bioprosthesis.
- Caution should be exercised in implanting a bioprosthesis in patients with clinically significant coronary artery disease.
- Patients with pre-existing mitral valve devices should be carefully assessed prior to implantation of the bioprosthesis to ensure proper bioprosthesis positioning and deployment.
- Patients presenting with combination AV low flow, low gradient should undergo additional evaluation to establish the degree of aortic stenosis.
- Do not use the bioprosthesis if the tamper evident seal is broken, the storage solution does not

completely cover the bioprosthesis, the temperature indicator has been activated, the bioprosthesis is damaged, or the expiration date has elapsed.

- Do not mishandle the RetroFlex 3 delivery system or use it if the packaging or any components are not sterile, have been opened or are damaged (e.g. kinked or stretched), or the expiration date has elapsed.
- Use of excessive contrast media may lead to renal failure. Measure the patient's creatinine level prior to the procedure. Contrast media usage should be monitored.
- Patient injury could occur if the delivery system is not un-flexed prior to removal.

## 5.0 Precautions

- Long-term durability has not been established for the bioprosthesis. Regular medical follow-up is advised to evaluate bioprosthesis performance.
- Glutaraldehyde may cause irritation of the skin, eyes, nose and throat. Avoid prolonged or repeated exposure to, or breathing of, the solution. Use only with adequate ventilation. If skin contact occurs, immediately flush the affected area with water; in the event of contact with eyes, seek immediate medical attention. For more information about glutaraldehyde exposure, refer to Material Safety Data Sheet available from Edwards Lifesciences.
- To maintain proper valve leaflet coaptation, do not overinflate the deployment balloon.
- Appropriate antibiotic prophylaxis is recommended post-procedure in patients at risk for prosthetic valve infection and endocarditis.
- Bioprosthetic valve recipients should be maintained on anticoagulant and antiplatelet therapy (e.g. clopidogrel or ticlopidine [75 mg/day]) for 6 months post procedure and aspirin (75-100 mg/day) for life, except when contraindicated, as determined by their physician.
- The safety of the bioprosthesis implantation has not been established in patients who have:
  - Pre-existing prosthetic heart valve in the aortic position
  - Severe ventricular dysfunction with ejection fraction <20%
  - Hypertrophic cardiomyopathy with or without obstruction (HOCM)
- Safety and effectiveness have not been established for patients who are candidates for surgical aortic valve replacement.
- Safety, effectiveness, and durability have not been established for valve-in-valve procedures.
- Safety and effectiveness have not been established for patients with the following

characteristics/comorbidities:

- Non-calcified aortic annulus
  - Congenital unicuspid or congenital bicuspid aortic valve
  - Mixed aortic valve disease (aortic stenosis and aortic regurgitation with predominant aortic regurgitation >3+)
  - Pre-existing prosthetic heart valve or prosthetic ring in any position
  - Severe mitral annular calcification (MAC), severe (>3+) mitral insufficiency, or Gorelin syndrome
  - Blood dyscrasias defined as: leukopenia (WBC <3000/mm<sup>3</sup>), acute anemia (Hb <9 mg%), thrombocytopenia (platelet count <50,000 cells/mm<sup>3</sup>), or history of bleeding diathesis or coagulopathy
  - Hypertrophic cardiomyopathy with or without obstruction (HOCM)
  - Echocardiographic evidence of intracardiac mass, thrombus, or vegetation
  - A known hypersensitivity or contraindication to aspirin, heparin, ticlopidine (Ticlid), or clopidogrel (Plavix), or sensitivity to contrast media, which cannot be adequately premedicated
  - Native aortic annulus size <18mm or >25mm as measured by echocardiogram
  - Patient has been offered surgery but has refused surgery
  - Significant aortic disease, including abdominal aortic or thoracic aneurysm defined as maximal luminal diameter 5 cm or greater; marked tortuosity (hyperacute bend), aortic arch atheroma (especially if thick [> 5 mm]; protruding, or ulcerated) or narrowing (especially with calcification and surface irregularities) of the abdominal or thoracic aorta, severe "unfolding" and tortuosity of the thoracic aorta
  - Iliofemoral vessel characteristics that would preclude safe placement of 22F or 24F introducer sheath such as severe obstructive calcification, severe tortuosity or vessels size less than 7 mm in diameter
- Bulky calcified aortic valve leaflets in close proximity to coronary ostia

## 6.0 Potential Adverse Events

- Potential risks associated with the overall procedure including potential access complications associated with standard cardiac catheterization for the transfemoral access procedure, balloon valvuloplasty, and the potential risks of local and/or general anesthesia:

- Death

- Stroke/transient ischemic attack clusters or neurological deficit
- Paralysis
- Permanent disability
- Respiratory insufficiency or respiratory failure
- Hemorrhage requiring transfusion or intervention
- Cardiovascular injury including perforation or dissection of vessels, ventricle, myocardium or valvular structures that may require intervention
- Pericardial effusion or cardiac tamponade
- Embolization including air, calcific valve material or thrombus
- Infection including septicemia and endocarditis
- Heart failure
- Myocardial infarction
- Renal insufficiency or renal failure
- Conduction system injury (defect) which may require a permanent pacemaker
- Arrhythmia
- Retroperitoneal bleed
- Femoral AV fistula or pseudoaneurysm
- Reoperation
- Peripheral ischemia or nerve injury
- Restenosis
- Pulmonary edema
- Pleural effusion
- Bleeding
- Anemia
- Abnormal lab values (including electrolyte imbalance)
- Hypertension or hypotension;
- Allergic reaction to anesthesia or to contrast media
- Hematoma
- Syncope
- Pain or changes at the access site
- Exercise intolerance or weakness
- Inflammation
- Angina
- Heart murmur
- Fever
- Additional potential risks specifically associated with the use of the bioprosthesis include, but may not be limited to the following:
- Cardiac arrest
- Cardiogenic shock
- Emergency cardiac surgery
- Cardiac failure or low cardiac output

- Coronary flow obstruction/transvalvular flow disturbance
- Device thrombosis requiring intervention
- Valve thrombosis
- Device embolization
- Device migration or malposition requiring intervention
- Valve deployment in unintended location
- Valve stenosis
- Structural valve deterioration (wear, fracture, calcification, leaflet tear/tearing from the stent posts, leaflets retraction, stent creep, suture line disruption of components of a prosthetic valve, thickening, stenosis)
- Device degeneration
- Paravalvular or transvalvular leak
- Valve regurgitation
- Hemolysis
- Device explants
- Nonstructural dysfunction
- Non-emergent reoperation

All listed risks may include symptoms associated with the above mentioned medical conditions.

## 7.0 Directions for Use

### 7.1 Required Equipment

- Standard cardiac catheterization lab equipment
- Fluoroscopy (fixed, mobile or semi-mobile fluoroscopy systems appropriate for use in percutaneous coronary interventions)
- Transesophageal or transthoracic echocardiography capabilities
- Exchange length 0.035 inch (0.89 mm) extra-stiff guidewire
- Temporary pacemaker (PM) and pacing lead
- Sterile rinsing basins, physiological saline, heparinized saline, and 15% diluted radiopaque contrast medium
- 20 cc-or-larger-luer-lock-syringe
- High-pressure 3-way stopcock
- Edwards SAPIEN Transcatheter Heart Valve
- RetroFlex 3 Delivery System
- 20 mm and/or 23 mm balloon catheter such as: RetroFlex balloon catheter Model 9120BC20 for use prior to 23 mm valve implantation and Model 9120BC23 for use prior to 26 mm valve implantation
- RetroFlex 3 Introducer Sheath Set Model 9120S23 for 23 mm valve procedure and Model 9120S26 for 26 mm valve procedure

- RetroFlex Dilator Kit Model 9100DKS7
- Crimper Model 9100CR23 for 23 mm valve procedure and Model 9100CR26 for 26 mm valve procedure
- Inflation device provided by Edwards Lifesciences for this application

### 7.2 Bioprosthesis Handling and Preparation

Follow sterile technique during device preparation and implantation.

#### 7.2.1 Bioprosthesis Rinsing Procedure

The bioprosthesis is packaged sterile in a plastic jar with a screw-cap closure and seal. Before opening, carefully examine the jar for evidence of damage (e.g., a cracked jar or lid, leakage, or broken or missing seals).

**CAUTION: Bioprosthetic valves from containers found to be damaged, leaking, without adequate sterilant, or missing intact seals must not be used for implantation.**

Step	Procedure
1	Set up two (2) sterile bowls with at least 500 mL of sterile physiologic saline to thoroughly rinse the glutaraldehyde sterilant from the bioprosthesis.
2	The bioprosthesis is contained in the jar within a holder. Carefully remove the bioprosthesis/holder assembly from the jar without touching the tissue. The holder is tagged with the bioprosthesis' serial identification number. Inspect the bioprosthesis for any signs of damage to the frame or tissue.
3	Rinse the bioprosthesis as follows: Place the bioprosthesis in the first bowl of sterile, physiological saline. Be sure the saline solution completely covers the bioprosthesis and holder. With the bioprosthesis and holder submerged, slowly agitate (to gently swirl the bioprosthesis and holder) back and forth for a minimum of 1 minute. Transfer the bioprosthesis and holder to the second rinsing bowl of physiological saline and gently agitate for at least one more minute. Ensure the rinse solution in the first bowl is not used. The bioprosthesis should be left in the final rinse solution until needed to prevent the tissue from drying.  <b>CAUTION: Do not allow the bioprosthesis to come in contact with the bottom or sides of the rinse bowl during agitation or swirling of the bioprosthesis. Care must be taken to ensure that the identification tag does</b>

Step	Procedure
	<b>not come in contact with the tissue and damage it. No other objects should be placed in the rinse bowls. The bioprosthesis should be kept hydrated throughout the rest of the preparation procedure to prevent the tissue from drying.</b>

### 7.2.2 Prepare Transfemoral Procedure Components

Step	Procedure
1	Refer to RetroFlex Dilator Kit, RetroFlex 3 Introducer Sheath Set and Crimper instructions for use on device preparation and handling.
2	Prime and flush the guidewire lumen of the delivery system with heparinized saline.
3	Insert an extra stiff guidewire [0.035 inch (0.89 mm) and $\geq$ 150 cm long] in the guidewire lumen, leaving a 2 to 3 cm segment of the guidewire protruding from the distal tip.
4	Flush the delivery system with heparinized saline through the flush port.
5	Place the loader cap onto the delivery system, ensuring that the inside of the loader cap is in the same direction as the tapered tip.
6	Prepare a 20 mL or larger luer-lock syringe with diluted contrast medium (15:85 contrast to heparinized saline) and attach it to a 3-way stopcock on the balloon inflation port.
7	Completely fill the inflation device provided by Edwards and attach to 3-way stopcock. Ensure there are no air bubbles in the balloon. If an air bubble is detected, eliminate it while deflating the balloon. Close the stopcock to the syringe.
8	Insert the balloon into the balloon gauge located on the crimper. Inflate the balloon and verify its diameter fits the gauge with minimal friction. While gently pulling and pushing the balloon, verify that the balloon moves with some resistance within the gauge. If the balloon does not reach the correct diameter when fully inflated, add or discard some of the inflating solution in the inflation device provided by Edwards until the correct diameter is reached. The inflation device must remain connected to the delivery system throughout the rest of the procedure.  <b>Note:</b> Correct balloon sizing is critical to successful valve deployment and valve function.
9	Close stopcock to the delivery system and remove any remaining contrast solution in inflation device provided by Edwards Lifesciences. Lock the inflation device.

