

EDWARDS PERICARDIAL MITRAL BIOPROSTHESIS, MODEL 11000M

Instructions for Use

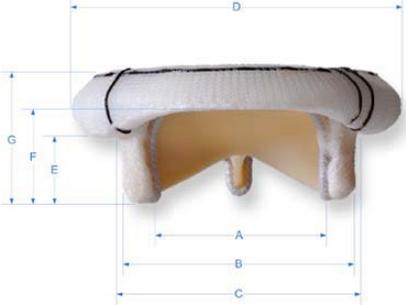
CAUTION: Federal (USA) Law restricts this device to sale by or on the order of a physician.

1. Device and Accessories Description

1.1 Device Description

The Edwards Pericardial Mitral Bioprosthesis, Model 11000M, is a stented trileaflet valve comprised of RESILIA bovine pericardial tissue that is mounted on a flexible frame. The valve is stored under dry packaging conditions and consequently does not require rinsing prior to implantation. The valve is available in sizes 25, 27, 29, 31 and 33 mm. See Table 1 for nominal dimensions.

Table 1. Nominal Dimensions

Edwards Pericardial Mitral Bioprosthesis, Model 11000M					
					
Size (mm)	25	27	29	31	33
A: Stent Diameter (Wireform, mm)	25	27	29	31	31
B: Tissue Annulus Diameter (mm)	28	29.5	31.5	33.5	33.5
C: External Stent Post Diameter (Tip, mm)	29	31	34	35	35
D: External Sewing Ring Diameter (mm)	36	38	40	42	44
E: Effective Profile Anterior (mm)	7	7.5	8	8.5	8.5
F: Effective Profile Posterior (mm)	10	10.5	11	11.5	11.5
G: Total Profile Height (mm)	15	16	17	18	18
Geometric Orifice Area (mm ²)	424	499	580	653	653
Note: For Sizing, See Section 10.4 Device Implantation					

RESILIA Tissue

RESILIA tissue is created with a novel technology called Edwards Integrity Preservation. The technology incorporates a stable-capping anticalcification process, which blocks residual aldehyde groups that are known to bind with calcium. The technology also incorporates tissue preservation with glycerol, which replaces the traditional storage in liquid-based solutions such as glutaraldehyde. The storage method eliminates tissue exposure to the residual unbound aldehyde groups commonly found in glutaraldehyde storage solutions

Valve Structure

The frame is designed to be compliant at the orifice as well as at the commissures. The compliance of the commissure supports is intended to reduce the loading shock at the valve commissures and free margin of the leaflets [Ref. 1]. The compliance of the orifice is intended to reduce the stress on the leaflets. The compliant orifice concept is based on the physiology and mechanics of natural heart valves and reported experience with implantation of unstented homografts [Refs. 2 & 3].

The lightweight wireform is made of a corrosion-resistant cobalt-chromium alloy, chosen because of its spring efficiency and fatigue-resistant characteristics, and is covered with a polyester fabric.

A thin cobalt-chromium alloy band and polyester band surround the base of the valve below the wireform frame providing structural support for the orifice. A silicone-rubber sewing ring that is covered with a porous, seamless polytetrafluoroethylene (PTFE) cloth is attached to the wireform frame, and facilitates tissue ingrowth and encapsulation. The sewing ring is scalloped along its anterior portion. Black silk suture markers on the anterior portion facilitate the orientation of the bioprosthesis and help avoid obstruction of the left ventricular outflow tract by a strut.

A black suture guide line circles the sewing ring. Placing sutures through the sewing ring and in the region form the suture guide line to the outer portion of the sewing ring eases needle penetration and provides variable compliance. The waffle has wider cells along the posterior portion, where calcifications or irregularities of the native mitral annulus are more frequent.

A holder is attached to the valve by means of sutures to facilitate handling and suturing the valve during implantation. The holder is detached by the surgeon. (See 11.4 Device Implantation).

Similar to other Edwards bioprosthetic valves, the cobalt-chromium alloy wireform in the model 11000M can be identified on fluoroscopy. This allows for identification of the valve's inflow and outflow edges.

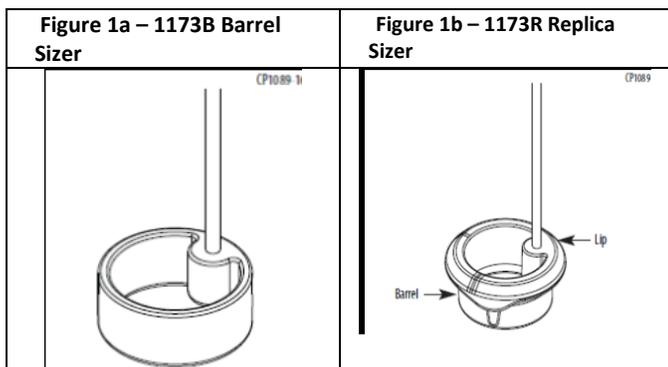
1.2 Sizers and Tray

Only sizers model 1173B (Figure 1a) or 1173R (Figure 1b) may be used with the 11000M bioprosthesis.

Caution: Do not use other manufacturer's valve sizers, or sizers for other Edwards Lifesciences valve prostheses to size the 11000M bioprosthesis.

Use only the sizers model 1173B or 1173R to determine the appropriate 11000M bioprosthesis size. Sizers model 1173B and 1173R permit direct observation of their fit within the annulus and are provided for each available 11000M bioprosthesis size. The barrel of the sizers model 1173B and 1173R indicate the external stent diameter at the base. The lip of the replica sizer 1173R replicates the sewing ring of the bioprosthesis, with its scalloped anterior portion and black markings, to determine the outcomes of specific suture or subvalvular apparatus preservation techniques.

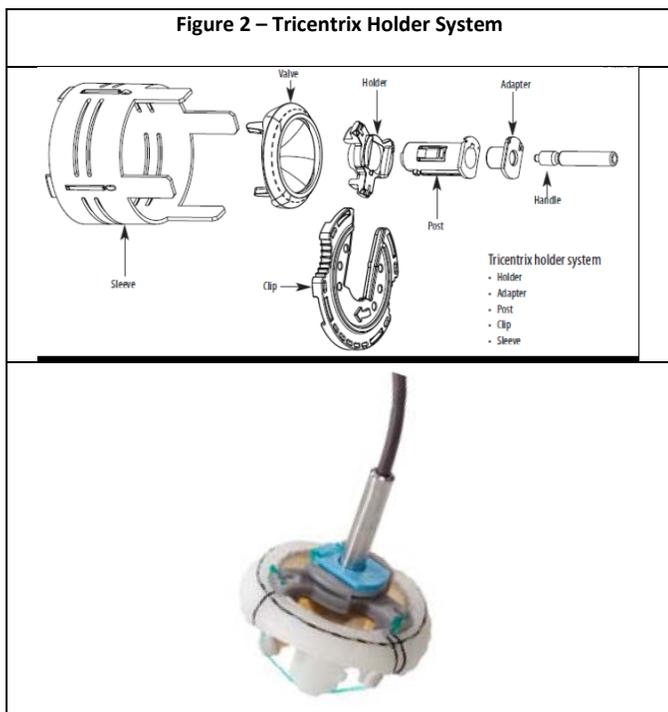
The sizers 1173B and 1173R are labeled with the bioprosthesis size. The complete set of sizers is housed in a tray, model SET1173, which can be reused and resterilized.



