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Carpentier-Edwards PERIMOUNT

Magna Ease Pericardial Bioprosthesis

Model 3300TFX Aortic

A PERI valve

For single use only

1.0 Device Description

The Edwards Carpentier-Edwards PERIMOUNT Magna Ease aortic pericardial bioprosthesis model 3300TFX (also referred to as the Magna Ease aortic bioprosthesis) is a trileaflet bioprosthesis comprised of bovine pericardium that has been preserved in a buffered glutaraldehyde solution and mounted on a flexible frame. The bioprosthesis is treated according to the Edwards ThermaFix process, which involves heat treatment of the tissue in glutaraldehyde and uses ethanol and polysorbate-80 (a surfactant). The bioprosthesis is packaged and terminally sterilized in glutaraldehyde. Glutaraldehyde is shown to both reduce the antigenicity of tissue xenograft bioprostheses and increase tissue stability (Refs. 10 & 12). Glutaraldehyde alone has not been shown to affect or reduce the calcification rate of the bioprosthesis.

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. 42). The compliance of the orifice is intended to reduce the stress on the leaflet. The compliant orifice concept is based on the physiology and mechanics of natural heart valves and reported experience with implantation of unstented homografts (Refs. 5 & 7).

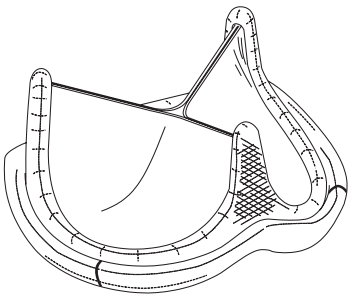
The lightweight wireform frame is made of Elgiloy, a corrosion-resistant alloy, chosen because of its superior spring efficiency and fatigue-resistant characteristics, and is covered with a woven polyester fabric.

A thin Elgiloy/polyester film laminate band surrounds the base of the wireform frame providing structural support for the orifice. To this frame is attached a soft, silicone-rubber suture ring that is covered with a porous, seamless polytetrafluoroethylene cloth to facilitate tissue ingrowth and encapsulation. The aortic sewing ring has been scalloped to conform to the natural aortic root.

The compliant nature of the suture ring facilitates coaptation between the bioprosthesis and an often irregular or calcific tissue bed.

An integral valve holder is attached to the valve by means of sutures to facilitate handling and suturing the valve during implantation. The holder is easily detached by the surgeon (see **11.2 Handling and Preparation Instructions**).

The sewing ring diameter and profile height on the Magna Ease aortic bioprosthesis has been reduced to facilitate implantation in patients with small aortic roots. The sewing ring has three equally spaced markers to aid in orientation.



Model 3300TFX PERIMOUNT Magna Ease Aortic Bioprosthesis

2.0 Indications for Use

Pericardial valves are indicated for use in patients suffering from valvular heart disease. Aortic valvular heart disease is a condition involving any of the following: obstruction of the aortic heart valve or stenosis; leakage of the aortic valve, known as regurgitation, incompetence, or insufficiency; and combinations of the two, sometimes referred to as mixed disease or combined lesions.

Aortic valvular heart disease may be caused by any number of factors, including congenital abnormalities, infection by various microorganisms, degenerative calcification, and rheumatic heart disease.

Pericardial valves are used particularly in those patients for whom long-term anticoagulation is contraindicated or who may be difficult to maintain on anticoagulation therapy.

The Magna Ease aortic bioprosthesis is intended for use in patients whose aortic valvular disease is sufficiently advanced to warrant replacement of their natural valve with a prosthetic one. It is also intended for use in patients with a previously implanted aortic valve prosthesis that is no longer functioning adequately and requires replacement. In the latter case, the previously implanted prosthesis is surgically excised and replaced by the replacement prosthesis. The bioprosthesis can be implanted in either the supra-annular or intra-annular position.

3.0 Contraindications

Do not use if surgeon believes such would be contrary to the best interests of the patient. The actual decision for or against the use of this bioprosthesis must remain with the surgeon who can evaluate all the various risks involved, including the anatomy and pathology observed at the time of surgery.

4.0 Warnings

FOR SINGLE USE ONLY. This device is designed, intended, and distributed for **SINGLE USE ONLY. DO NOT RE-STERILIZE OR REUSE THIS DEVICE**. There are no data to support the sterility, non-pyrogenicity, and functionality of the device after reprocessing. Exposure of the bioprosthesis or container to irradiation, steam, ethylene oxide, or other chemical sterilants will render the bioprosthesis unfit for use. Such action could lead to illness or an adverse event, as the device may not function as originally intended.