10	Close the stopcock to the 20 mL syringe and verify the balloon is sized appropriately with the gauge. Remove the syringe. Unlock inflation device and deflate the balloon while creating a three-wing fold configuration, and ensure no fluid is left behind. Lock the inflation device.
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### 7.2.3 Mount and Crimp the Bioprosthesis on the Delivery System

Step	Procedure
1	Remove the bioprosthesis from the holder and gently place the bioprosthesis into the crimper aperture.
2	Gradually crimp the bioprosthesis to a diameter of approximately 12 mm.
3	Remove the bioprosthesis from the crimper and place it on the delivery system with the inflow (fabric cuff end) of the bioprosthesis towards the distal end of the balloon catheter. Ensure that the inflow of the bioprosthesis is aligned with the proximal end of the tapered catheter tip.
4	Place the bioprosthesis back in the crimper aperture, and completely crimp until it fits inside the crimp gauge.  <b>CAUTION: The physician must verify correct mounting/orientation of the bioprosthesis prior to its implantation.</b>
5	Press on the balloon shoulders circumferentially to facilitate insertion into the flex catheter and loader.
6	Pull the proximal end of the balloon into the flex catheter until the proximal edge of the bioprosthesis is flush against the distal end of the flex catheter.
7	Flush the loader with sterile heparinized saline and insert the crimped bioprosthesis inside the loader.
8	Advance the bioprosthesis into the loader until the distal end of the delivery system tip is exposed.
9	Screw the loader cap to the loader, re-flush the flex catheter and close the stopcock to the delivery system.  <b>Note:</b> Keep bioprosthesis hydrated until ready for implantation.
10	Remove guidewire and flush guidewire lumen.

### 7.3 Valvuloplasty and Bioprosthesis Delivery

Valvuloplasty and bioprosthesis delivery should be performed under local and/or general anesthesia with hemodynamic monitoring in a catheterization lab/hybrid operating room with fluoroscopic and

electrocardiographic imaging capabilities.

Administer heparin to maintain the ACT at  $\geq 250$  sec.

**CAUTION: Use of excessive contrast media may lead to renal failure. Measure the patient's creatinine level prior to the procedure. Contrast media usage should be monitored.**

**CAUTION: Use of the retrograde approach may require a femoral artery cut-down with surgical closure of the puncture site due to the large size of the arteriotomy.**

### 7.3.1 Baseline Parameters

Step	Procedure
1	Perform a supra-aortic angiogram with the projection of the native aortic valve perpendicular to the view.
2	Evaluate the height between the inferior aspect of the annulus and the inferior aspects of the lowest coronary ostium for subsequent prosthetic aortic valve implantation.
3	Introduce a pacemaker (PM) lead until its distal end is positioned in the right ventricle.
4	Set the stimulation parameters, and test pacing.

### 7.3.2 Valvuloplasty

Refer to RetroFlex Balloon Catheter Instructions for Use (IFU) for information on device preparation and handling.

**Note:** Rapid ventricular pacing should be performed when using the RetroFlex balloon catheter for valvuloplasty prior to aortic transcatheter valve implantation.

After placement of the balloon at the intended site, begin rapid ventricular pacing. Once the blood pressure has decreased to 50 mmHg or below, balloon inflation can commence.

**CAUTION: Prosthetic valve implantation should not be carried out if the balloon cannot be fully inflated during valvuloplasty.**

### 7.3.3 Bioprosthesis Delivery

Step	Procedure
1	Dilate the femoro-iliac vessel using the RetroFlex dilator kit. Refer to RetroFlex Dilator Kit IFU for information on device preparation and handling.
2	Insert the introducer sheath. Refer to the RetroFlex 3 Introducer Sheath Set IFU for

	additional information on device preparation and handling:
3	Insert the loader into the sheath.
4	Push the delivery system through the sheath. <b>CAUTION: The bioprosthesis should not be advanced through the sheath if the sheath tip is not past the aortic bifurcation.</b>
5	Retract loader to the proximal end of RetroFlex 3 delivery system.
6	The catheter articulates in a direction opposite from the flush port, and the flush port should be pointed away from the physician. Advance the RetroFlex 3 delivery system up the descending aorta; deflect the delivery system by rotating its handle "clockwise".
7	Cross the native aortic valve and position the bioprosthesis within the diseased valve.
8	Maintain the position of the bioprosthesis and retract the flex catheter, leaving the bioprosthesis in position. Verify that the flex catheter is completely off of the balloon before it is inflated and the bioprosthesis is deployed.
9	Position the mid-point of the bioprosthesis at the plane of the hinge points of the native valve leaflets.
10	Verify the correct location of the bioprosthesis with respect to the calcified valve.
11	<p>Begin bioprosthesis deployment:</p> <ul style="list-style-type: none"> <li>• Unlock the inflation device.</li> <li>• Begin rapid pacing; once arterial blood pressure has decreased to 50 mmHg or below, balloon inflation can commence.</li> <li>• Deploy the bioprosthesis by inflating the balloon with the entire volume in the inflation device. When the delivery system has been completely deflated, turn off the pacemaker.</li> <li>• De-articulate the delivery system and remove it from the sheath.</li> </ul> <p><b>CAUTION: Patient injury could occur if the delivery system is not un-flexed prior to removal.</b></p>
12	Remove sheath when the ACT level is appropriate (e.g., reaches $< 150$ sec). Close puncture site.

## 8.0 How Supplied

**STERILE:** The bioprosthesis is supplied sterilized with glutaraldehyde solution. The delivery system is supplied sterilized with ethylene oxide gas.

## 8.1 Storage

The bioprosthesis must be stored between 10 °C-25 °C (50 °F-77 °F). Each jar is shipped in an enclosure containing a temperature indicator to detect exposure of the bioprosthesis to extreme temperature.

The RetroFlex 3 delivery system should be stored in a cool, dry place.

## 9.0 MR Safety



MR Conditional

Non-clinical testing has demonstrated that the Edwards SAPIEN THV (implant) is MR Conditional. It can be scanned safely under the following conditions:

- Static magnetic field of 1.5 Tesla (T) or 3 Tesla.
- Spatial gradient field of 2500 Gauss/cm or less.
- Maximum whole-body-averaged specific absorption rate (SAR) of 2 W/kg for 15 minutes of scanning.
- Normal mode operation, as defined in IEC 60601-2-33 Ed. 3.0, of the MR system.

In non-clinical testing and analysis, the implant was determined to produce a temperature rise of less than 1.1 °C above background for a whole body SAR of 2.0 W/kg for 15 minutes of MR scanning in a 1.5 T cylindrical whole body MR system, assessed using a GE Signa whole body coil and a phantom designed to simulate human tissue. The phantom average SAR calculated using calorimetry was 2.2 W/kg and local background SAR at the site of the implant was 5.6 W/kg. The measured rise above background was 0.7 °C for a whole body SAR of 2 W/kg in a 3.0 T cylindrical bore whole body MR system, assessed using a GE Signa HDx whole body active shield MR scanner with software version 14/LX/MR and a phantom designed to simulate human tissue. The phantom average SAR calculated using calorimetry was 2.9 W/kg and local background SAR at the site of the implant was 8.4 W/kg.

The image artifact extended as far as 15 mm from the implant for spin echo images and 40 mm for gradient images when scanned in non-clinical testing in a 3.0 T GE Signa HDx MR system. The implant has not been evaluated in MR systems other than 1.5 or 3.0 T.

## 10.0 Patient Information

A patient implant card is provided in the patient information brochure and should be given to every patient after the procedure prior to discharge. The

serial number and model number may be found on the package.

## 11.0 Recovered Clinical Bioprosthesis

The explanted bioprosthesis should be placed into a suitable histological fixative such as 10% formalin or 2% glutaraldehyde and returned to the company. Refrigeration is not necessary under these circumstances. Contact Edwards Lifesciences to request an Explant Kit.

## Disposal of Used Delivery Devices

Used delivery devices may be disposed of in the same manner that hospital waste and biohazardous materials are handled. There are no special risks related to the disposal of these devices.

## 12.0 Clinical Studies

The Placement of Aortic Transcatheter Valves (PARTNER) trial (Cohort B), a prospective, randomized-controlled, multi-center pivotal trial, evaluated the safety and effectiveness of the Edwards SAPIEN™ Transcatheter Heart Valve via transfemoral delivery to a group of inoperable patients with severe symptomatic aortic stenosis. These inoperable patients were eligible for Cohort B due to coexisting conditions that resulted in the probability of death or irreversible morbidity exceeding 50%. Patients in Cohort B were also evaluated for vascular access and those meeting the criteria were 1:1 randomized to either transfemoral delivery of the Edwards SAPIEN valve or to a control group. Patients in the control group were treated with medication and/or balloon valvuloplasty. Patients in Cohort B who did not meet the criteria for vascular access were not eligible for the trial. The following data summarize the results from Cohort B.

A total of 358 patients with severe aortic stenosis underwent 1:1 randomization at 22 centers (18 in the United States) with baseline characteristics described in Table 1. Severe aortic stenosis was defined as an aortic-valve area of less than 0.8 cm<sup>2</sup>, a mean aortic-valve gradient of 40 mmHg or more, or a peak aortic-jet velocity of 4.0 m per second or more. The primary end point was the rate of death from any cause over the duration of the trial. At 1 year, the rate of death from any cause (Kaplan-Meier analysis) was 30.7% with TAVR, as compared with 50.7% in the group not receiving the valve (hazard ratio with TAVR, 0.51; 95% confidence interval [CI], 0.39 to 0.68; P < 0.0001) (Figure 3). A total of 141 of the 179 (78.8%) patients in the control group underwent balloon aortic valvuloplasty (BAV). In addition, 11 patients (6.1%)

