Edwards SAPIEN Transcatheter Heart Valve with the Ascendra Balloon Catheter

Instructions for Use

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

Transapical 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.**

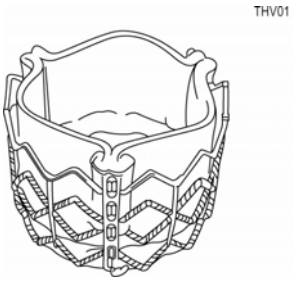
STERILE: The bioprosthesis is supplied sterilized with gluteraldehyde solution. The delivery system is supplied sterilized with ethylene oxide gas.

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



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

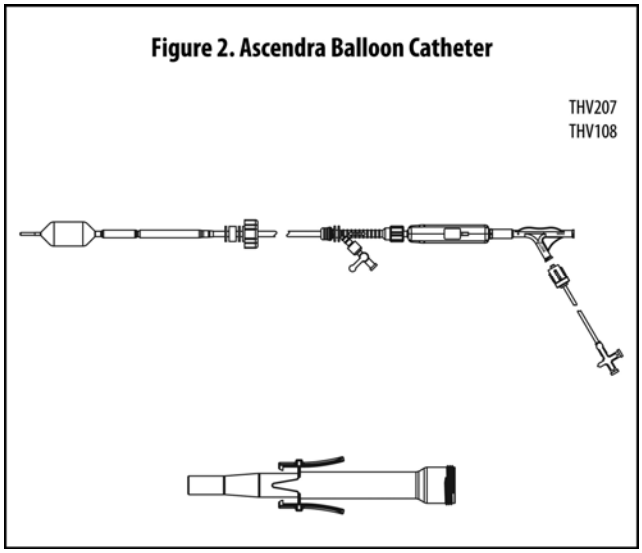
The following table identifies the bioprosthesis size that should be used based on native valve annulus size, as measured by transesophageal echocardiography (TEE).

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

- Ascendra Balloon Catheter – Model 9100BCL23 for 23 mm valve procedure and 9100BCL26 for 26 mm valve procedure (Figure 2)

The Ascendra Balloon Catheter is used for delivery of the Edwards SAPIEN Transcatheter Heart Valve. The balloon catheter has radiopaque markers for visualization under fluoroscopy and a balloon for deployment of the bioprosthesis. The system also comes with a loader that is used to cover the bioprosthesis during delivery. An extension tubing is supplied for use with the balloon catheter during inflation.

Figure 2. Ascendra Balloon Catheter



2.0 Indications

The Edwards SAPIEN™ Transcatheter Heart Valve, model 9000TFX, sizes 23mm and 26mm, is indicated for transapical delivery in patients with severe symptomatic native aortic valve stenosis who have been determined by two cardiac surgeons to be at high risk for surgical aortic valve replacement, not suitable for transfemoral delivery per heart team decision, and in whom existing co-morbidities would not preclude the expected benefit from correction of the aortic stenosis.

The Ascendra Balloon Catheter is indicated for the transapical 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, or the bioprosthesis is damaged, or the expiration date has elapsed.
- Do not mishandle the Ascendra Balloon Catheter 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.
- Care should be exercised in patients with hypersensitivities to chromium, nickel, molybdenum, manganese, copper, silicon, and/or polymeric materials
- The procedure should be conducted under fluoroscopic guidance. Some fluoroscopically guided procedures are associated with a risk of radiation injury to the skin. These injuries may be painful, disfiguring, and long-lasting.
- The safety and efficacy of the transapical procedure has not been evaluated in for only those patient populations where the transfemoral procedure delivery is not suitable.

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, 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^3), acute anemia (Hb <9 mg%), thrombocytopenia (platelet count <50,000 cells/mm^3), 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 <18 mm or >25 mm as measured by echocardiogram
- 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
- 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 transapical 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
- Mechanical failure of delivery system and/or accessories

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
- Injury at the site of ventricular access that may require repair
- 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, leaflet retraction, stent creep, suture line disruption of components of a prosthetic valve, thickening, stenosis)
- Device degeneration
- Paravalvular or transvalvular leak
- Injury to the mitral valve
- 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) soft, standard and extra-stiff guidewires
- 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
- 60 cc or larger luer-lock syringe
- High-pressure 3-way stopcock
- Edwards SAPIEN Transcatheter Heart Valve
- Ascendra Balloon Catheter
- 20 mm balloon valvuloplasty catheter such as Ascendra Balloon Aortic Valvuloplasty Catheter Model 9100BAVC
- Ascendra Introducer Sheath Set Model 9100IS
- 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: Bioprostheses 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 physiological 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 1 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 Transapical Procedure Components