1.3 Valve Holder and Handle

Tricentrix Holder System and Handles

The holder/handle assembly consists of two components; the Tricentrix holder system (Figure 2) that is mounted to the 11000M bioprosthesis, and a handle (1111, 1117, 1173 or 1126) that is attached to the Tricentrix holder system at the time of surgery. The holder is detached by the surgeon. (See 11.4 Device Implantation).



The following handles (Table 2) may be used with the 11000M Bioprosthesis:

Table 2. Accessory Handles				
Model	Shaft Material	Overall Length		Reusable
		Inch	cm	
1111	Stainless Steel	7.0	17.8	Yes
1117	Nitinol	9.1	23.2	Yes
1126	Stainless Steel	11.5	29.2	No
1173	Nitinol	11.3	28.6	Yes

Handles with a nitinol shaft are more flexible than stainless steel. With each sterilization cycle, they return to their original straight shape for easier attachment to the holder.

2. Intended Use and Indications for Use

The Edwards Pericardial Mitral Bioprosthesis, Model 11000M, is intended for use as a heart valve replacement.

The Edwards Pericardial Mitral Bioprosthesis, Model 11000M, is indicated for the replacement of native or prosthetic mitral heart valves.

3. Contraindications

There are no known contraindications with the use of the Edwards Pericardial Mitral Bioprosthesis.

4. Warnings

FOR SINGLE USE ONLY. This device is designed, intended, and distributed for single use only. Do not resterilize or reuse this device. There are no data to support the sterility, non-pyrogenicity, and functionality of the device after sterile reprocessing.

DO NOT FREEZE OR EXPOSE THE VALVE TO EXTREME HEAT.

Exposure of the valve to extreme temperatures will render the device unfit for use. (Refer to Section 10.2 Storage, for recommended storage conditions).

DO NOT USE the valve:

- If the foil pouch, sealed trays or lids are opened, damaged, or stained
- If the expiration date has elapsed, or
- If it is dropped, damaged, or mishandled in any way. Should a valve be damaged during insertion, do not attempt repair.

DO NOT EXPOSE the valve to any solutions, chemicals, antibiotics, etc., except for sterile physiological saline solution. Irreparable damage to the leaflet tissue, which may not be apparent under visual inspection, may result.

DO NOT GRASP the leaflet tissue of the valve with instruments or cause any damage to the valve. Even the most minor leaflet tissue perforation may enlarge in time to produce significant impairment of valve function.

DO NOT OVERSIZE. Oversizing may cause valve damage or localized mechanical stresses, which may in turn injure the heart or result in leaflet tissue failure, stent distortion and regurgitation.

As with any implanted medical device, there is a potential for patient immunological response. Some components of the model 11000M are a metal alloy that contains cobalt, chromium, nickel, molybdenum, manganese, carbon, beryllium and iron. Care should be exercised in patients with hypersensitivities to these materials. This device was not made with natural rubber latex, but may have been produced in a latex-containing environment.

5. Adverse Events

5.1 Observed Adverse Events

As with all prosthetic heart valves, serious adverse events, sometimes leading to death, may be associated with the use of tissue valves. In addition, adverse events due to individual patient reaction to an implanted device or to physical or chemical changes

to the components, particularly those of biological origin, may occur at varying intervals (hours or days) necessitating reoperation and replacement of the prosthetic device.

The Edwards Pericardial Mitral Bioprosthesis, Model 11000M is similar in design to the Carpentier-Edwards PERIMOUNT Magna Mitral Ease Pericardial Bioprosthesis, Model 7300TFX.

Adverse events associated with the use of Carpentier-Edwards PERIMOUNT Pericardial Bioprostheses compiled from the literature and from reports received through the product surveillance system in accordance with the United States regulations establishing Good Manufacturing Practices, section 820.198, include stenosis, regurgitation through an incompetent valve, perivalvular leak, endocarditis, hemolysis, thromboembolism, thrombotic obstruction, bleeding diatheses related to the use of anticoagulation therapy, and malfunctions of the valve due to distortion at implant, fracture of the wireform, or physical or chemical deterioration of valve components. Types of tissue deterioration include infection, calcification, thickening, perforation, degeneration, suture abrasion, instrument trauma, and leaflet detachment from the valve stent posts. These complications may present clinically as abnormal heart murmur, shortness of breath, exercise intolerance, dyspnea, orthopnea, anemia, fever, arrhythmia, hemorrhage, transient ischemic attack, stroke, paralysis, low cardiac output, pulmonary edema, congestive heart failure, cardiac failure, and myocardial infarction.

5.2 Potential Adverse Events

Adverse events potentially associated with the use of valves and the surgical procedure include:

- Allergic reaction/immunological response
- Angina
- Annulus (damage, dissection, tear)
- Arterial dissection
- Asystole and/or cardiac arrest
- Bleeding
 - Peri- or post-procedural
 - Anticoagulant related
 - Pericardial tamponade
 - Hematoma
 - Hemorrhage
 - Cerebrovascular
- Blood – Coagulopathy
- Blood – Hemolysis/Hemolytic Anemia
- Blood – Anemia
- Blood Pressure alteration (hypotension, hypertension)
- Cardiac – Arrhythmias/Conduction Disturbances
- Cardiogenic shock
- Coronary artery ostia occlusion
- Deep vein thrombosis (DVT)
- Disseminated intravascular coagulation (DIC)
- Embolism
- Esophageal tear/rupture
- Endocarditis
- Hypoxemia
- Infection – local, wound or systemic
- Myocardial infarction
- Multi-system organ failure (MOF)
- Neurologic Events
 - Stroke (CVA)

- Transient Ischemic Attack (TIA)
- Pericardial effusion
- Pleural effusion
- Pulmonary edema
- Pneumonia
- Prosthetic Insufficiency – Regurgitation/Stenosis
- Reduced exercise tolerance
- Renal failure, acute
- Renal insufficiency
- Respiratory failure
- Thrombocytopenia, (Non-HIT)
- Thrombocytopenia, heparin induced (HIT)
- Thromboembolism
 - Arterial, venous, peripheral, central
- Transvalvular or Valvular Leaking
- Valve dislodgement/instability
- Valve - Nonstructural dysfunction
 - Paravalvular Leak
 - Leaflet impingement
 - Leaflet tissue damage (instruments /sutures)
 - Pannus
 - Prosthesis Mismatch (PPM) (due to inappropriate sizing)
 - Distortion at implant
- Valve – Structural dysfunction/deterioration
- Valve – Thrombosis

It is possible that these complications may lead to:

- Reoperation
- Explantation
- Permanent disability
- Death

6. Clinical Studies

The clinical safety and effectiveness of the Edwards Pericardial Mitral Bioprosthesis, Model 11000M was established based on the outcome data of the COMMENCE trial, which assessed the safety and effectiveness of the Model 11000A (aortic) and Model 11000M (mitral) valves.