underwent aortic valve replacement. 5 patients (2.8%) received an LV-descending aortic conduit, and 4 patients (2.2%) received a THV outside the US. The coprimary composite end point was time of death from any cause or the time to the first occurrence of repeat hospitalization. The rate of the composite end point of death from any cause or repeat hospitalization was 43.6% with TAVR as compared with 71.6% in the control group (hazard ratio, 0.45; 95% CI, 0.35 to 0.59;  $P < 0.0001$ ) (Figure 4). Prespecified secondary end points included the rate of death from cardiovascular causes (Figure 5), NYHA functional class (Figure 6), valve performance (Figure 7, 8), and the distance covered during a 6-minute walk test. Among survivors at 1 year, the rate of cardiac symptoms (New York Heart Association class III or IV) was lower among patients who had undergone TAVR than among those in the control group (23.9% vs. 60.8%,  $P < 0.001$ ). When interpreting NYHA results, consider that the evaluation was unblinded. As with other heart valve trials, the patients are aware of their treatment group. Accordingly there is the potential for bias in the NYHA values, and there is no statistical method for estimating the bias. At 30 days, TAVR, as compared with the control, was associated with a higher incidence of strokes (7.3% vs. 1.7%,  $P = 0.02$ ) and major vascular complications (16.8% vs. 1.1%,  $P < 0.001$ ). The time from index procedure to stroke in the TAVR group was as follows: 1 stroke at 12 days before the index procedure but after randomization, 4 strokes on the day of the index procedure, 2 strokes on the first post-operative day and 2 on the second post-operative day, and one stroke each on days 3, 5, 10, 23, 39, 51, 75, 120, 136, and 151. At 1 year, the rate of hemorrhagic vascular complication was 55.9% in the TAVR group, as compared to 14.0% in the control group. At 1 year, the rate of bleeding events was 17.3% in the TAVR group, as compared to 2.2% in the control group. Additionally, at 1 year, the rate of

endocarditis was 1.1% in the TAVR group, as compared to 0.6% in the control group. Mean total hospital stay was 18.4 days for the TAVR group, as compared to 13.8 days for the control group. Mean days alive out of hospital was 273.8 days for the TAVR group and 210.2 days for the control group. At 1 year, rate of aortic regurgitation for the TAVR group was as follows: 2% of patients at 4+, 13% of patients at 3+, 50% of patients at 2+, 20% of patients at 1+, and 11% of patients with no regurgitation. In comparison, rate of aortic regurgitation of the control group was as follows: 17% of patients at 3+, 40% of patients at 2+, 37% of patients at 1+, and 7% of patients with no regurgitation. In the control group, the rate of AV reintervention was as follows: 66 patients (37%) had a cardiac reintervention with a BAV. 11 patients (6.1%) underwent aortic valve replacement. 1 patient (0.6%) received an LV-descending aortic conduit. 4 patients (2.2%) received a THV outside the US. In the TAVR group, at 1 year, 10 patients (5.6%) had undergone reintervention of the aortic valve.

Procedure data for the TAVR group is summarized in Table 2. Clinical outcomes of TAVR as compared with the control are summarized in Table 3. In the year after TAVR, there was no deterioration in the functioning of the bioprosthetic valve, as assessed by evidence of stenosis or regurgitation on an echocardiogram.

In patients with severe aortic stenosis who were not suitable candidates for surgery, TAVR, as compared with the control, significantly reduced the rates of death from any cause, the composite end point of death from any cause or repeat hospitalization, and cardiac symptoms, despite the higher incidence of stroke and major vascular events.

These products are manufactured and sold under one or more of the following US patent(s): US Patent No. 5,411,552; 5,840,081; 5,931,969; 6,168,614; 6,210,957; 6,214,054; 6,547,827; 6,561,970; 6,582,462; 6,893,460; 6,908,481; 7,214,344; 7,510,575; 7,530,253; 7,585,321; 7,618,446; 7,780,723; 7,789,909; and RE40570 and corresponding foreign patents. Additional patents are pending.

Characteristic	TAVR (N = 179)	Control Group (N = 179)	P Value
Age — yr	83.1 ± 8.6	83.2 ± 8.3	0.95
Male sex — no. (%)	82 (45.8)	84 (46.9)	0.92
STS score†	11.2 ± 5.8	11.9 ± 4.8	0.14
NYHA class — no. (%)			0.68
II	14 (7.8)	11 (6.1)	
III or IV	165 (92.2)	168 (93.9)	
Coronary artery disease — no. (%)	121 (67.6)	133 (74.3)	0.20
Previous myocardial infarction — no./total no. (%)	33/177 (18.6)	47/179 (26.3)	0.10
Previous intervention — no./total no. (%)			
CABG	58/179 (32.4)	73/179 (40.8)	0.12
PCI	47/179 (26.3)	39/179 (21.8)	0.39
Balloon aortic valvuloplasty	25/154 (16.2)	39/160 (24.4)	0.09
Cerebral vascular disease — no./total no. (%)	48/175 (27.4)	46/171 (26.9)	1.00
Peripheral vascular disease — no./total no. (%)	55/178 (30.9)	45/179 (25.1)	0.24
COPD — no. (%)			
Any	74 (41.3)	94 (52.5)	0.04
Oxygen-dependent	38 (21.2)	46 (25.7)	0.38
Creatinine > 2 mg/dL (177 μmol/liter) — no./total no. (%)	8/179 (4.5)	16/178 (9.0)	0.10
Atrial fibrillation — no./total no. (%)	28/85 (32.9)	39/80 (48.8)	0.04
Permanent pacemaker — no./total no. (%)	35/179 (19.6)	31/179 (17.3)	0.68
Pulmonary hypertension — no./total no. (%)	50/118 (42.4)	53/121 (43.8)	0.90
Extensively calcified aorta — no. (%)	34 (19.0)	20 (11.2)	0.05
Deleterious effects of chest-wall irradiation — no. (%)	16 (8.9)	15 (8.4)	1.00
Chest-wall deformity — no. (%)	15 (8.4)	9 (5.0)	0.29
Liver disease — no./total no. (%)	6/177 (3.4)	6/178 (3.4)	1.00
Echocardiographic findings			
Aortic-valve area — cm <sup>2</sup>	0.6 ± 0.2	0.6 ± 0.2	0.97
Mean aortic-valve gradient — mmHg	44.5 ± 15.7	43.0 ± 15.3	0.39
Mean LVEF — %	53.9 ± 13.1	51.1 ± 14.3	0.06
Moderate or severe mitral regurgitation — no./total no. (%)‡	38/171 (22.2)	38/165 (23.0)	0.90

\* Plus-minus values are means ± SD. To convert the value for creatinine to micromoles per liter, multiply by 88.4. CABG denotes coronary-artery bypass grafting, COPD chronic obstructive pulmonary disease, LVEF left ventricular ejection fraction, NYHA New York Heart Association, PCI percutaneous coronary intervention, and TAVR transcatheter aortic-valve replacement.

† The Society of Thoracic Surgeons (STS) score measures patient risk at the time of cardiovascular surgery on a scale that ranges from 0% to 100%, with higher numbers indicating greater risk. An STS score higher than 10% indicates very high surgical risk.

‡ Moderate or severe mitral regurgitation was defined as regurgitation of grade 3+ or higher.

Table 2: TAVR Procedure Data	
Variable	Mean or % of patients (min – max)
Total time of procedure (min)	262 (139-616)
Skin to skin time (min)	150 (34 – 553)
Fluoroscopy time (min)	29 (10-68)
Volume of contrast (ml)	132 (10-450)
Use of CPB	1.1%
Use of general anesthesia	100%
# of devices used	
0	4.6%
1	89.1%
2	5.7%
3	0.6%
Valve in Valve procedure	2.3%
Emergent operation due to device or procedure	1.1%
Valve Size	
23 mm	56.6%
26 mm	43.4%
Adverse event during procedure	39.4%
Device malfunction	3.4%
Device Success (deployment, AVA >0.9, AI <3+, 1 valve)	78.2%
Procedure Success (Device success, no MACCE <30d)	71.8%

**Table 3. Clinical Outcomes at 30 Days and 1 Year (ITT Population)**

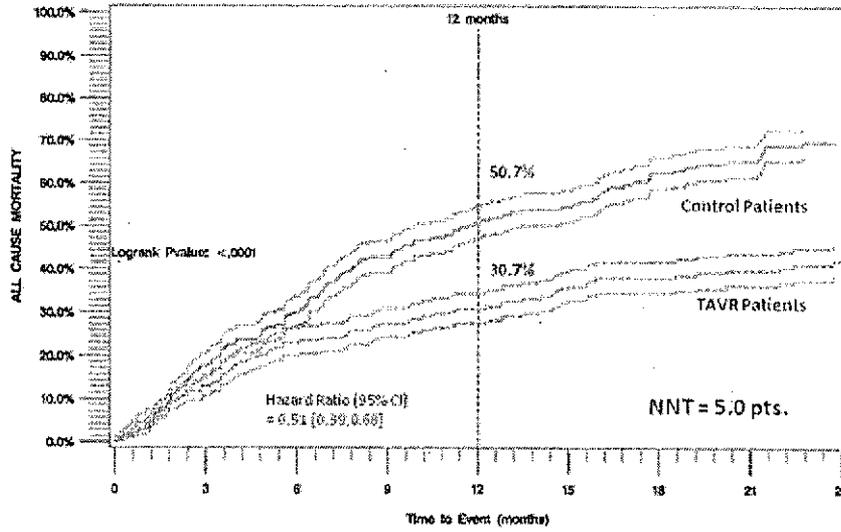
Outcome	30 Days		1 Year	
	Transfemoral TAVR N = 179	Control Group N = 179	Transfemoral TAVR N = 179	Control Group N = 179
Death	9 (5.0)	5 (2.8)	55 (30.7)	89 (49.7)
From any cause From cardiovascular cause <sup>a</sup>	8 (4.5)	3 (1.7)	35 (19.6)	75 (41.9)
Repeat hospitalization <sup>b</sup>	10 (5.6)	18 (10.1)	40 (22.3)	79 (44.1)
Death from any cause or repeat hospitalization <sup>b</sup>	20 (11.2)	22 (12.3)	78 (43.6)	126 (70.4)
TIA	0	0	1 (0.6)	0
All Stroke	13 (7.3)	3 (1.7)	20 (11.2)	8 (4.5)
Myocardial Infarction				
All	0		1 (0.6)	1 (0.6)
Peri-procedural	0	0	0	0
Hemorrhagic Vascular Complication <sup>f</sup>	90 (50.3)	25 (14.0)	100 (55.9)	25 (14.0)
Major Vascular Complication	30 (16.8)	2 (1.1)	31 (17.3)	4 (2.2)
Renal Failure	2 (1.1)	2 (1.1)	4 (2.2)	5 (2.8)
Renal Insufficiency	1 (0.6)	0 (0.0)	2 (1.1)	3 (1.7)
Bleeding Event <sup>g</sup>	29 (16.2)	4 (2.2)	31 (17.3)	4 (2.2)
Cardiac reintervention				
Balloon aortic valvuloplasty	1 (0.6) <sup>c</sup>	11 (6.1)	5 (2.8)	66 (36.9) <sup>d</sup>
Repeat TAVR <sup>e</sup>	3 (1.7)	NA	4 (2.2)	NA
Aortic-valve replacement	0	3 (1.7)	1 (0.6) <sup>c</sup>	11 (6.1)
Endocarditis	0	0	2 (1.1)	1 (0.6)
New Atrial Fibrillation	1 (0.6)	2 (1.1)	1 (0.6)	3 (1.7)
New pacemaker	6 (3.4)	9 (5.0)	8 (4.5)	14 (7.8)

NA = not applicable, TAVR = transcatheter aortic valve replacement, TIA = transient ischemic attack.

