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.

Please verify that you have the latest version of the instructions for use prior to using the device.

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.

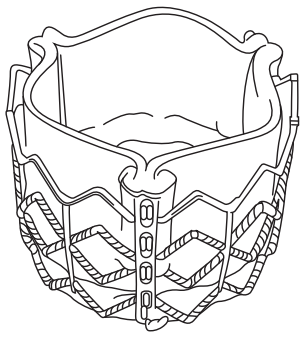
1.0 Device Description

- Edwards SAPIEN Transcatheter Heart Valve – Model 9000TFX (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

THV01



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

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

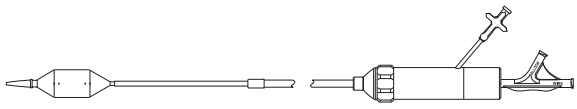
Native Valve Annulus Size (Tissue Annulus Diameter)	Bioprosthesis Diameter
18-22 mm	23 mm
21-25 mm	26 mm

- 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 markers as indicated in Figure 2.

Figure 2. RetroFlex 3 Delivery System

THV112



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, and RetroFlex 3 Delivery System are indicated for transfemoral delivery in patients with severe aortic 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.

3.0 Contraindications

The bioprosthesis is contraindicated in patients with:

- Non-calcified aortic annulus;
- Congenital unicuspid or congenital bicuspid aortic valve;
- Evidence of intracardiac mass, thrombus or vegetation, active infection or endocarditis.

4.0 Warnings

- 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.
- Observation of the pacing lead throughout the procedure is essential to avoid the potential risk of pacing lead perforation.
- 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, or 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.
- 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)

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.

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: abnormal lab values (including electrolyte imbalance); allergic reaction to anesthesia or to contrast media; anemia; angina; arrhythmia; bleeding; cardiovascular injury including perforation or dissection of vessels, ventricle, myocardium or valvular structures that may require intervention; conduction system injury (defect) which may require a permanent pacemaker; death; embolization including air, calcific valve material or thrombus; exercise intolerance or weakness; femoral AV fistula or pseudoaneurysm; fever; heart failure; heart murmur; hematoma; hemorrhage requiring transfusion or intervention; hypertension or hypotension; infection including septicemia and endocarditis; inflammation; myocardial infarction; pain or changes at the access site; paralysis; pericardial effusion or cardiac tamponade; peripheral ischemia or nerve injury; permanent disability; pleural effusion; pulmonary edema; renal insufficiency or renal failure; reoperation; respiratory insufficiency or respiratory failure; restenosis; retroperitoneal bleed; stroke/transient ischemic attack, clusters or neurological deficit; syncope.
- Additional potential risks specifically associated with the use of the bioprosthesis include, but may not be limited to the following: bleeding; cardiac arrest; cardiac failure or low cardiac output; cardiogenic shock; coronary flow obstruction/transvalvular flow disturbance; device degeneration; device embolization; device explant; device migration or malposition requiring intervention; device thrombosis requiring intervention; emergency cardiac surgery; endocarditis; hemolysis; hemorrhage; injury at the site of venous, arterial or ventricular access that may require repair; non-emergent reoperation; nonstructural

dysfunction; paravalvular/or transvalvular leak; 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, or other); valve regurgitation; valve stenosis; valve deployment in unintended location; valve thrombosis.

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. **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 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.**

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 ≥ 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.

Step	Procedure
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. **Note:** 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 provided by Edwards Lifesciences to syringe. 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.

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. **CAUTION: The physician must verify correct mounting/orientation of the bioprosthesis prior to its implantation.**
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 and re-flush the flex catheter and close the stopcock to the delivery system. **Note:** 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 ≥ 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.

Note: 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.