The COMMENCE trial is an open-label, prospective, non-randomized, multicenter trial without concurrent or matched controls. Following a pre-surgical assessment, subjects are followed for one year to assess primary safety and effectiveness. Subjects are followed annually thereafter for a minimum of five years post-surgical experience.

The trial population in the mitral arm consisted of adult subjects (18 years or older) diagnosed with mitral valve disease requiring a planned replacement of the native or prosthetic mitral valve. Concomitant coronary bypass surgery and ascending aorta resection and replacement from the sinotubular junction without the need for circulatory arrest are permitted.

Trial candidates with prior valve surgery which included the implant of a prosthetic valve or annuloplasty ring that will remain *in situ* are excluded. Concomitant valve repair or replacement are excluded. Surgical procedures outside the cardiac area are not permitted. Various clinical presentations and histories may cause exclusion from the trial.

The reporting period for the COMMENCE trial is January 2013 through August 2017. At the time of the database lock, 777 subjects

were enrolled at thirty-four (34) investigational sites in the US and Europe. Of the enrolled population, 99.2% (771/777) of the subjects were successfully implanted with a trial valve. This includes 689 subjects treated with the Model 11000A at twenty-seven (27) sites and eighty-two (82) subjects treated with the Model 11000M at seventeen (17) sites.

Table 3 provides trial demographics, NYHA Classification and Risk Scores; Table 4 lists the combined observed adverse event rates during study; Table 5 lists the observed adverse event rates during study for the mitral cohort only; Table 6 gives the linearized late rates compared to the objective performance criteria (OPC); Table 7 lists linearized late rates for valve-related events compared to the OPC; Table 8 provides NYHA Classification data at baseline and 1-year follow-up; and Table 9 lists hemodynamic parameters at 1-year.

In the clinical study, the analysis of effectiveness is based on NYHA functional classification and echocardiography data at one (1) year. Improvement in NYHA classification from baseline to the one year visit was observed based on subjects with available data at both time intervals. Based on Echocardiographic Core Lab assessments of echocardiography data, 88.4% (61/69) of 11000M patients have no detectable or trivial mitral regurgitation at one year. Based on core lab assessments of echocardiography data, mean effective orifice areas (EOA) and mean gradients are consistent with current literature regarding other stented aortic bioprostheses and indicate acceptable hemodynamic performance of the Edwards Pericardial Mitral Bioprosthesis, Model 11000M.

The results from the COMMENCE clinical trial demonstrate a 0.1% observed rate of structural valve deterioration (SVD), with a 95% upper confidence interval of 0.7%, which is statistically less than 1% after 1-year of follow-up. All objective performance criteria (OPC)-defined adverse events are lower than the established standard of twice the FDA's Objective Performance Criteria for a bioprosthetic valve, with the exception of all bleeding and major bleeding. In the COMMENCE combined aortic and mitral cohorts, the upper 95% confidence limit for the linearized rate for all bleeding was 4.0% and major bleeding was 2.1%. For the mitral cohort alone, the upper 95% confidence limit for the linearized rate for all bleeding was 14.2% and for major bleeding was 9.8% which exceeds the FDA criterion of twice the OPC (all bleeding: 2.8% and major bleeding: 1.8%). However, detailed analysis of the major bleeding events showed no clear indication that the major bleeding events were directly related to Model 11000A or Model 11000M valves. The CEC adjudicated valve-related events are provided in Table 6.

Table 3. COMMENCE Trial Study Demographics Combined Aortic and Mitral Cohorts**Mitral Cohort Only**

Age at Implant	N: Mean ± SD (Min - Max)	N: Mean ± SD (Min - Max)
Age (years)	771: 67.2±11.4 (20.0, 90.0)	82: 68.9 ± 9.4
Sex	% (n / N)	
Female	31.4% (242/771)	58.5% (48/82)
Male	68.6% (529/771)	41.5% (34/82)
NYHA Classification	% (n/N)	% (n/N)
Class I	21.9% (169 / 771)	6.1% (5/82)
Class II	48.4% (373 / 771)	35.4% (29/82)
Class III/IV	29.7% (229 / 771)	58.5% (48/82)
Class III	26.2% (202 / 771)	41.5% (34/82)
Class IV	3.5% (27 / 771)	17.1% (14/82)
Risk Scores	N: Mean ± SD (Min - Max)	N: Mean ± SD (Min - Max)
STS risk of mortality (%) ¹	578: 2.2±2.3 (0.3, 23.3)	40: 4.8±4.7 (0.6, 23.3)
EuroSCORE II (%)	771: 3.1±4.0 (0.5, 36.0)	82: 8.0±7.5 (0.7, 36.0)

N is the number of subjects with available data for the given parameter.

¹STS scores only calculated for aortic arm subjects undergoing isolated AVR or AVR+CABG, and mitral arm subjects undergoing MVR or MVR+CABG.

Table 4. Observed Adverse Events – Combined Aortic and Mitral Cohort

Adverse Event or Outcome	Early¹ (N=771) n, m (%)	Late² (LPY³ = 1671.84) n, m, (%/pt-yr)	Freedom-from Event at 1 Year (POD 390) (SE)⁴
All mortality	9, 9, (1.2%)	39, 39, (2.3%)	0.972 (0.006)
Valve-related mortality	4, 4, (0.5%)	10, 10, (0.6%)	0.989 (0.004)
Reoperation	1, 1, (0.1%)	8, 8, (0.5%)	0.997 (0.002)
Explant	0, 0, (0.0%)	6, 6, (0.4%)	0.997 (0.002)
Thromboembolism	18, 19, (2.3%)	32, 35, (2.1%)	0.962 (0.007)
Valve thrombosis	0, 0, (0.0%)	0, 0, (0.0%)	1.000 (0.000)
All bleeding	7, 7, (0.9%)	48, 54, (3.2%)	0.948 (0.008)
Major bleed	6, 6, (0.8%)	24, 26, (1.6%)	0.972 (0.006)
All Paravalvular Leak	2, 2, (0.3%)	2, 2, (0.1%)	0.996 (0.002)
Major PVL	1, 1, (0.1%)	2, 2, (0.1%)	0.997 (0.002)
Endocarditis	0, 0, (0.0%)	11, 11, (0.7%)	0.995 (0.003)
Hemolysis	0, 0, (0.0%)	0, 0, (0.0%)	1.000 (0.000)
Structural Valve Deterioration	0, 0, (0.0%)	1, 1, (0.1%)	0.999 (0.001)

¹ For 'Early Events' (events occurring thru post-implant day 30): For 'Early' m is the number of events; n is the number of subjects experiencing an event; % = n/N.