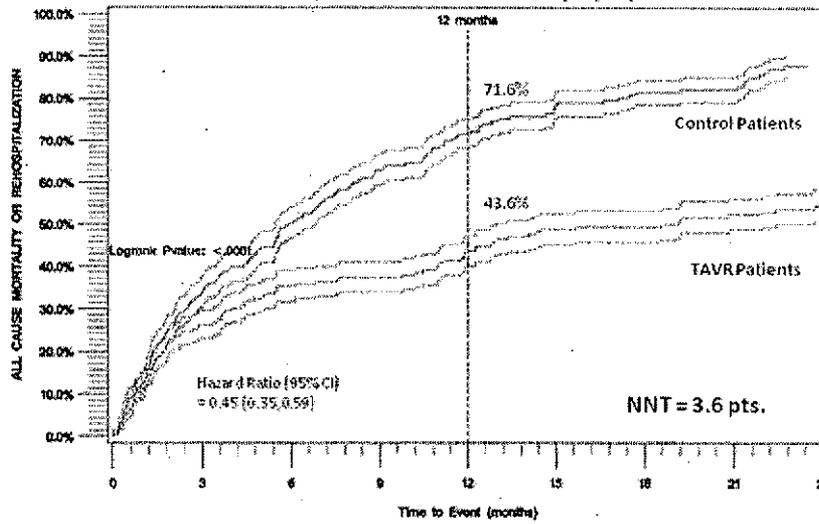
Data presented as n (%). of patients.

- a. Deaths from unknown causes were assumed to be deaths from cardiovascular causes.
- b. Repeat hospitalizations were included if they were due to aortic stenosis or complications of the valve procedure (e.g., TAVR).
- c. One patient in the TAVR group did not receive TAVR (because of failed access) and subsequently underwent balloon aortic valvuloplasty, followed by aortic-valve replacement.
- d. 30 patients underwent repeat BAV after the index BAV procedure that had been performed in the first 30 days after randomization, and 36 patients underwent a first BAV more than 30 days after randomization.
- e. Three patients underwent a repeat TAVR within 24 hours after the index TAVR procedure; four patients in the control group who underwent TAVR at a nonparticipating, ex-US site are not included here.
- f. Stroke was defined as follows: Neurological deficit lasting  $\geq$  24 hours or lasting less than 24 hours with a brain imaging study showing an infarction.
- g. Bleeding event is defined as  $\geq$  2 units within the index procedure
- h. Hemorrhagic vascular complications are defined as vascular complications that include hematoma at the access site of  $>$  5 cm, false aneurysm, arterio-venous fistula, retroperitoneal bleeding, peripheral ischemia/nerve injury, any transfusion or vascular surgical repair within 30 days of the procedure.

**Figure 3 Primary Endpoint: All Cause Mortality**  
(68% confidence limits displayed)



**Figure 4 Co-Primary Endpoint: Mortality or Repeat Hospitalization**  
(68% confidence limits displayed)



**Figure 5 Secondary Endpoint: Death from Cardiovascular Cause**  
(68% confidence limits displayed)

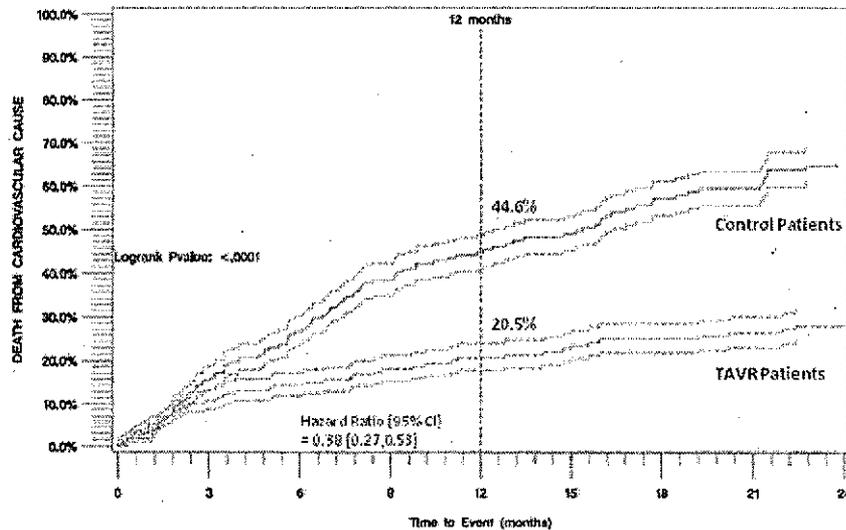


Figure 6 Secondary Endpoint: NYHA Symptoms Over Time

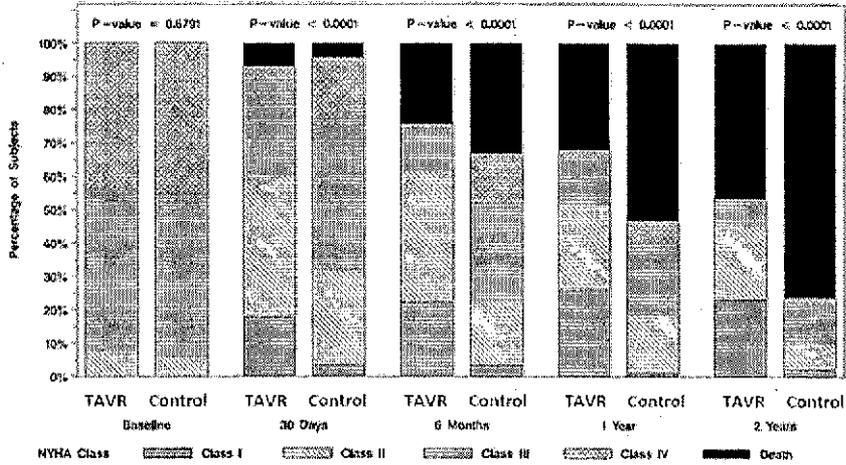


Figure 7 Secondary Endpoint: AVA Over Time (one standard deviation displayed)

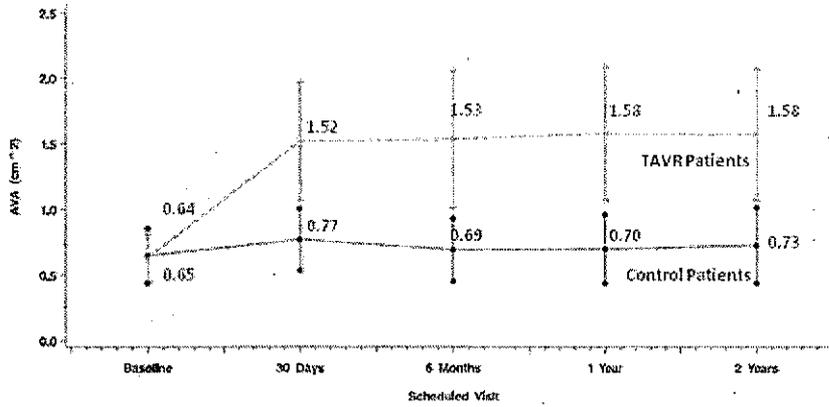
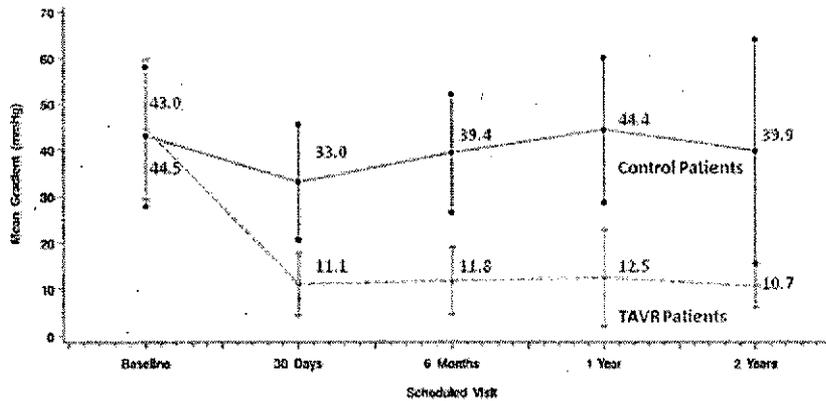


Figure 8 Secondary Endpoint: Mean Gradient Over Time (one standard deviation displayed)





Edwards

# RetroFlex Balloon Catheter

## Instructions for Use

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

Please verify that you have the latest version of the instructions for use prior to using the device by visiting <http://THVIFU.edwards.com> or by calling 1.800.822.9837. In order to access the instructions for use, an IFU Code will be required.

**STERILE:** The balloon catheter is supplied sterilized by ethylene oxide.

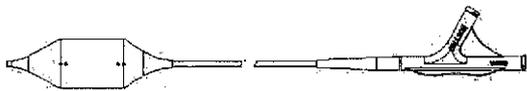
### 1.0 Device Description

The RetroFlex Balloon Catheter consists of a shaft and balloon with radiopaque markers indicating working length of the balloon. At the proximal end of the device, there is a standard "Y-connector" for balloon inflation and the guidewire lumen. The inflation parameters are as follows:

Table 1. Inflation Parameters

Model	Balloon Dimensions	Inflation Volume
9120BC20	20 mm x 3 cm	13 mL
9120BC23	23 mm x 3 cm	16 mL

RetroFlex Balloon Catheter



Black dots indicate position of radiopaque markers.

Device Compatibility:

- Maximum guidewire diameter: 0.035" (0.89 mm)
- Minimum sheath compatibility: 14F (4.62 mm)

NOTE: For proper volume sizing, the balloon catheter should be used with the inflation device provided by Edwards Lifesciences.

Edwards Lifesciences, the stylized E logo, Edwards and RetroFlex are trademarks of Edwards Lifesciences Corporation.

## 2.0 Indications

The RetroFlex balloon catheter is indicated for valvuloplasty of a stenotic cardiac valve prior to implantation of a transcatheter heart valve.

## 3.0 Contraindications

- Other than standard risks associated with insertion of a cardiovascular catheter, there are no known contraindications for valvuloplasty. The patient's medical condition could affect successful use of this catheter.

## 4.0 Warnings

- The device is designed, intended, and distributed for single use only. **Do not resterilize or reuse the device.** There are no data to support the sterility, nonpyrogenicity, and functionality of the device after reprocessing.
- Do not mishandle the device or use it if the packaging or any components are not sterile, have been opened or are damaged (e.g. kinked or stretched), or the expiration date has elapsed.

## 5.0 Precautions

- For special considerations associated with the use of this device prior to transcatheter heart valve implantation, refer to the bioprosthesis Instructions for Use.
- Use only appropriate balloon inflation medium. Do not use air or gaseous medium to inflate the balloon.
- The device is not intended for post-dilatation of deployed transcatheter heart valves.
- While exposed within the body, device advancement and retrieval should not be done without the aid of fluoroscopy. Do not advance or retract the device unless the balloon is fully deflated under vacuum.