Step	Procedure
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. **CAUTION: The bioprosthesis should not be advanced through the sheath if the sheath tip is not past the aortic bifurcation.**
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	Begin bioprosthesis deployment: • Unlock the inflation device. • Begin rapid pacing; once arterial blood pressure has decreased to 50 mmHg or below, balloon inflation can commence. • 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. • De-articulate the delivery system and remove it from the sheath. **CAUTION: Patient injury could occur if the delivery system is not un-flexed prior to removal.**
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 sterilized with glutaraldehyde solution. The delivery system is 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 Devices

Used 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 (see Ref. 1)

The Placement of Aortic Transcatheter Valves (PARTNER) trial, a prospective, randomized-controlled, multi-center pivotal trial, evaluated the safety and effectiveness of the Edwards SAPIEN™ Transcatheter Heart Valve via transfemoral and transapical delivery to the standard therapy of patients in a stratified population of high-risk and inoperable patients with severe symptomatic aortic stenosis. Patients were stratified into two cohorts based on their risk of operability for standard aortic valve replacement surgery - those who were considered high surgical risk were eligible for Cohort A, while inoperable patients were eligible for Cohort B due to coexisting conditions that resulted in the probability of death or irreversible morbidity exceeding 50%. In Cohort A, patients were evaluated for transfemoral access, and those meeting the criteria were 1:1 randomized to either Transfemoral delivery of the Edwards SAPIEN valve or surgical aortic valve replacement. Patients stratified into 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 best medical management. Patients receiving best medical management 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 1-year 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^2, 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% with standard therapy (hazard ratio with TAVR, 0.51; 95% confidence interval [CI], 0.39 to 0.68; $P < 0.001$) (Figure 3). 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% with standard therapy (hazard ratio, 0.45; 95% CI, 0.35 to 0.59; $P < 0.001$) (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 (Figure 9). 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 who had received standard therapy (23.9% vs. 60.8%, $P < 0.001$). At 30 days, TAVR, as compared with standard therapy, 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%, $P < 0.001$). Clinical outcomes of TAVR as compared with standard therapy are summarized in Table 2. 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 standard therapy, 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 major strokes and major vascular events.

13.0 References

1. Leon, Martin et al. Transcatheter Aortic Valve Implantation for Aortic Stenosis in Patients Who Cannot Undergo Surgery. *N Engl J Med.* 2010, 1-11. This article (10.1053/NEJMoa1008232) was published on September 22, 2010 at NEJM.org

Table 1: Baseline Characteristics of the Patients and Echocardiographic Findings*			
	TAVR	Standard Therapy	
Characteristic	(N = 179)	(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
Logistic EuroSCORE‡	26.4 ± 17.2	30.4 ± 19.1	0.04
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)	0.2
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)	0.9
Frailty — no./total no. (%)§	21/116 (18.1)	33/118 (28.0)	0.09
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
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
Echocardiographic findings			
Aortic-valve area — cm^2	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)	0.9

* 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 implantation.

† 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.

‡ The logistic European System for Cardiac Operative Risk Evaluation (EuroSCORE), which measures patient risk at the time of cardiovascular surgery, is calculated with the use of a logistic-regression equation. Scores range from 0% to 100%, with higher scores indicating greater risk. A logistic EuroSCORE higher than 20% indicates very high surgical risk.

§ Frailty was determined by the surgeons according to prespecified criteria.