² For 'Late Events' (events occurring after post-implant day 30): m is the number of events; n is the number of subjects experiencing an event; and % = m/LPY.

³ LPY: Late patient-years; LPY are calculated from post-implant day 31 until the last patient contact

⁴ Based on Kaplan-Meier analysis of time to first occurrence (early or late). Standard Error (SE) based on Greenwood's formula.

Table 5. Observed Adverse Events – Mitral Cohort Only

Adverse Event or Outcome	Early ¹ (N=82) n, m (%)	Late ² (LPY ³ = 114.65) n, m, (%/pt-yr)	Freedom-from Event at 1 Year (SE) ⁴
All-cause mortality	1, 1 (1.2)	7, 7 (6.1)	0.938 (0.027)
Valve-related mortality	1, 1 (1.2)	1, 1 (0.9)	0.988 (0.012)
Reoperation	0, 0 (0.0)	3, 3 (2.6)	0.983 (0.017)
Explant	0, 0 (0.0)	2, 2 (1.7)	0.983 (0.017)
Thromboembolism	2, 3 (2.4)	2, 2 (1.7)	0.963 (0.021)
Valve thrombosis	0, 0 (0.0)	0, 0 (0.0)	1.000 (0.000)
All bleeding	1, 1 (1.2)	9, 10 (8.7)	0.912 (0.032)
Major bleeding	1, 1 (1.2)	6, 6 (5.2)	0.937 (0.027)
All paravalvular leak	0, 0 (0.0)	0, 0 (0.0)	1.000 (0.000)
Major paravalvular leak	0, 0 (0.0)	0, 0 (0.0)	1.000 (0.000)
Endocarditis	0, 0 (0.0)	1, 1 (0.9)	1.000 (0.000)
Hemolysis	0, 0 (0.0)	0, 0 (0.0)	1.000 (0.000)
Structural Valve Deterioration	0, 0 (0.0)	1, 1 (0.9)	0.986 (0.014)

¹ For 'Early Events' (events occurring thru post-implant day 30): m is the number of events; n is the number of subjects experiencing an event; % = n/N.

² For 'Late Events' (events occurring after post-implant day 30): m is the number of events; n is the number of subjects experiencing an event; and % = m/LPY.

³ LPY: Late patient-years; LPY are calculated from post-implant day 31 until the last patient contact

⁴ Based on Kaplan-Meier analysis of time to first occurrence (early or late). Standard Error (SE) based on Greenwood's formula.

Table 6. Linearized late rates compared to the OPC – Combined Aortic and Mitral Cohort

Adverse Event or Outcome	Late ¹ (LPY ² = 1671.84) n, m, (%/pt-yr)	95% UCL ³	2X OPC ⁴
Thromboembolism	32, 35, (2.1%)	2.7%	5.0
Valve thrombosis	0, 0, (0.0%)	0.1%	0.4
All bleeding	48, 54, (3.2%)	4.0%	2.8
Major bleeding	24, 26, (1.6%)	2.1%	1.8
All paravalvular leak	2, 2, (0.1%)	0.3%	2.4
Major paravalvular leak	2, 2, (0.1%)	0.3%	1.2
Endocarditis	11, 11, (0.7%)	1.1%	2.4

¹ For 'Late Events' (events occurring after post-implant day 30): m is the number of events; n is the number of subjects experiencing an event; and % = m/LPY.

² LPY: Late patient-years; LPY are calculated from post-implant day 31 until the last patient contact

³ UCL is the one-sided 95% Upper Confidence Limit for the linearized rate.

⁴ FDA Objective Performance Criterion for tissue valves as described in Table R.1 of EN ISO 5840:2009, Annex R.1.

Table 7. Linearized late rates for valve-related events compared to the OPC – Combined Aortic and Mitral Cohort

OPC Event	Late Events Late pt-yrs = 1671.84 n, m (%/pt-yr)	Upper 95% CI	2X OPC
Thromboembolism	2, 2 (0.1)	0.3	5.0
Bleeding	0, 0 (0.0)	0.1	2.8
Major Bleeding	0, 0 (0.0)	0.1	1.8
Paravalvular Leak	2, 2 (0.1)	0.3	2.4
Major Paravalvular Leak	2, 2 (0.1)	0.3	1.2
Endocarditis	11, 11 (0.7)	1.1	2.4
Valve Thrombosis	0, 0 (0.0)	0.1	0.4
OPC Event	14, 15 (0.9)	1.3	.

'n' is the number of subjects with the event.

'm' is the number of events.

Major PV leaks are any PV Leak events resulting in surgical intervention or classified as an SAE.

Minor PV leaks are +3 or +4 on an echo core lab for a subject with without a major PV leak. The first echo reading of +3/+4 is considered the onset of the minor PV Leak. A +2 PV leak on a core lab echo is also considered a minor leak if associated with a hemolysis AE.

Table 8. NYHA Classification at Baseline and 1-Year

Cohort	NYHA Class	Baseline NYHA % (n / N ¹)	1-Year NYHA ² % (n / N ¹)
Combined Aortic and Mitral	Class I	21.8% (155 / 711)	82.8% (589 / 711)
	Class II	49.2% (350 / 711)	15.6% (111 / 711)
	Class III	26.0% (185 / 711)	1.3% (9 / 711)
	Class IV	3.0% (21 / 711)	0.3% (2 / 711)
Mitral Only	Class I	5.5% (4 / 73)	90.4% (66 / 73)
	Class II	38.4% (28 / 73)	9.6% (7 / 73)
	Class III	43.8% (32 / 73)	0.0% (0 / 73)
	Class IV	12.3% (9 / 73)	0.0% (0 / 73)

¹ N is the number of subjects who have both preoperative and 1 year NYHA data

² Improvement in NYHA observed demonstrated by a *p*-value < 0.0001 based on the test for marginal homogeneity after converting NYHA Class to numeric values (Class I = 1, Class II = 2, Class III = 3, Class IV = 4). Values of 0 were replaced with 0.5 to avoid sparseness of data.