## 6.0 Potential Adverse Events

Complications associated with standard catheterization, balloon valvuloplasty, and the use of angiography include, but are not limited to, allergic reaction to anesthesia or to contrast media, injury including perforation or dissection of vessels, thrombus formation, plaque dislodgement and embolization that may result in myocardial infarction, stroke, distal peripheral occlusion and/or death, arrhythmia development, cardiac perforation, conduction system injury, hematoma, infundibulum injury, annular tear or rupture and/or valve leaflet dehiscence, severe valve insufficiency, valve restenosis, valve damage, balloon rupture.

### 7.0 Directions for Use

Step	Procedure
1	Prepare vascular access site for valvuloplasty balloon catheter insertion and position guidewire using standard techniques.
2	Flush the valvuloplasty balloon catheter with heparinized saline. Attach a high pressure 3-way stopcock to the balloon inflation port.
3	Prepare a 20 mL syringe with 5 mL diluted contrast solution (15:85 contrast to heparinized saline) and attach to the stopcock.
4	Completely fill the inflation device provided by Edwards with diluted contrast solution and attach in the locked position to the stopcock; close the stopcock to the inflation device.
5	Slowly pull vacuum with the 20 mL syringe repeatedly to remove air, leaving neutral pressure in the system.
6	Close the stopcock to the balloon catheter. Gradually remove contrast medium into the 20 mL syringe to achieve the appropriate volume by rotating the knob of the inflation device. Close the stopcock to the 20 mL syringe and remove the 20 mL syringe from the system.
7	Remove balloon cover and hydrate the length of the balloon catheter.

Step	Procedure
8	Advance the balloon catheter over the guidewire, through the introducer sheath, across the valve, and position the balloon markers at the intended site.
9	Fully inflate the balloon with the inflation device.
10	Completely deflate the balloon, and gently withdraw the valvuloplasty balloon catheter and remove from the sheath.

### 8.0 How Supplied

STERILE: The balloon catheter is supplied sterilized by ethylene oxide.

### 9.0 Storage

Store in a cool, dry place.

### 10.0 Device Disposal

Used devices may be handled and disposed of in the same manner as hospital waste and biohazardous materials. There are no special risks related to the disposal of these devices.



Edwards

# Crimper

## Model 9100CR23/ 9100CR26

### Instructions for Use

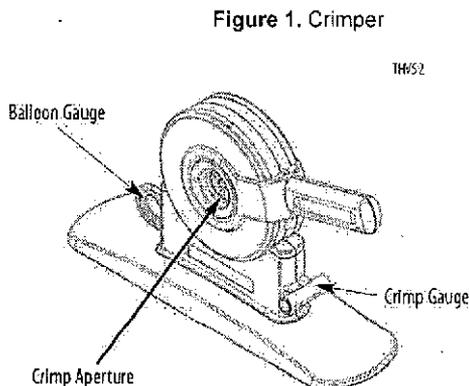
**Caution:** Federal (USA) law restricts this device to sale by or on the order of a physician.

Please verify that you have the latest version of the instructions for use prior to using the device by visiting <http://THVIFU.edwards.com> or by calling 1.800.822.9837. In order to access the instructions for use, an IFU Code will be required.

**STERILE:** The crimper is supplied sterilized by ethylene oxide.

### 1.0 Device Description

The Crimper is comprised of a housing and a compression mechanism, creating an aperture that is opened and closed by means of a handle. The Crimper includes a balloon gauge to verify diameter of an inflated balloon catheter. The Crimper is available in two sizes, 23 mm and 26 mm, with a corresponding balloon gauge for each size. It also includes a crimp gauge to verify collapsed diameter of the device.



### 2.0 Indications

The Crimper is indicated for use in preparing the Edwards SAPIEN Transcatheter Heart Valve for implantation.

### 3.0 Contraindications

No known contraindications.

Edwards Lifesciences, the stylized E logo and Edwards are trademarks of Edwards Lifesciences Corporation.

### 4.0 Warnings

- The device is designed, intended, and distributed for single use only. **Do not resterilize or reuse the device.** There are no data to support the sterility, nonpyrogenicity, and functionality of the device after reprocessing.
- Do not mishandle the device or use it if the packaging or any components are not sterile, have been opened or are damaged, or the expiration date has elapsed.

### 5.0 Precautions

For special considerations associated with the use of this device prior to transcatheter heart valve implantation, refer to the bioprosthesis Instructions for Use.

### 6.0 Potential Adverse Events

No known potential adverse events.

### 7.0 Directions for Use

1. Remove the bioprosthesis from its package and gently place the bioprosthesis into the crimper aperture.
2. Crimp the bioprosthesis by rotating the handle to close the aperture.

### 8.0 How Supplied

**STERILE:** The Crimper is supplied sterilized by ethylene oxide.

### 9.0 Storage

The Crimper should be stored in a cool, dry place.

### 10.0 Device Disposal

Used crimpers may be handled and disposed of in the same manner as hospital waste and biohazardous materials. There are no special risks related to the disposal of these devices.

These products are manufactured and sold under one or more of the following US patent(s): US Patent No. 7,530,253 and corresponding foreign patents. Additional patents are pending.

# Transcatheter Aortic Valve Replacement for Patients Who Cannot Have Open-Heart Surgery

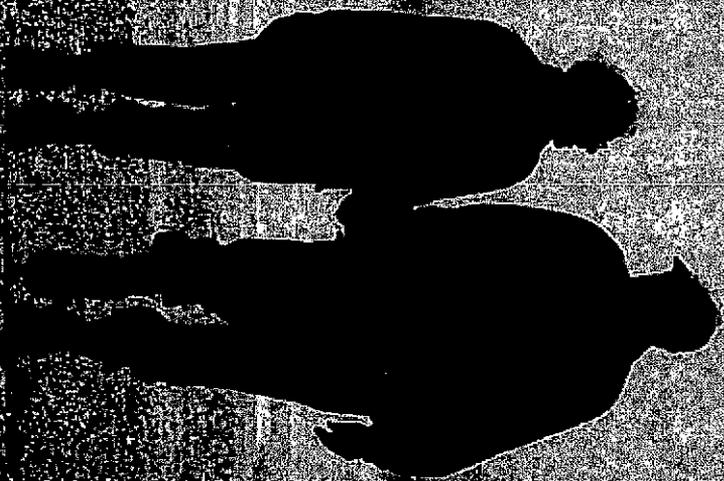
What You and  
Your Loved Ones  
Should Know



This pamphlet was created for patients who feel sick from severe aortic stenosis (a narrowing of the aortic valve opening that does not allow normal blood flow) and who cannot have open-heart surgery. This information will help you and your loved ones learn more about your heart, how it works, and aortic stenosis. In addition, you will learn about a new procedure called transcatheter aortic valve replacement (TAVR).

Be sure to ask your doctor to explain your treatment options, and their risks, to help you decide which option is best for you.

See pages 13-14 to review the risks of the TAVR procedure.



## Table of Contents

<b>How Does Your Heart Work?</b> .....	<b>3-4</b>
Chambers and Valves.....	3
<b>What is Severe Aortic Stenosis?</b> .....	<b>5-6</b>
<b>Transcatheter Aortic Valve Replacement</b> .....	<b>7-16</b>
Who Should Not Have the Transcatheter Aortic Valve Replacement Procedure?.....	7
Which Products Will Be Used During the Transcatheter Aortic Valve Replacement Procedure?.....	8
What Do You Need to Do Before the Transcatheter Aortic Valve Replacement Procedure?.....	8
What Will Happen During the Transcatheter Aortic Valve Replacement Procedure?.....	9
What Are the Possible Benefits and Risks 1 Year After the Transcatheter Aortic Valve Replacement Procedure?.....	11
What Are the Specific Procedural Risks 30 Days After the Transcatheter Aortic Valve Replacement Procedure?.....	13
What Happens After the Transcatheter Aortic Valve Replacement Procedure?.....	15
<b>Warnings</b> .....	<b>17</b>
<b>Precautions</b> .....	<b>18</b>
<b>How Long Will Your New Valve Last?</b> .....	<b>18</b>
<b>Additional Information</b> .....	<b>18</b>
<b>Patient Implant Card</b> .....	<b>18</b>

Please remember, this information is not meant to tell you everything you need to know about your treatment options for aortic stenosis, or about the TAVR procedure. Regular check-ups with your doctor are essential. Call or see your doctor whenever you have questions or concerns about your health, especially if you experience unusual symptoms or changes in your overall health.

## HOW DOES YOUR HEART WORK?

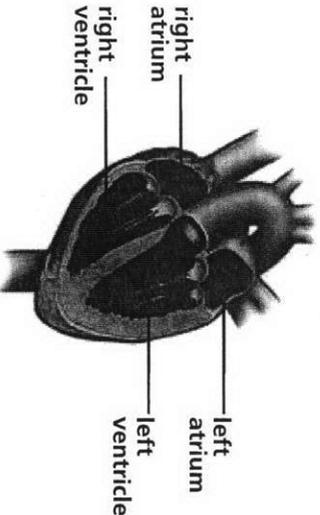
The heart is a muscular organ located in your chest between your lungs. The heart is designed to pump blood through your body. The right side of your heart pumps blood through the lungs, where the blood picks up oxygen. The left side of the heart receives this blood and pumps it to the rest of your body.

**Your heart beats between 60 and 100 times per minute. At 60 beats per minute, that's approximately 31.5 million beats per year.**

## Chambers and Valves

The heart is divided into four main areas, or chambers—two upper chambers (called the left and right atrium) and two lower chambers (called the left and right ventricle).

There are four valves that control the flow of blood through your heart. They are called the aortic, mitral, pulmonary, and tricuspid valves, and each is made of flaps of tissue called leaflets. (See *Figure on page 4*)



**NOTE:** The left and the right side of the heart is pictured as the heart sits in your body.

Each time your heart beats, it pumps blood through these valves by contracting (squeezing) its chambers. These valves open in one direction, like one-way gates, allowing blood to flow forward. In between beats, the heart's chambers quickly relax, and its valves close, preventing blood from flowing backward.

There are two common problems that can develop in heart valves:

- When your valve is narrowed and does not completely open because of things like a build-up of calcium (mineral deposits), high cholesterol (a waxy fat), age, or genetics (such as a birth defect), this is called stenosis.
- When your valve does not fully close and allows blood to leak backwards through the valve, this is called regurgitation.