DO NOT RESTERILIZE THE BIOPROSTHESIS BY ANY METHOD. Exposure of the bioprosthesis or container to irradiation, steam, ethylene oxide, or other chemical sterilants will render the bioprosthesis unfit for use.

DO NOT FREEZE OR EXPOSE THE BIOPROSTHESIS TO EXTREME HEAT. Exposure of the bioprosthesis to extreme temperatures will render the device unfit for use. Each bioprosthesis is contained in a carton with a temperature indicator displayed through a window on the side panel. The temperature indicator is intended to monitor the temperature that the device is exposed to during transit and storage. If the indicator displays any reading other than "OK" do not use the bioprosthesis.

DO NOT USE the bioprosthesis if the tamper evident seal is broken.

DO NOT USE the bioprosthesis if expiration date has elapsed. There are no data to support the function and performance of the device beyond the expiration date.

DO NOT USE the bioprosthesis if the container is leaking, damaged, or the glutaraldehyde solution does not completely cover the bioprosthesis. Failure to maintain tissue moisture may lead to compromised sterility and/or bioprosthesis function.

DO NOT EXPOSE the bioprosthesis to any solutions, chemicals, antibiotics, etc., except for the storage solution or sterile physiological saline solution, as irreparable damage to the leaflet tissue may result that is not apparent under visual inspection.

DO NOT ALLOW the bioprosthesis to dry. It must be kept moist at all times. Maintain tissue moisture with sterile physiological saline irrigation on both sides of the leaflet tissue. Failure to maintain tissue moisture may lead to compromised bioprosthesis function.

DO NOT PASS CATHETERS, transvenous pacing leads, or any surgical instrument across the bioprosthesis with the exception of a surgical mirror used to examine suture placement. Other surgical devices may cause tissue damage.

DO NOT USE the bioprosthesis if it has been dropped, damaged, or mishandled in any way. Should a bioprosthesis be damaged during insertion, do not attempt repair. Such action could lead to illness or an adverse event, as the device may not function as originally intended.

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

DO NOT OVERSIZE. 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 valve regurgitation.

Clinical data that establish the safety and efficacy of the bioprosthesis for use in patients under the age of 20 are not available; therefore, we recommend careful consideration of its use in younger patients.

The decision to use a tissue valve must ultimately be made by the physician on an individual basis after a careful evaluation of the short- and long-term risks and benefits to the patient and consideration of alternative methods of treatment. Long-term durability has not been established for bioprostheses.

As with any implanted device, there is potential for an immunological response. Some components of the model 3300TFX 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.

Serious adverse events, sometimes leading to replacement of the bioprosthesis and/or death, may be associated with the use of prosthetic valves (see **6.0 Adverse Events**). A full explanation of the benefits and risks should be given to each prospective patient before surgery.

Note: Bioprostheses should be used with caution in the presence of severe systemic hypertension or when the anticipated patient longevity is longer than the known longevity of the prosthesis (see 7.0 Clinical Studies).

Careful and continuous medical follow-up (at least by an annual visit to the physician) is advised so that bioprosthesis-related complications, particularly those related to material failure, can be diagnosed and properly managed.

Recipients of prosthetic heart valves who are undergoing dental procedures should receive prophylactic antibiotic therapy to minimize the possibility of prosthetic infection.

Bioprosthetic heart valve recipients should be maintained on anticoagulant therapy (except where contraindicated) during the initial healing stages after implantation, approximately 2 to 3 months. Anticoagulants should then be discontinued over a period of 10 days, except in those patients for whom indefinite anticoagulant protection is indicated, i.e., in the absence of sinus rhythm and in patients with a dilated left atrium, calcification of the atrial wall, or history of previous atrial thrombus. However, the appropriate anticoagulation therapy must be determined by the physician on an individual basis (Ref. 1).

Adequate rinsing with physiological saline, as described in the Technique section, is mandatory before implantation to reduce the glutaraldehyde concentration. No other solutions, drugs, chemicals, antibiotics, etc., should ever be added to the glutaraldehyde or rinse solutions, as irreparable damage to the leaflet tissue, which may not be apparent under visual inspection, may result.