Table 9. Hemodynamic Parameters at 1-Year – Mitral Cohort Only

Parameter	25 mm Mean ± SD (N ¹)	27 mm Mean ± SD (N ¹)	29 mm Mean ± SD (N ¹)	31 mm Mean ± SD (N ¹)	33 mm Mean ± SD (N ¹)
Mean Gradient (mmHg)	4.9 ± 1.2 (4)	4.1 ± 1.4 (25)	4.1 ± 1.5 (20)	3.9 ± 2.0 (12)	3.3 ± 1.4 (6)
EOA (cm ²)	1.1 ± 0.4 (4)	1.2 ± 0.3 (23)	1.5 ± 0.6 (20)	1.4 ± 0.5 (12)	1.5 ± 0.7 (6)

¹N represents the number of subjects with evaluable data for the specified valve size.

7. Post-Operation Management

Bioprosthetic heart valve recipients should be maintained on anticoagulation therapy, except where contraindicated, during the initial stages after implantation as determined by the physician on an individual basis. Long-term anticoagulation and/or antiplatelet therapy should be considered for patients with risk factors for thromboembolism.

8. Patient Selection

The ultimate judgment regarding care of a particular patient must be made by the healthcare provider and patient in light of all the circumstances presented by that patient (Ref. 4). A bioprosthesis is recommended for MVR in patients of any age who will not take warfarin or who have major medical contraindications to warfarin therapy. Patient preference is a reasonable consideration in the selection of mitral valve operation and valve prosthesis. A mechanical prosthesis is reasonable for MVR in patients under 65 years of age who do not have a contraindication to anticoagulation. A bioprosthesis is reasonable for MVR in patients under 65 years of age who elect to receive this valve for lifestyle considerations after detailed discussions of the risks of anticoagulation versus the likelihood that a second MVR may be necessary (Ref. 4).

8.1 Specific Patient Populations

The safety and effectiveness of the model 11000M valve has not been established for the following specific populations because it has not been studied in these populations:

- Patients who are pregnant;
- Nursing mothers;
- Patients with abnormal calcium metabolism (e.g., chronic renal failure, hyperparathyroidism);
- Patients with aneurysmal aortic degenerative conditions (e.g., cystic medial necrosis, Marfan's syndrome);
- Children, adolescents, and young adults
- Patients with hypersensitivity to metal alloys that contain cobalt, chromium, nickel, molybdenum, manganese, carbon, beryllium and iron.
- Patients with hypersensitivity to latex.

9. Patient Counseling Information

Careful and continued medical follow up (at least by an annual visit to the physician) is advised so that valve-related complications, particularly those related to material failure, can be diagnosed and properly managed. Patients with valves are at risk from bacteremia (e.g., undergoing dental procedures) and should be advised about prophylactic antibiotic therapy. Patients should be encouraged to carry their Patient Identification Card at all times and to inform their healthcare providers that they have an implant when seeking care.

10. How Supplied

10.1 Packaging

The Edwards Pericardial Mitral Bioprosthesis, Model 11000M, is provided sterile and nonpyrogenic, in a double barrier tray package. The double tray package is in a foil pouch which is in a carton. Upon receipt of the carton, inspect the exterior for signs of damage.

Each valve is contained in a carton with a temperature indicator displayed through a window on the side panel. The temperature indicator is intended to identify products that were exposed to transient temperature extremes. Upon receipt of the valve, immediately inspect the indicator and refer to the carton label to confirm a "Use" condition. If the "Use" condition is not apparent, do not use the valve and contact the local supplier or Edwards Lifesciences representative to make arrangements for return authorization and replacement.

Warning: Carefully inspect the valve before implantation for evidence of extreme temperature exposure or other damage. Exposure of the valve to extreme temperatures will render the device unfit for use.

10.2 Storage

The Edwards Pericardial Mitral Bioprosthesis, Model 11000M, should be stored at 10 °C to 25 °C (50-77 °F), in the foil pouch and shelf carton.

11. Directions for Use

11.1 Physician Training

The techniques for implanting this valve are similar to those used for any stented mitral surgical valve. Only surgeons who have received appropriate training in surgical valve implantation should use the device.

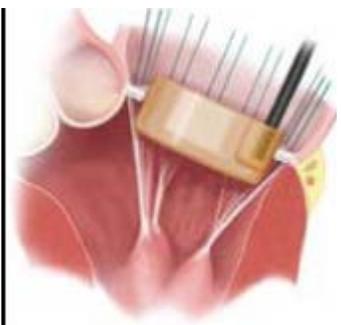
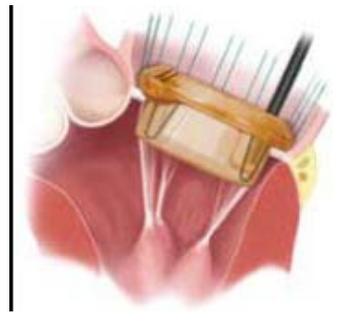
11.2 Sizing

Warning: Fragments of handles and sizers are not radio-opaque and cannot be located by means of an external imaging device.

Caution: Do not use other manufacturer's valve sizers, or sizers for other Edwards Lifesciences valves, to size the Edwards Pericardial Mitral Bioprosthesis, Model 11000M.

Caution: Examine sizers for signs of wear, such as dullness, cracking or crazing, prior to use. Replace sizer if any deterioration is observed.

Using the Model 1173B and 1173R sizers, select the cylindrical end of the largest diameter sizer that comfortably fits in the patient's annulus. The sizers 1173B and 1173R are labeled with the bioprosthesis size.

Step	Procedure
1	<p>Sizing with barrel sizer 1173B: To size with barrel sizer 1173B, pass the barrel portion of the sizer through the mitral annulus. Ensure the barrel portion is directly in plane of the mitral annulus.</p> 
2	<p>Sizing with replica sizer 1173R: To size with replica sizer 1173R, pass the barrel portion of the replica sizer through the mitral annulus so that the tip of the sizer, which simulates the sewing ring portion of the bioprosthesis, rests on the superior aspect of the annulus.</p> 

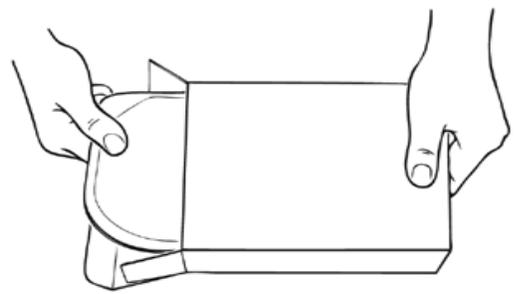
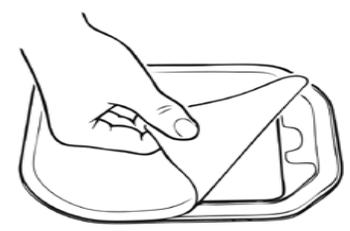
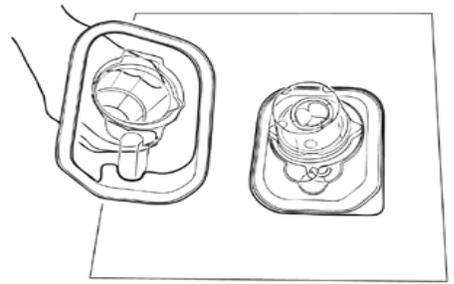
Some techniques such as use of pledgets, leaflet reefing, or mitral subvalvular apparatus preservation may further reduce the size of the mitral annulus which can result in the need for a smaller bioprosthesis to be implanted (Ref. 8). When using these techniques, it is recommended to re-size the annulus to avoid oversizing of the bioprosthesis. The consistent performance of the Edwards Pericardial Mitral Bioprostheses, Model 11000M makes oversizing unnecessary to achieve the desired hemodynamic performance in most patients.