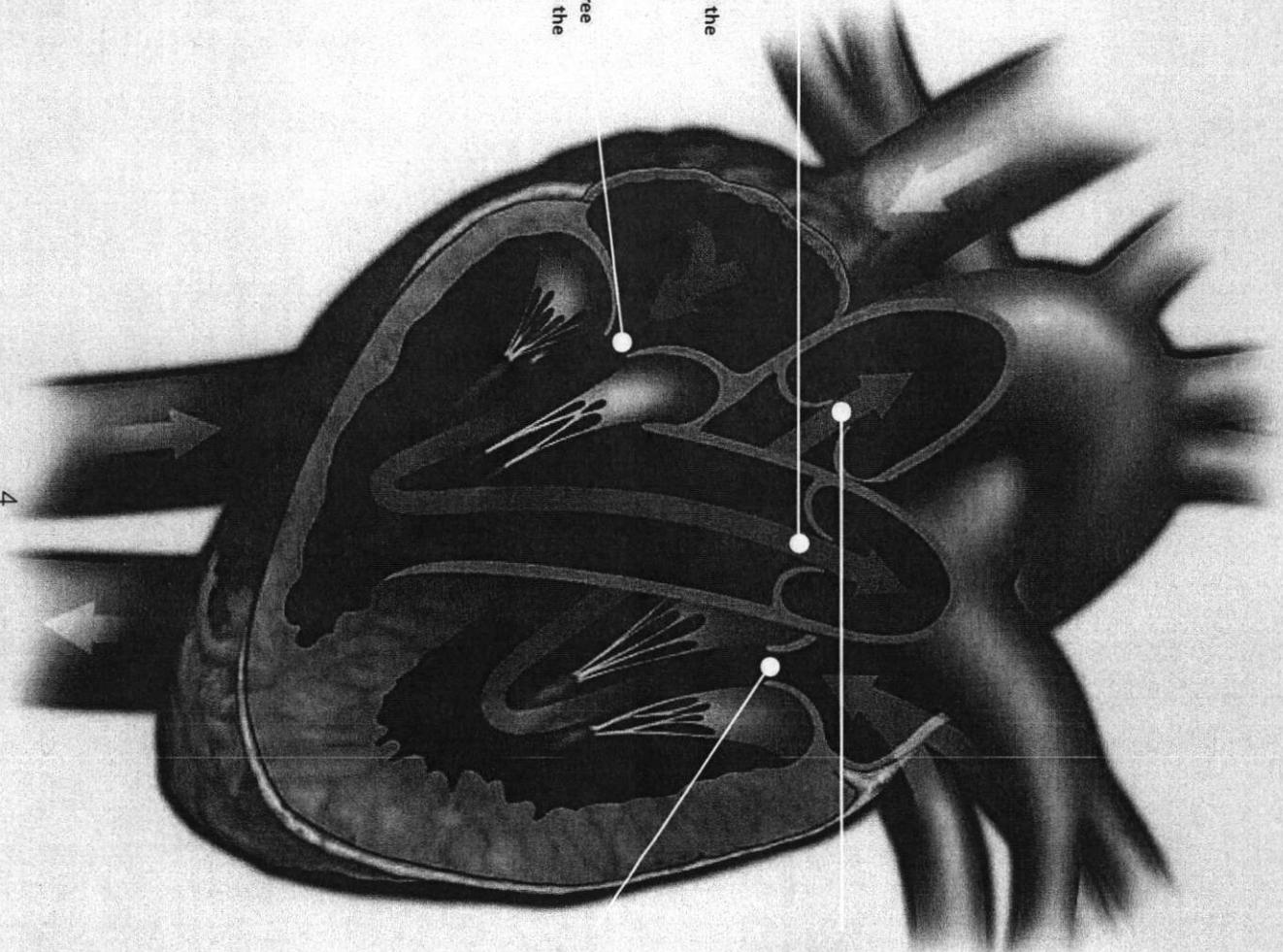
With either problem, your heart needs to work harder and may not pump enough oxygen-rich blood to your body.

**The pulmonary valve**  
has three leaflets. It controls blood flow from the right ventricle to the pulmonary artery, sending blood to the lungs to pick up oxygen.

**The tricuspid valve** has three leaflets. It controls blood flow from the right atrium to the right ventricle.

**The aortic valve** has three leaflets. It controls blood flow from the left ventricle to the aorta, sending blood to the rest of the body.

**The mitral valve** has two leaflets. It controls blood flow between the left atrium and left ventricle.





## WHAT IS SEVERE AORTIC STENOSIS?

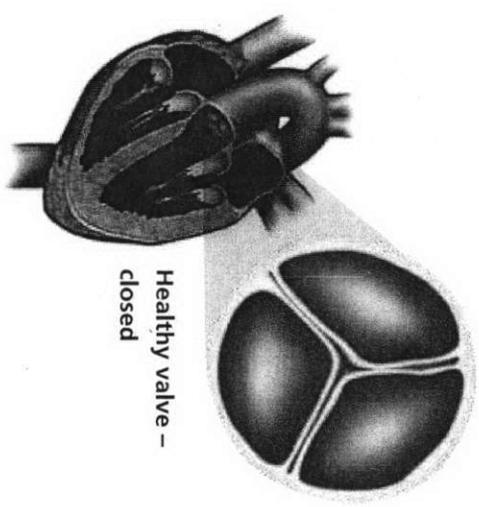
Severe aortic stenosis is a narrowing of your aortic valve opening that does not allow normal blood flow. It can be caused by a birth defect, rheumatic fever, or radiation therapy, or can be related to age.

In elderly patients, severe aortic stenosis is often caused by the build-up of calcium (mineral deposits) on the aortic valve's leaflets. Over time the leaflets become stiff, reducing their ability to fully open and close. When the leaflets don't fully open, your heart must work harder to push blood through the aortic valve to your body.

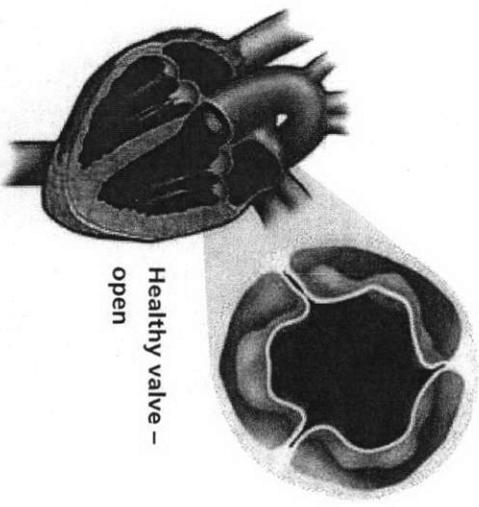
Eventually, your heart gets weaker, increasing the risk of heart failure (your heart cannot supply enough blood to your body). Severe aortic stenosis is a very serious problem. Without treatment, half of the people who feel sick from this problem die within an average of 2 years.



### HEALTHY AORTIC VALVE

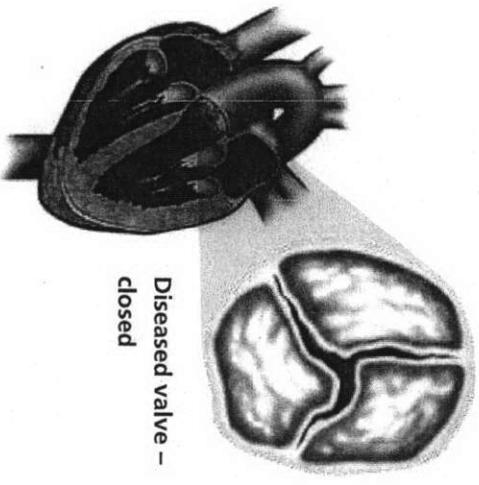


Healthy valve - closed

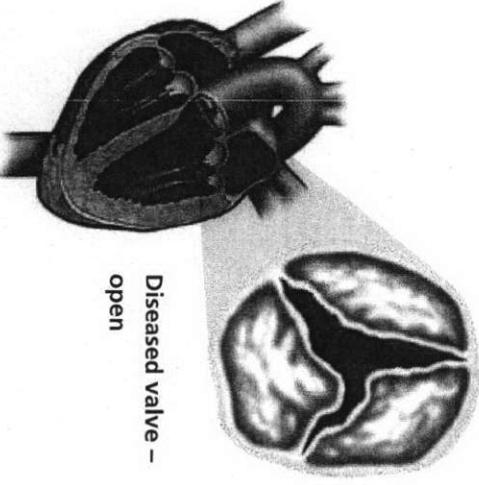


Healthy valve - open

### DISEASED AORTIC VALVE



Diseased valve - closed



Diseased valve - open

## TRANSCATHETER AORTIC VALVE REPLACEMENT

If a cardiac surgeon determines that you are too sick for open-heart surgery and if medicine is not helping you feel better, transcatheter aortic valve replacement (TAVR) may be an alternative. This less invasive procedure allows your aortic valve to be replaced with a new valve while your heart is still beating.

### TAVR

Anesthesia	General
Cardiopulmonary bypass	Usually not required
Entry site	Out in leg
Average total procedure duration*	4-5 hours
Average hospital stay	8 days

\* The time required to perform the procedures necessary for the entire procedure

**The TAVR procedure is not right for everyone. In certain cases, the risks of the procedure may outweigh the benefits. See pages 13-14 to review the risks of the TAVR procedure.**

### Who Should Not Have the Transcatheter Aortic Valve Replacement Procedure?

The Edwards SAPIEN transcatheter heart valve should not be used in the following people:

- Patients whose aortic valve is not calcified
- Patients whose aortic valve only has one or two leaflets (usually due to a birth defect)
- Patients who have a blood clot or an abnormal growth
- Patients who have an infection in the heart or infections elsewhere
- Patients who already have a prosthetic (man-made) valve or repair device implanted in any of their four heart valves.
- Patients who have aortic stenosis along with aortic regurgitation (when your valve does not fully close and allows blood to leak backwards through the valve)
- Patients who have severe disease with their mitral valve
- Patients whose aortic valve is either too small or too big

- Patients who have severe disease in their vessels leading to the heart, small vessels, or vessels that have a lot bends that would not allow passage of the products necessary to perform the procedure
  - Patients who have thick aortic leaflets which are very close to the arteries that supply the heart with blood
  - Patients who have severe problems with bleeding or blood clotting
  - Patients who have a condition in which the heart muscle becomes thick
  - Patients who cannot take aspirin, heparin, ticlopidine (Ticlid), or clopidogrel (Plavix), or have sensitivity to contrast medium (fluid used to see your internal structures during the procedure)
  - Patients who can have open-heart surgery
- If the Edwards SAPIEN transcatheter heart valve is used in the patients mentioned above, it may not work properly. This could make you feel very sick, or even cause death.

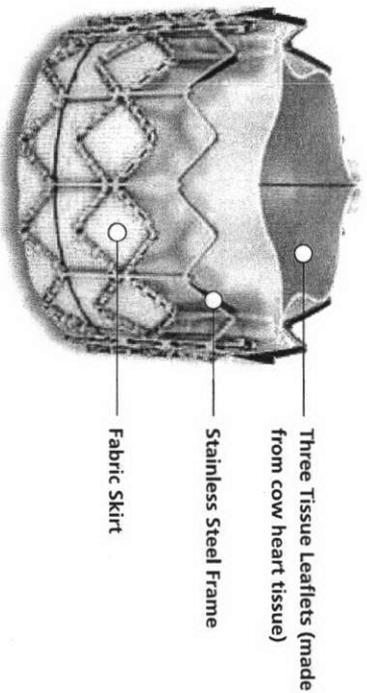
### Which Products Will Be Used During the Transcatheter Aortic Valve Replacement Procedure?