Step	Procedure
1	Refer to Ascendra Introducer Sheath Set and Crimper instructions for use on device preparation and handling.
2	Remove the balloon cover from the Ascendra Balloon Catheter
3	Loosen the pusher nut and slide the pusher as far proximal as possible. Rotate the pusher nut to secure the pusher. Slide the loader cap, washers, and seal as far proximal as possible. **CAUTION: Overtightening the pusher nut may result in improper balloon inflation.**
4	Prime and flush the guidewire lumen of the balloon catheter with heparinized saline.
5	Insert an extra stiff guidewire (0.035" [0.89 mm] and ≥ 100 cm long) in the guidewire lumen, leaving a 2 to 3 cm segment of the guidewire protruding from the distal tip.
6	Flush the balloon catheter with heparinized saline through the flush port.
7	Attach extension tubing to balloon inflation port.
8	Prepare a 60 mL or larger luer-lock syringe with diluted contrast medium (15:85 contrast to heparinized saline) and attach it to the balloon extension tubing.
9	Completely fill the inflation device provided by Edwards Lifesciences with diluted contrast medium and attach to the balloon extension tubing.
10	Close stopcock to inflation device. De-air the balloon catheter.
11	Close the stopcock to the syringe. 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 balloon gauge. If the balloon does not reach the correct diameter when fully inflated, add or discard some of the inflation solution in the inflation device provided by Edwards Lifesciences until the correct diameter is reached.

Step	Procedure
	The inflation device must remain connected to the balloon catheter throughout the rest of the procedure. **Note:** Correct balloon sizing is critical to successful valve deployment and valve function.
12	Close stopcock to the balloon catheter and remove any remaining diluted contrast medium in the inflation device to the syringe. Lock the inflation device provided by Edwards Lifesciences.
13	Close the stopcock to the syringe and verify the balloon is sized appropriately with the balloon gauge. Remove the syringe.
14	Unlock inflation device provided by Edwards Lifesciences and deflate the balloon while creating a three-wing fold configuration, and ensure no diluted contrast medium is left behind. Lock the inflation device provided by Edwards Lifesciences.

7.2.3 Mount and Crimp the Bioprosthesis on the Balloon Catheter

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 balloon catheter with the inflow (fabric cuff end) of the bioprosthesis towards the proximal end of the balloon catheter. Center bioprosthesis between the radiopaque markers.
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	Loosen the pusher nut and advance the pusher to align the pusher tip with the proximal end of the crimped bioprosthesis. Rotate the pusher nut to secure the pusher in place. **CAUTION: Overtightening the pusher nut may result in improper balloon inflation.**
6	Flush the loader with sterile heparinized saline and slide the threaded end of the loader over the crimped bioprosthesis.
7	Slide the washers and seal on the balloon catheter shaft distally to the pusher. Insert into loader. Ensure washers and seal are flat against each other within the loader to prevent leakage. Slide loader cap distally over balloon catheter so it sits flat against the washers and seal and rotate the loader cap onto the base of loader. Check that the thread is not exposed. This indicates that the loader cap and seal are fully engaged around the pusher tubing. Do not overtighten the loader cap. **Note:** The loader must fully cover the bioprosthesis.
8	Re-flush the balloon catheter through the flush port and close stopcock to the balloon catheter. **Note:** Keep bioprosthesis hydrated until ready for implantation.
9	Remove guidewire and flush guidewire lumen.

7.3 Valvuloplasty and Bioprosthesis Delivery

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

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 Ascendra Balloon Aortic Valvuloplasty Catheter Instructions for Use (IFU) for information on device preparation and handling.

Note: Rapid ventricular pacing should be performed when using the Ascendra Balloon Aortic Valvuloplasty 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	Insert the introducer sheath. Refer to the Ascendra Introducer Sheath Set IFU for additional information on device preparation and handling.
2	Insert loader into the sheath until it locks. Tap lightly on the loader and loosen the loader cap to de-air. Tighten cap until loader is sealed and catheter can move with minimal resistance. Check that the thread is not exposed. This indicates that the loader cap and seal are fully engaged around the pusher tubing. Do not overtighten.
3	Cross the native aortic valve and position the bioprosthesis within the diseased valve.

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