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

Figure 3

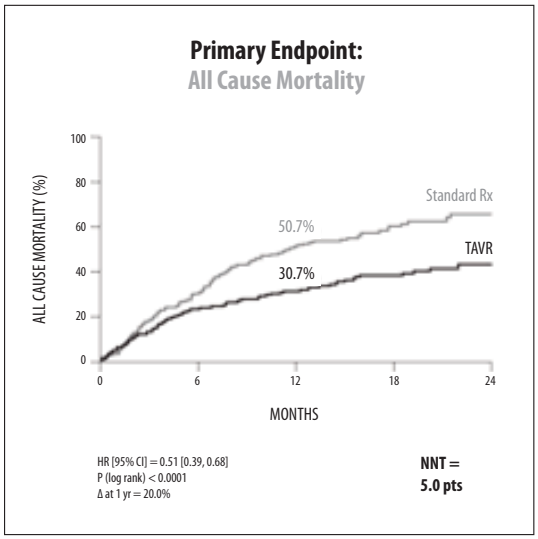


Figure 4

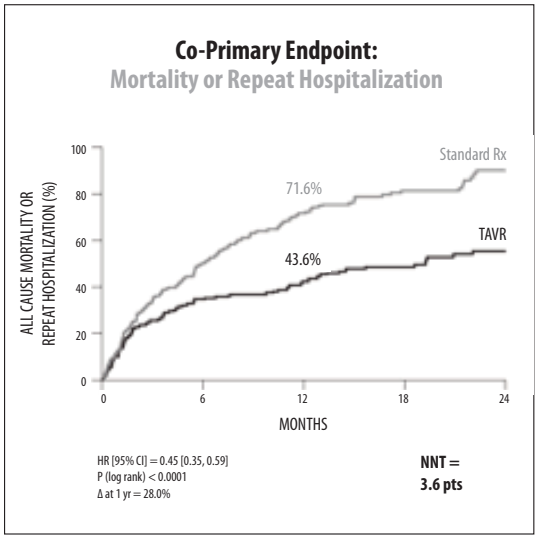


Figure 5

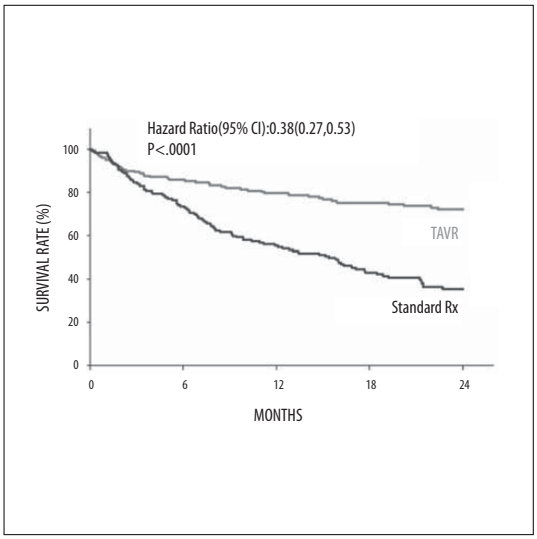


Figure 6

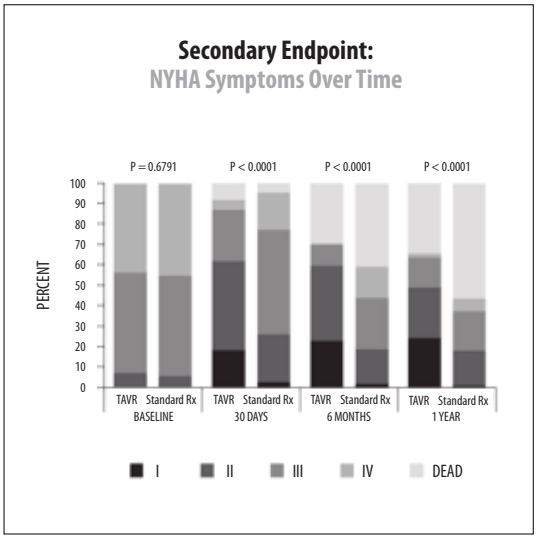


Figure 7

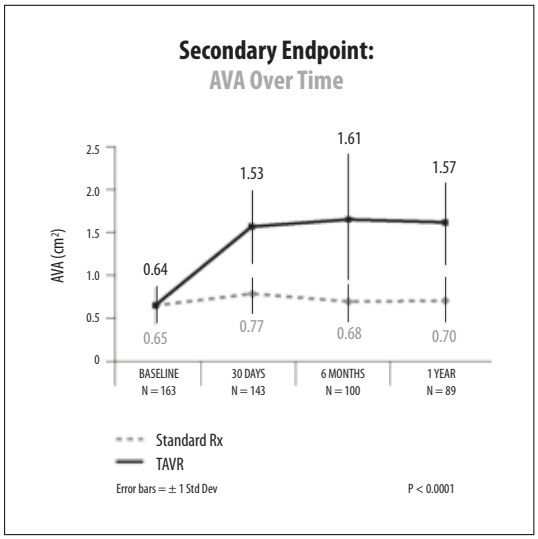


Figure 8

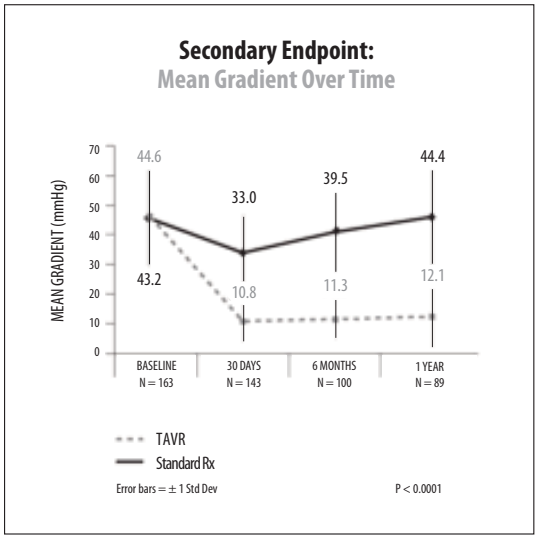


Figure 9

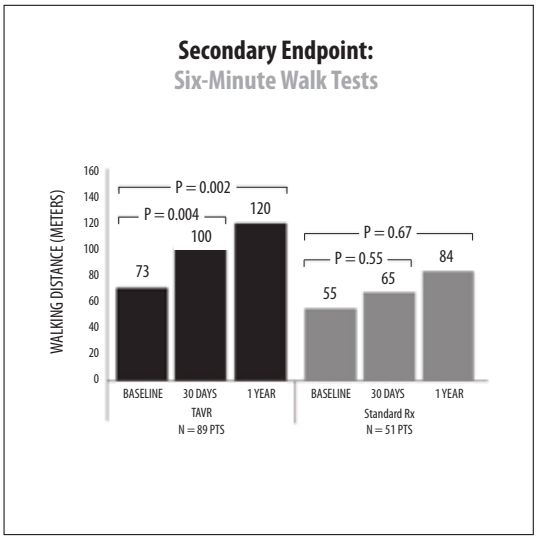


Table 2. Clinical Outcomes at 30 Days and 1 Year (ITT Population)						
	30 Days			1 Year		
Outcome	Transfemoral TAVR N = 179	Standard Care N = 179	*P*-Value[a]	Transfemoral TAVR N = 179	Standard Care N = 179	*P*-Value[a]
Death						
From any cause	9 (5.0)	5 (2.8)	0.41	55 (30.7)	89 (49.7)	< 0.001
From cardiovascular cause	8 (4.5)	3 (1.7)	0.22	35 (19.6)	75 (41.9)	< 0.001
Repeat hospitalization	10 (5.6)	18 (10.1)	0.17	40 (22.3)	79 (44.1)	< 0.001
Death from any cause or repeat hospitalization	20 (11.2)	22 (12.3)	0.74	78 (43.6)	126 (70.4)	< 0.001