The Edwards SAPIEN transcatheter heart valve and other accessories are used to perform the TAVR procedure. The Edwards SAPIEN transcatheter heart valve is a biological (made from animal tissue) valve that replaces your aortic valve. It is provided in two sizes, 23 mm and 26 mm in diameter. Your doctor will determine the right size for you.

### What Do You Need to Do Before the Transcatheter Aortic Valve Replacement Procedure?

Be sure to tell your doctor what medicine you are taking and whether you have any allergies. Your doctor may ask you to change the medicine you are on before the procedure. Your doctor will also explain the procedure and answer any questions you may have.

The Edwards SAPIEN transcatheter heart valve (that replaces your diseased aortic valve) is pictured to the right. Image is larger than actual valve size.



## What Will Happen During the Transcatheter Aortic Valve Replacement Procedure?

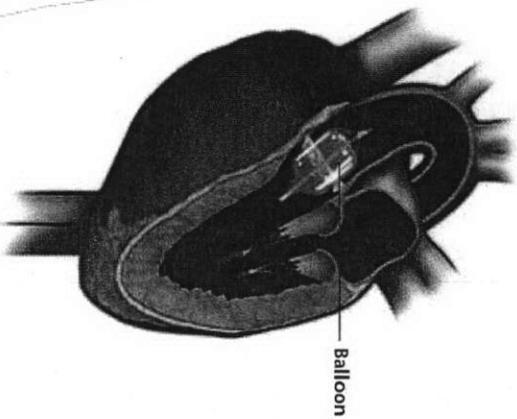
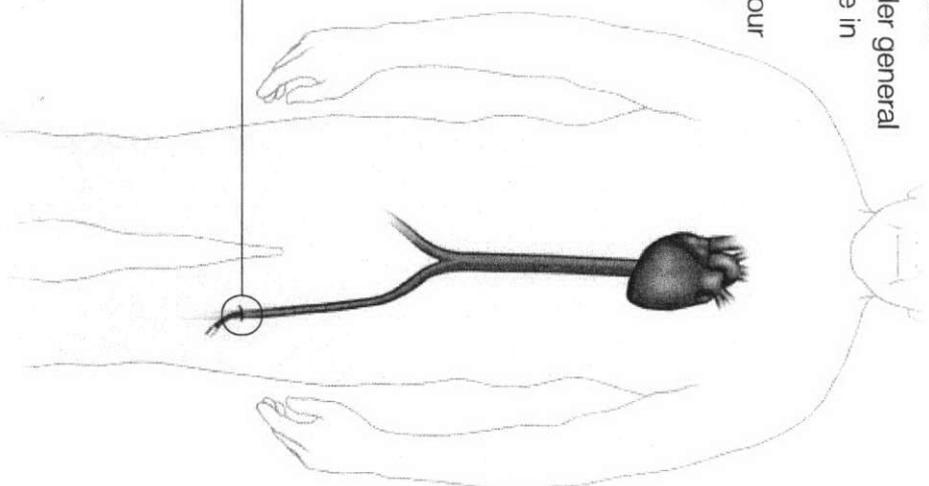
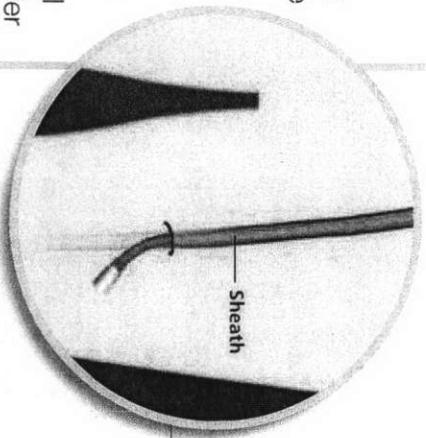
The procedure will be performed in the hospital. General anesthesia will be given to put you into a deep sleep. After you are asleep, a tube will be placed down your throat and connected to a mechanical ventilator (a machine that will help you breathe during the procedure).

Your heart's pumping function will be briefly suspended twice during the procedure. To do this your doctor will place a temporary pacing wire in your heart which causes the heart to race. This makes it hard for your heart to pump blood through your body well, which may result in low blood flow to your brain, kidneys, and other organs for a few seconds. After the procedure is done, the temporary pacing wire is removed.

The doctor will use fluoroscopy (a type of X-ray) during the procedure. The doctor will also use contrast medium (fluid used to see your internal structures during the procedure) in order to see your aortic valve. Some patients may have kidney problems or an allergic reaction as a result of the contrast medium. The

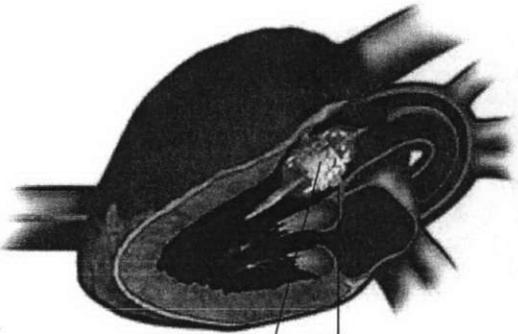
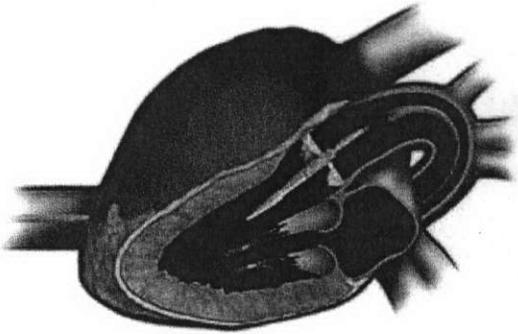
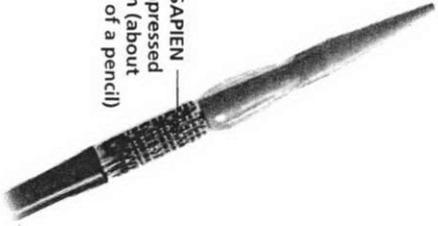
doctor will also use echocardiography (a type of ultrasound) to see your aortic valve. The average time required to perform the procedure is 4 to 5 hours.

1. You will be placed under general anesthesia (you will be in a deep sleep).
2. A cut will be made in your leg, where your doctor will put in a sheath (a short hollow tube) that is slightly larger than the width of a pencil.

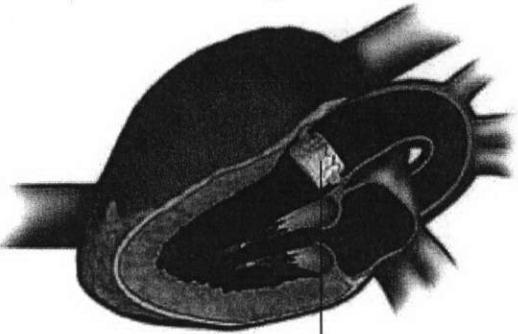


3. Your doctor will take a small balloon and put it through the sheath into your blood vessel to reach your aortic valve. The balloon will be inflated with fluid to open your narrowed valve, deflated, and then removed.

Edwards SAPIEN  
valve compressed  
on balloon (about  
the width of a pencil)



Diseased  
valve  
Expanded  
Edwards  
SAPIEN  
valve



Edwards  
SAPIEN  
valve in  
place

4. The Edwards SAPIEN transcatheter heart valve will be placed on the delivery system (long tube with a small balloon on the end), and compressed on the balloon (using a crimper) to make it small enough to fit through the sheath. It will be about the width of a pencil.

5. The delivery system carrying the valve will be placed through the sheath and pushed up to your aortic valve, guided by a type of X-ray.

6. The balloon of the delivery system carrying the valve will be inflated with fluid, expanding this new valve within your diseased valve. The new valve will push the leaflets of your diseased valve aside. The frame of the new valve is very strong and it will use the leaflets of your diseased valve to anchor securely in place. Next, the balloon will be deflated.

7. Your doctor will make sure that your new valve is working properly before removing the delivery system and closing the cut in your leg. If your new valve is not working properly, your doctor may need to do something else which may include open-heart surgery or other additional surgery.

## **What Are the Possible Benefits and Risks 1 Year After the Transcatheter Aortic Valve Replacement Procedure?**

In the United States, The PARTNER Trial studied the safety and effectiveness of the Edwards SAPIEN transcatheter heart valve in 358 patients whose doctors had determined them to be unable to undergo open-heart surgery. Half of the patients were treated with the Edwards SAPIEN transcatheter heart valve and half were treated with standard medical therapy. Patients were examined at 30 days, 6 months, and 1 year after the procedure, and will continue to be examined every year for 5 years.<sup>1</sup>

**Standard medical therapy may have included medicine or other procedures that treat aortic stenosis such as balloon aortic valvuloplasty (procedure to stretch the aortic valve opening).**

The study results showed that patients who received the Edwards SAPIEN transcatheter heart valve lived longer and felt better, but had a higher stroke rate, than those patients who did not receive a new valve (most of whom had balloon aortic valvuloplasty).<sup>1</sup>

- 69 out of every 100 patients with severe aortic stenosis were alive at 1 year after receiving a new valve.
- In comparison, only 50 out of every 100 patients who did not receive a new valve were alive at 1 year.
- Additionally, the study showed that patients who received a new valve had improved heart function and felt much better at 1 year compared to patients who did not receive a new valve.

**The major risks of the TAVR procedure with the Edwards SAPIEN transcatheter heart valve include:<sup>1</sup>**

- Death from any cause. Death occurred in 31 out of 100 patients within 1 year after receiving a new valve.
- Stroke – a condition when blood stops flowing to the brain, which may cause partial or severe disability.

Stroke occurred in 11 out of every 100 patients within 1 year after receiving a new valve, which was approximately two and a half times as often as seen in patients who did not receive a new valve (most of whom had balloon aortic valvuloplasty).

- Major vascular complications – a tear or hole in blood vessels or the heart, or a hematoma (a blood clot under the skin), which will require another procedure. Major vascular complications occurred in 17 out of every 100 patients within 1 year after receiving a new valve, which was approximately 8 times as often as seen in patients who did not receive a new valve (most of whom had balloon aortic valvuloplasty).

- Bleeding event – a loss of blood that requires 2 or more units of a blood transfusion within the indexed procedure. A bleeding event occurred in 17 out of every 100 patients within 1 year after receiving a new valve, which was approximately 8 times as often as seen in patients who did not receive a new valve (most of whom had balloon aortic valvuloplasty).

The following table is a summary of the clinical risks observed at 1 year in The PARTNER Trial.<sup>1</sup> The frequency is shown as the number of patients out of every 100.