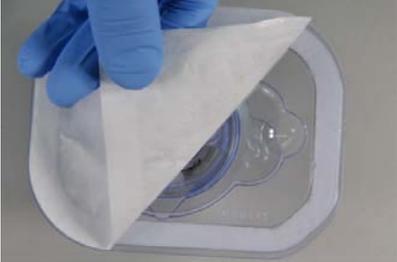
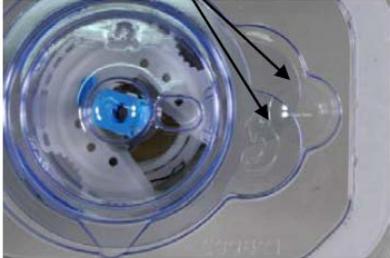
Due to the elastic nature of a chord, it may be extended by the Tricentrix holder system during implantation but retract back around the post once the holder is removed, entrapping leaflets and impairing function. Sizers 1173B and 1173R are made of a transparent material to allow visualization of the subvalvular apparatus during sizing. Make sure no chord will be in the way of the struts.

Caution: Exercise special care when using subvalvular apparatus preservation techniques to avoid chordae entrapment by a strut.

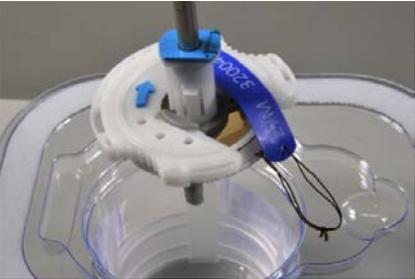
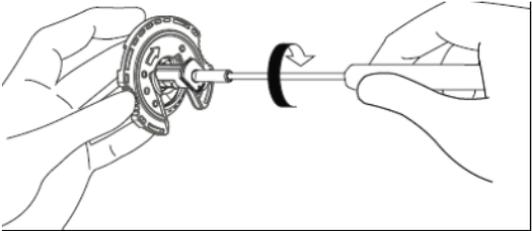
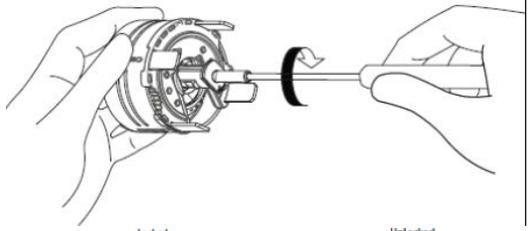
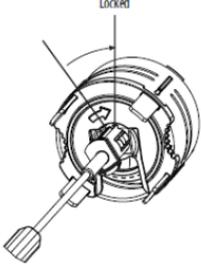
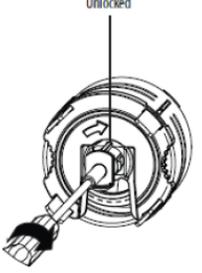
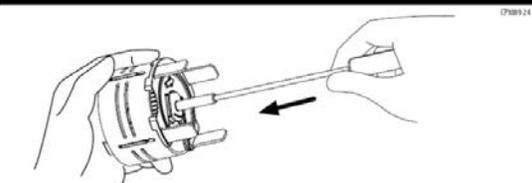
Warning: Avoid oversizing the bioprosthesis. Oversizing may cause bioprosthesis damage or localized mechanical stresses, which may in turn injure the heart or result in leaflet tissue failure, stent distortion and regurgitation.

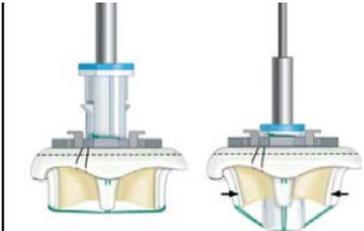
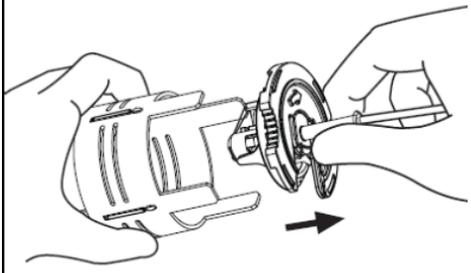
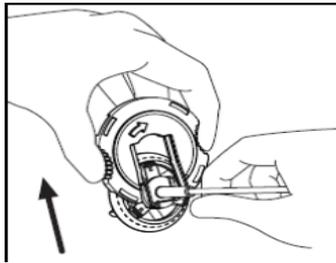
11.3 Handling and Preparation Instructions

Step	Procedure
1	<p>Warning: Check expiration date on packaging before use. Do not use product if expiration date has elapsed.</p> <p>Warning: Do not open foil pouch into sterile field. Foil pouch is a protective cover only. The innermost package tray may be introduced into the sterile field.</p> <p>Caution: Do not open the Edwards Pericardial Mitral Bioprosthesis, Model 11000M package until implantation is certain.</p>
2	<p>Once the appropriate size valve is chosen, remove the foil pouch from the carton in the non-sterile field. Before opening, examine the package for evidence of damage and broken or missing seals. Open pouch and remove tray in the non-sterile field.</p>  <p style="text-align: right;">HVT24</p>
3	<p>Near the sterile field, hold the base of the outer tray and peel the lid from the outer tray.</p>  <p style="text-align: right;">HVT25</p>
4	<p>The inner tray and contents are sterile. Transfer the inner tray to the sterile field. The contents of the inner tray must be handled using a sterile surgical technique to prevent contamination.</p>  <p style="text-align: right;">HVT26</p>

Step	Procedure
5	<p>Caution: Do not open the inner package until implantation is certain and the surgeon is ready to place the valve.</p> <p>Caution: The valve is not secured to the inner tray. Care should be taken while peeling the lid and opening the plastic tab.</p> <p>Before opening, examine the inner tray and lid for evidence of damage, stains, and broken or missing seals. Hold the base of the inner tray and peel the lid from the inner tray.</p>  <p>To access the bioprosthesis, remove the plastic cover by pulling up on both tabs. Discard the plastic cover.</p>  