TIA	0	0	-	1 (0.6)	0	1
All Stroke[g]	13 (7.3)	3 (1.7)	0.02	20 (11.2)	8 (4.5)	0.03
Major Stroke	10 (5.6)	2 (1.1)	0.04	15 (8.4)	7 (3.9)	0.12
Myocardial Infarction						
All	0	0	-	1 (0.6)	1 (0.6)	1
Peri-procedural	0	0	-	0	0	-
Hemorrhagic Vascular Complication[h]	90 (50.3)	25 (14.0)	< 0.0001	100 (55.9)	25 (14.0)	< 0.0001
Major Vascular Complication	30 (16.8)	2(1.1)	< 0.0001	31 (17.3)	4 (2.2)	< 0.0001
Renal Failure	2 (1.1)	2 (1.1)	1	4 (2.2)	5 (2.8)	0.59
Renal Insufficiency	1 (0.6)	0 (0.0)	1	2 (1.1)	3 (1.7)	1
Bleeding Event[h]	29 (16.2)	4 (2.2)	< 0.0001	31 (7.3)	4 (2.2)	< 0.0001
Cardiac reintervention						
Balloon aortic valvuloplasty	1 (0.6)[d]	2 (1.1)	1	1 (0.6)	66 (36.9)[e]	< 0.001
Repeat TAVR	3 (1.7)	NA	-	3 (1.7)	NA	-
Aortic-valve replacement	0	3 (1.7)	0.25	2 (1.1)[d]	17 (9.5)	< 0.001
Endocarditis	0	0	-	2 (1.1)	1 (0.6)	0.31
New Atrial Fibrillation	1 (0.6)	2 (1.1)	1	1 (0.6)	3 (1.7)	0.62
New pacemaker	6 (3.4)	9 (5.0)	0.6	8 (4.5)	14 (7.8)	0.27