**Risks Within 1 Year After the TAVR Procedure<sup>1</sup>**

	TAVR	Standard Medical Therapy
<b>Death</b>		
From any cause	31 out of 100 patients	50 out of 100 patients
From cardiovascular (heart-related) causes	20 out of 100 patients	42 out of 100 patients
<b>Repeat hospitalizations</b>	22 out of 100 patients	44 out of 100 patients
<b>Major vascular complications</b>	17 out of 100 patients	2 out of 100 patients
<b>Bleeding event</b>	17 out of 100 patients	2 out of 100 patients
<b>Stroke</b>	11 out of 100 patients	5 out of 100 patients
<b>New pacemaker (device that can help regulate the heart) implantation</b>	5 out of 100 patients	8 out of 100 patients
<b>Need for additional procedures on the operated valve</b>		
Balloon aortic valvuloplasty (procedure to stretch the aortic valve opening)	3 out of 100 patients	37 out of 100 patients
Repeat transcatheter aortic valve replacement	2 out of 100 patients	N/A
Surgical aortic valve replacement	1 out of 100 patients	6 out of 100 patients
<b>Kidney failure</b>	2 out of 100 patients	3 out of 100 patients
<b>Myocardial infarction (heart attack)</b>	1 out of 100 patients	1 out of 100 patients
<b>Endocarditis (inflammation or infection of any internal heart structures, including the valves)</b>	1 out of 100 patients	1 out of 100 patients
<b>New atrial fibrillation (abnormal heartbeat)</b>	1 out of 100 patients	2 out of 100 patients

## What Are the Specific Procedural Risks 30 Days After the Transcatheter Aortic Valve Replacement Procedure?

As with any medical intervention, there is a possibility that complications may occur during or after receiving the Edwards SAPIEN transcatheter heart valve, even after leaving the hospital.

The major risks of the TAVR procedure with the Edwards SAPIEN transcatheter heart valve include:<sup>1</sup>

- Death from any cause. Death occurred in 5 out of every 100 patients within 30 days after receiving a new valve.
- Stroke – a condition when blood stops flowing to the brain, which may cause partial or severe disability. Stroke occurred in 7 out of every 100 patients within 30 days after receiving a new valve, which was approximately 4 times as often as seen in patients who did not receive a new valve (most of whom had balloon aortic valvuloplasty).
- Major vascular complications – a tear or hole in blood vessels or the heart, or a hematoma (a blood clot under the skin), which will require another surgery. Vascular complications occurred in 17 out of every 100 patients within 30 days after receiving a new valve, which was 15 times as often as seen in patients who did not receive a new valve (most of whom had balloon aortic valvuloplasty).
- Bleeding event – a loss of blood that requires 2 or more units of a blood transfusion within the indexed procedure. A bleeding event occurred in 16 out of every 100 patients within 30 days after receiving a new valve, which was approximately 8 times as often as seen in patients who did not receive a new valve (most of whom had balloon aortic valvuloplasty).



Additional possible risks listed below are organized by how often they occurred in patients within 30 days of the TAVR procedure.<sup>1</sup>

### Risks Within 30 Days After the TAVR Procedure<sup>1</sup>

Abnormal blood test results	20 out of 100 patients
Infection (including bacteremia, which is usually a temporary inflammation or infection of the entry site, or infection in the blood)	19 out of 100 patients
Arrhythmia (irregular heartbeat)	15 out of 100 patients
Blood leakage around the valve	15 out of 100 patients
Difficulty exercising	10 out of 100 patients
Pain or change at the entry site (where the doctor inserted the catheter with the valve)	10 out of 100 patients
Respiratory insufficiency or failure (any problems with breathing)	10 out of 100 patients
High blood pressure or low blood pressure	9 out of 100 patients
Heart failure (poor heart function, reduced ability of the heart to supply enough blood to the body)	5 out of 100 patients
Hematoma (small collection of blood under the skin) or changes at the entry site	5 out of 100 patients
Fever	4 out of 100 patients
Blood vessel blockage	3 out of 100 patients
Angina (cardiac chest pain or tightness)	2 out of 100 patients
Aortic valve reintervention (need for another procedure or surgery on your aortic valve)	2 out of 100 patients

### In addition, the following risks occurred in 1 or fewer out of 100 patients:

- Acute kidney injury (renal failure, when the kidneys cannot work properly), which can require hemodialysis
  - Allergic reaction to anesthesia, contrast medium (fluid used to see your internal structures during the procedure), or medicine
  - Anemia (low red blood cell count)
  - Damage to the nerves
  - Decreased kidney function
  - Device embolization (movement of the valve after placement)
  - Narrowing of the valve
  - Syncope (fainting)
  - Bleeding into the heart sac
  - Coronary obstruction (blockage in the coronary vessels around the heart)
  - Device breakdown or degeneration
  - Failure or poor function of the implanted valve
  - Mechanical malfunction of the valve delivery system
  - Need for valve explant (removal)
  - Shortness of breath
- In addition, there is a possibility that you may experience other problems that are not listed above that have not been previously observed with this procedure.



### **What Happens After the Transcatheter Aortic Valve Replacement Procedure?**

After the procedure, you will be moved to the intensive care unit (ICU) for careful monitoring. You may be given blood-thinning medicine. Patients who receive a transcatheter heart valve may be given blood-thinning medicine for 6 months after the procedure and aspirin for the rest of their lives, unless otherwise specified by their doctor. Patients who do not take blood-thinning medicine may be at increased risk of developing a dangerous blood clot after the procedure which may result in a stroke. Blood-thinning medicine may increase the risk of bleeding in the brain (stroke).

While in the hospital after the TAVR procedure, the following examinations will be completed:

- Physical exam
- Chest X-ray
- Blood tests
- Electrocardiography (ECG or EKG) (a test that records your heart's electrical activity)
- Ultrasound of your heart

You will remain in the ICU until your doctor feels you can be transferred to a regular hospital room, where you will continue to be monitored until you leave the hospital. The average ICU time is 4 days and the average hospital stay for the TAVR procedure is 8 days.

You should feel better soon after your procedure. Your doctor will give you specific instructions to help you with your recovery, which may include a special diet, exercise, and medicine. It is important to carefully follow your doctor's directions, especially if blood-thinning drugs are prescribed. Your doctor will monitor your medicine and advise you when or if you can stop taking it.

Regular check-ups by your doctor are very important. It is easier for patients with a replacement heart valve to get infections, which could lead to future heart damage. Call or see your doctor whenever you have questions or concerns about your health, especially if you experience any unusual problems such as bleeding, pain or other discomfort, or changes in your overall health.

Even after you have fully recovered from the procedure, your doctor may want to check your progress occasionally. You will need to take any medicine as prescribed and have your heart checked from time to time. Be sure to discuss all your medicine (including over-the-counter medicine) with your doctor, and don't change any dosage unless instructed to, even if you feel better.

**Always inform other doctors about your heart valve replacement before any medical or dental procedure. Before undergoing an MRI (magnetic resonance imaging) procedure, always notify the doctor (or medical technician) that you have an implanted heart valve. Failure to do so may result in damage to the valve that could result in death.**



## WARNINGS

- The safety of the valve implantation has not been established in patients who have:
  - A prosthetic heart valve already implanted in the aortic position.
  - Severe dysfunction of their left ventricle with an ejection fraction (fraction of blood pumped out of the left ventricle with each heart beat) < 20% (normal ejection fraction ranges between 50 and 65%).
  - A condition in which the heart muscle becomes thick. The thickening makes it harder for blood to leave the heart, forcing the heart to work harder to pump blood.
- The safety of the valve implantation has only been established in patients who have:
  - Senile degenerative aortic stenosis

14

## PRECAUTIONS

- Antibiotic medicine is recommended after the procedure in patients at risk for infection. Patients who do not take antibiotics may be at increased risk of infection.
- Patients who receive a transcatheter heart valve should stay on blood-thinning medicine for 6 months after the procedure and aspirin for the rest of their lives, unless otherwise specified by their doctor. Patients who do not take blood-thinning medicine may be at increased risk of developing a dangerous blood clot after the procedure which may result in a stroke. Blood-thinning medicine may increase the risk of bleeding in the brain (stroke).
- Long-term durability has not been established for the valve. Regular medical follow-up is advised to evaluate valve performance.

## HOW LONG WILL YOUR NEW VALVE LAST?

How long your new valve will last is unknown at this time. Edwards Lifesciences has tested the valve in the laboratory to replicate 5-year durability. All valves tested for 5-year durability passed the test. The first Edwards transcatheter heart valve was implanted in 2002.

The most common reason that a biological valve may fail is a gradual build-up of calcium (mineral deposits). In this situation, the valve may not work properly, which may cause your aortic stenosis to return, and possibly chest pain, shortness of breath, irregular heartbeat, and fatigue. Talk to your doctor if you experience any of these symptoms. Regular medical follow-up is essential to evaluate how your valve is performing.

## ADDITIONAL INFORMATION

For More Information on the Edwards TAVR Procedure

To contact Edwards Lifesciences for any inquiries:

**Toll free phone in the USA:**  
1.800.424.3278

**Phone from outside the USA:**  
+1.949.250.2500

**Email Address:**  
Tech\_Support@edwards.com

**Mail:**  
Edwards Lifesciences LLC  
1 Edwards Way  
Irvine, CA 92614 USA

**Online:**  
[www.yourheartvalve.com](http://www.yourheartvalve.com)  
(Under Resources)  
[www.edwards.com](http://www.edwards.com)  
(Click on "FOR PATIENTS")

## PATIENT IMPLANT CARD

**Edwards SAPIEN**

**Transcatheter Heart Valve**

**Instructions:** Please carry this card at all times after your procedure and show it to any medical personnel who may be treating you. If you do not receive one of these cards after your procedure, please contact your doctor.

**References**

1. Data on file at Edwards Lifesciences.

**CAUTION:** Federal (United States) law restricts the Edwards SAPIEN transcatheter heart valve to sale by or on the order of a physician. This device has been approved by the FDA for specific indications for use. See instructions for use for full prescribing information, including indications, contraindications, warnings, precautions and adverse events.

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Irvine, USA | Nyon, Switzerland | Tokyo, Japan | Singapore, Singapore | São Paulo, Brazil  
edwards.com





**MR Conditional**

Non-clinical testing has demonstrated that the Edwards SAPIEN THV (implant) is MR Conditional. It can be scanned safely under the following conditions:

- Static magnetic field of 1.5 Tesla (T) or 3.0 Tesla.
  - Spatial gradient field of 2500 Gauss/cm or less.
  - Maximum whole-body-averaged specific absorption rate (WB-SAR) of 2 W/kg for 15 minutes of scanning.
  - Normal mode operation, as defined in IEC 60601-2-33 Ed. 3.0, of the MR system.
- In non-clinical testing and analysis, the device was determined to produce a temperature rise of less than 1.1°C above background for a WB-SAR of 2 W/kg for 15 minutes of MR scanning in 1.5 T and 3.0 T cylindrical bore whole body MR systems.

The image artifact extended as far as 15 mm from the device for spin echo images and 40 mm for gradient images when scanned in non-clinical testing in a 3 T GE Signa HDx MR system. The implant has not been evaluated in MR systems other than 1.5 or 3.0 T.

Edwards Lifesciences MRI information available at [www.edwardsmri.com](http://www.edwardsmri.com).

Tel (USA) 800.424.3278

Tel (outside USA) 949.250.2500



Edwards

**Edwards Lifesciences Implanted Device ID Card**

Patient

Device Description

Follow-up Physician

Model

Implanting Physician

Implant Date

Serial No.

Hospital

Position

Size