Step	Procedure
6	<p>Attach the handle, Models 1111, 1117, 1126 or Model 1173, to the Tricentrix valve holder system while the valve is still in the tray. To attach, align the handle with the threaded hole in the valve holder and turn clockwise until a positive resistance is felt.</p>  <p>Caution: Do not grasp the valve with hands or surgical instruments.</p> <p>Caution: Examine the handle for signs of wear, such as dullness, cracking or crazing, prior to use. Replace handle if any deterioration is observed.</p> <p>Caution: The handle/holder assembly is required for implantation and should not be removed until the valve is sutured to the annulus.</p> <p>Caution: Care should be taken to avoid entangling the serial tag in the handle during attachment.</p>

Step	Procedure
7	<p>Once the handle is attached, remove the whole assembly (i.e. plastic sleeve, clip, the Tricentrix holder system and bioprosthesis) from the tray. The plastic sleeve is loosely fitted to the clip and may remain in the tray. This will not affect deployment.</p>  <p>Grasping the plastic sleeve or clip, continue the rotation to overcome the resistance until the white holder post reaches the unlock position.</p>  <p>Or</p>   
8	<p>Apply the required push force on the handle until the white holder post slides across the leaflets and snaps into its fully deployed position. An audible click may be heard as the deployment position is reached.</p> 

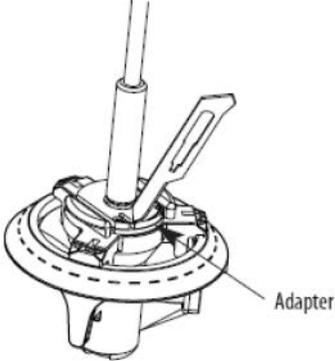
Step	Procedure
9	<p>Caution: If an adequate push force is not applied to the handle when deploying the Tricentrix holder system, the tenting system will not be secured and will not be able to minimize the potential for suture entrapment.</p> <p>Always check for proper deployment. There should be no more space between the blue adapter and the grey holder. The handle/post assembly should no longer be able to slide.</p> <p>The white holder post should protrude through the leaflets while the three commissures should deflect slightly towards the center of the bioprosthesis. The leaflets will temporarily be wrinkled by the deployed white holder post. When the holder is removed following implantation, the leaflets will return to their normal position.</p> 
10	<p>After deployment, remove the sleeve (if attached) by holding the handle and pulling the sleeve off the clip.</p> 
11	<p>Remove the clip by sliding it off the holder in a sideways direction.</p>  <p>Both sleeve and clip should be discarded.</p>

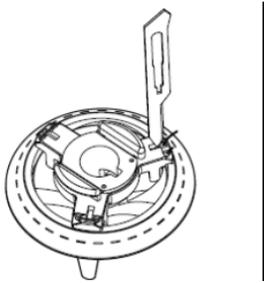
Step	Procedure
12	<p>A serial number tag is attached to the sewing ring of each bioprosthesis by a suture. This serial number should be confirmed with the number on the bioprosthesis package and bioprosthesis implant data card. This tag should not be detached from the bioprosthesis until implantation is certain.</p> <p>Caution: If any difference in serial number is noted, the bioprosthesis should be returned unused.</p> <p>Caution: Care should be exercised to avoid cutting or tearing the sewing ring cloth during removal of the serial number tag.</p> <p>Caution: To prevent damage to the sewing ring cloth, avoid pulling the knot of the serial tag suture through the sewing ring.</p>
13	<p>The model 11000M, DOES NOT REQUIRE RINSING prior to implantation.</p> <p>Caution: If the valve is rinsed prior to implantation, it must then be kept hydrated with sterile physiological saline irrigation on both sides of the leaflet tissue throughout the remainder of the surgical procedure. Rinsing every one to two minutes is recommended.</p> <p>Caution: Avoid contact of the leaflet tissue with towels, linens, or other sources of particulate matter that may be transferred to the leaflet tissue.</p>

Step	Procedure
1	<p>The surgeon should be familiar with the recommendations for proper sizing and placement in the supra-annular and/or intra-annular position (See 11.2 Sizing).</p> <p>Because of the complexity and variation of cardiac valve replacement surgery, the choice of surgical technique, appropriately modified in accordance with the previously described Warnings, is left to the discretion of the individual surgeon. In general, the following steps should be employed:</p> <ol style="list-style-type: none"> 1. Surgically remove the diseased or damaged valve leaflets and all associated structures deemed necessary. 2. Surgically remove any calcium from the annulus to ensure proper seating of the sewing ring of the valve to avoid damage to the delicate leaflet tissue. 3. Measure the annulus using only the mitral sizers, Models 1173B and 1173R (see Figures 1a – 1b.) 4. Proper seating of the prosthesis; 5. Tying sutures with the holder in place to minimize the potential for suture looping or chordal entrapment; 6. Examination of the bioprosthetic leaflets for distortion or leak during tying. <p>Caution: When choosing a valve for a given patient, the size, age, and physical condition of the patient in relation to the size of the valve must be taken into consideration to minimize the possibility of obtaining a suboptimal hemodynamic result. The selection of a valve, however, must ultimately be made by the physician on an individual basis after carefully weighing all of the risks and benefits to the patient.</p> <p>Caution: Adequate removal of calcium deposits from the patient’s annulus must be performed before implantation to avoid damage to the delicate bioprosthesis leaflet tissue as a result of contact with calcium deposits. Insert the sizer into the mitral annulus. The barrel of the sizer should always fit comfortably in the annulus.</p> <p>Caution: Use only sizers 1173B or 1173R during the selection of the bioprosthesis size; other sizers may result in improper valve selection (see 1.2 Accessory Description). Like other mitral bioprostheses, the Edwards Pericardial Mitral Bioprosthesis, Model 11000M is usually implanted using pledgeted mattress sutures. It is recommended to size the annulus after the sutures have been placed, as sutures may decrease the size of the bioprosthesis that can be implanted.</p>

11.4 Device Implantation

Step	Procedure
2	<p>Proper orientation of the bioprosthesis: Caution: The wireform frame of the Model 11000M bioprosthesis is symmetrical, and the three commissure supports (struts) are equally spaced. However, the sewing ring is designed for a specific orientation of the bioprosthesis. The scalloped part of the sewing ring, between the two silicone protrusions, should be placed across the intercommissural anterior portion of the annulus and straddle the left ventricular outflow tract.</p> <p>The contrasting suture markers in the sewing ring are intended to aid in proper orientation and denote a typical intercommissural distance. However, this distance may vary for each individual patient. On the left side, two close black sutures indicate where the first stitch should be placed and correspond to the anterior commissure. On the right side, only one black suture indicates the approximate location of the posterior commissure. Using these orientation aids, the third post should naturally fall in place in or around the middle of the posterior leaflet location.</p> <p>Caution: Special care must be exercised to avoid placing a strut in front of the left ventricular outflow tract, as it may impair the long-term hemodynamic performance.</p>