NA = not applicable, TAVR = transcatheter aortic valve replacement, TIA = transient ischemic attack.
Data presented as n (%) of patients.

a. *p*-values are for between-group comparisons of the frequency of the event at each time point. Analyses were conducted using Fisher's exact test.
b. Deaths from unknown causes were assumed to be deaths from cardiovascular causes.
c. Repeat hospitalizations were included if they were due to aortic stenosis or complications of the valve procedure (e.g., TAVR).
d. 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.
e. 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.
f. Three patients underwent a repeat TAVR within 24 hours after the index TAVR procedure; four patients in the standard of care group who underwent TAVR at a nonparticipating, ex-US site are not included here.
g. Stroke per protocol definition as follows: Neurological deficit lasting ≥ 24 hours or lasting less than 24 with a brain imaging study showing an infarction
h. Per additional analysis requested by FDA with new definition.

06/11

Manufacturer
Edwards Lifesciences LLC
One Edwards Way
Irvine, CA 92614-5686 USA
Made in USA

Telephone 949.250.2500
800.424.3278
FAX 949.250.2525

Web IFU
199470001 A

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.

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

THV114

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.

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.
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

Supplied pouched and 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

Manufacturer
Edwards Lifesciences LLC
One Edwards Way
Irvine, CA 92614-5686 USA
Made in USA

Telephone 949.250.2500
800.424.3278
FAX 949.250.2525

Web IFU
199473001 A

Crimper
Model 9100CR23/ 9100CR26

Instructions for Use

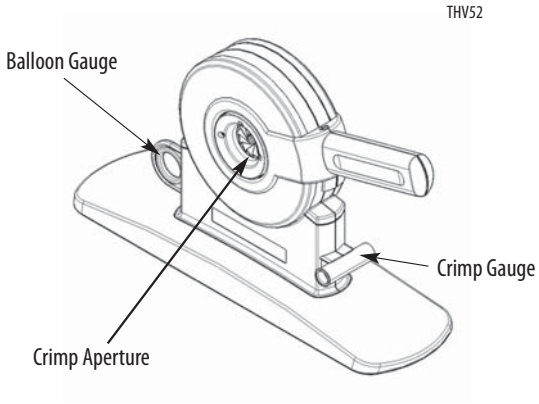
Caution: Federal (USA) law restricts this device to sale by or on the order of a physician.

Please verify that you have the latest version of the instructions for use prior to using the device.

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.

Figure 1. Crimper



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.

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

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.

Manufacturer
Edwards Lifesciences LLC
One Edwards Way
Irvine, CA 92614-5686 USA
Made in USA

Telephone 949.250.2500
800.424.3278
FAX 949.250.2525

Web IFU
199474001 A