Step	Procedure
3	<p>Suture Placement: A black suture guide line circles the sewing ring. When placing sutures through the sewing ring, sliding drag forces are reduced when sutures are placed straight through the sewing ring and in the region from the suture guide line to the outer portion of the sewing ring.</p> <p>Firm tension must be maintained on the sutures as the bioprosthesis is lowered into the annulus; this minimizes the potential for formation of suture loops that might entrap a leaflet. This, when combined with the fully retracted stent posts when the Tricentrix holder system is in place, helps guide the sutures into their correct position behind the struts and onto the sewing ring.</p> <p>Remove the handle prior to tying the sutures. The handle and blue adapter must be removed as an assembly. Maintain the bioprosthesis placement in the annulus by gently placing forceps or gloved hands onto the holder and cutting the green thread on the blue adapter. Remove the blue adapter and handle assembly as one unit.</p>  <p>The diagram shows a top-down view of the bioprosthesis assembly. A central handle with a long shaft is inserted into the device. A blue adapter is attached to the base of the handle. A dashed line indicates the suture guide line around the sewing ring. A label 'Adapter' points to the blue component.</p>

Step	Procedure
4	<p>Caution: Avoid looping or catching a suture around the open cages, free struts, or commissure supports of the bioprosthesis, which would interfere with proper valvular function. To minimize the potential for suture looping, it is essential to leave the deployed holder in place until all knots are tied.</p> <p>However, if leaving the holder in place obstructs the surgeon's view, all the sutures adjacent to each of the three frame struts must be tied down before cutting the three green holder attachment threads to remove the holder.</p> <p>Caution: If the deployed holder attachment threads are cut before these adjacent sutures are tied down, the holder will no longer minimize the potential for suture looping around the frame struts.</p> <p>Special attention must be given to avoid tying the sutures on top of the corners of the holder's grey legs. Before tying each suture, examine the leaflets while holding the two strands of the suture under tension. Distortion or movement of the leaflets during this maneuver suggests that the suture is looped around a strut. At no point before or after holder removal should tension on the sutures be released as this may facilitate formation of loops in the sutures and possible entrapment. It is recommended to place a surgical mirror through the leaflets after the holder removal in order to examine each strut and proper suture placement.</p> <p>Caution: When using interrupted sutures, it is important to cut the sutures close to the knots and to ensure that exposed suture tails will not come into contact with the leaflet tissue (Ref. 8).</p> <p>The Tricentrix holder system is removed as a unit at the completion of the suturing procedure as follows:</p>  <ol style="list-style-type: none"> 1. Cut each of the three (3) exposed green sutures using a scalpel or scissor placed only in the cutting channel. Never attempt to cut a suture below a partially separated holder as a part of the attaching suture may fall in the ventricle. Avoid cutting or damaging the stent or leaflet tissue when cutting the sutures. 2. When all three (3) attaching sutures have been properly cut, remove the Tricentrix holder system from the bioprosthesis as a unit, along with attaching sutures, using sterile gloved hands or protected forceps. 3. Following surgery, remove the holder and discard.

11.5 Accessory Cleaning and Sterilization

The accessories for the Edwards Pericardial Mitral Bioprosthesis, Model 11000M, are packaged separately. Handle model 1126 is provided sterile and is intended for single use only. Handle models 1111, 1117 and 1173 and sizer models 1173B and 1173R are supplied nonsterile and must be cleaned and sterilized before use. The handles, sizers, tray base and tray lid must be cleaned and

resterilized prior to each use. Refer to the Instructions for Use supplied with the reusable accessories for cleaning and sterilization instructions.

11.6 Return of Valves

Edwards Lifesciences is interested in obtaining recovered clinical specimens of the Edwards Pericardial Mitral Bioprosthesis, Model 11000M, for analysis. Contact the local representative for return of recovered valves.

- Unopened Package with Sterile Barrier Intact: If the foil pouch or trays have not been opened, return the valve in its original packaging.
- Package Opened but Valve is Not Implanted: If the tray is opened, the valve is no longer sterile. If the valve is not implanted, it 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.
- Explanted Valve: The explanted valve 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.

12. MRI Safety Information



Non-clinical testing has demonstrated that the Edwards Pericardial Mitral Bioprosthesis, Model 11000M, is MR Conditional. A patient with the Edwards Pericardial Mitral Bioprosthesis, Model 11000M, can be scanned safely under the following conditions:

- Static magnetic field of 1.5 tesla or 3 tesla only.
- Maximum spatial gradient magnetic field of 3,000 gauss/cm (30 T/m) or less.
- Maximum MR system-reported, whole-body averaged specific absorption rate (SAR) of 2.0 W/kg in Normal Operating Mode.

Under the scan conditions defined above, the Edwards Pericardial Mitral Bioprosthesis, Model 11000M, is expected to produce a maximum in vivo temperature rise of 2.3°C after 15 minutes of continuous scanning.

In non-clinical testing, the image artifact extends approximately 11.5 mm from the model 11000M valve when imaged with a spin echo pulse sequence and 36 mm from the device when imaged with a gradient echo pulse sequence and a 3 tesla MRI system. The artifact obscures the device lumen.

13. Patient Labeling

13.1 Patient Identification Card

A Patient Identification Card is provided to each patient implanted with the Edwards Pericardial Mitral Bioprosthesis, Model 11000M.

13.2 Patient Information

Patient information materials may be obtained from Edwards or an Edwards clinical sales specialist.

14. References

1. Reis, Robert L., et al. The Flexible Stent. A new concept in the fabrication of tissue heart valve prostheses. J. Thorac Cardiovasc Surg 1971, 62(5):683:689.
2. Barrat-Boyes, B.G. and A.H.G. Roche. A review of aortic valve homografts over a six and one-half year period. Ann Surg 1969, 170:483-492.
3. Brewer, R.J., et al. The dynamic aortic root. Its role in aortic valve function. J Thorac Cardiovasc Surg 1976, 72:413-417. Reis, Robert L., et al.
4. The Flexible Stent. A New Concept in the Fabrication of Tissue Heart Valve Prostheses. J Thorac Cardiovasc Surg 1971, 62(5):683-689 and 693-695.
5. Bonow R.O., et al. ACC/AHA Guidelines for the Management of Patients with Valvular Heart Disease: A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee on Management of Patients With Valvular Heart Disease). J Am Coll Cardiol 2014, 63:e57-185.

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