5.0 Precautions

- The outside of the jar is not sterile and must not be placed in the sterile field.
- Adequate rinsing with physiological saline must be performed before implantation to reduce the glutaraldehyde concentration.
- Adequate removal of calcium deposits from the patient's annulus must be performed before implantation to avoid damage to the delicate prosthetic valve leaflet tissue as a result of contact with calcium deposits.
- Glutaraldehyde may cause irritation of the skin, eyes, nose, and throat. Avoid prolonged or repeated exposure 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 the eyes, seek immediate medical attention. For more information about glutaraldehyde exposure, please refer to the Material Safety Data Sheet MSDI0424 available from Edwards Lifesciences.

- The Magna Ease aortic bioprosthesis has a unique configuration designed to fit above the patient annulus or within the annulus. The surgeon should be familiar with the recommendations for proper sizing and placement in the supra-annular or intra-annular position. Refer to the Device Implantation section (11.3) for further details.
- Handle the bioprosthesis only with Edwards Lifesciences accessories. Only Edwards sizers should be used during the selection of the bioprosthesis size; other sizers may result in improper bioprosthesis selection.
- **When choosing a bioprosthesis for a given patient, the size, age, and physical condition of the patient in relation to the size of the prosthesis must be taken into consideration to minimize the possibility of obtaining a suboptimal hemodynamic result. The selection of a bioprosthesis, however, must ultimately be made by the physician on an individual basis after carefully weighing all of the risks and benefits to the patient.**
- Due to the relative flexibility of the frame, **care must be exercised to prevent folding or deformation of the stent** that may lead to regurgitation, altered hemodynamics, and/or leaflet disruption rendering the bioprosthesis incompetent. In this regard oversizing must be avoided.
- The spacing of the sutures in the remnant of the valvular orifice and the prosthesis suture ring must be carefully matched to avoid folding of the leaflets or distortion of the orifice. Edwards Lifesciences has received reports in which individual mattress sutures, spanning a distance of 10 to 15 mm, produced a pursestring effect causing compression of the valve orifice.
- 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. Cases have been reported in which bioprostheses developed severe regurgitation and had to be replaced as a result of wear due to contact with sutures (Ref. 2).
- Unlike rigid mechanical valves, the stent wall is soft and will not resist needle penetration. Accordingly, extreme care must be exercised when placing sutures through the sewing margin to avoid penetration of the side wall of the stent and possible laceration of the leaflet tissue.
- As with all prostheses that have open cages, free struts, or commissure supports, care must be exercised to avoid looping or catching a suture around the commissure, which would interfere with proper valvular function.
- The stent of the aortic bioprosthesis is symmetrical, and the commissure supports (struts) are equally spaced. The struts should correspond to the remnants of the natural commissures so as not to obstruct the coronary ostia.
- A serial number tag is attached to the sewing ring of each bioprosthesis by a suture. This serial number should be checked against the number on the jar and implantation data card; if any difference is noted, the bioprosthesis should be returned unused. This tag should not be detached from the bioprosthesis until implant is imminent. Care should be exercised to avoid cutting or tearing the suture ring cloth during removal.
- Careful handling is required for all implantable devices. If the bioprosthesis is dropped, damaged, or mishandled in any way, it must not be used for human implantation.
- Based on reports in the literature on tissue valves (Refs. 3, 18, 23, 26, 48, 49, & 54), there appears to be an increased incidence of leaflet calcification in patients under the age of 20. When feasible, repeated intravenous injections containing calcium should be avoided during the postoperative period, and excessive milk or dairy product consumption should be avoided in children. Animal research studies (Ref. 11) show that a high systemic calcium level can lead to early calcification.

6.0 Adverse Events

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

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 (Federal) 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 anticoagulant therapy, and malfunctions of the valve due to distortion at implant, fracture of the Elgiloy 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 infarct.

Note: Based on reports in the literature on tissue valves (Refs. 3, 18, 23, 26, 36, 48, 49 & 54), there appears to be an increased incidence of leaflet calcification in patients under the age of 20. In this regard, animal research studies (Ref. 11) show that a high systemic calcium level can lead to early calcification. Furthermore, at least one published report describes a potential relationship between the consumption of daily calcium supplements and early leaflet calcification in an adult (Ref. 34). When feasible, repeated intravenous injections containing calcium should be avoided during the postoperative period; and excessive milk or dairy product consumption should be avoided in children. There are no clinical data presently available demonstrating increased resistance of Magna Ease aortic bioprostheses to calcification as compared to other commercially available bioprostheses.

6.2 Potential Adverse Events

Adverse events potentially associated with the use of bioprosthetic heart valves include:

- Angina
- Cardiac arrhythmias
- Endocarditis
- Local and/or systemic infection
- Heart failure
- Hemolysis
- Hemolytic anemia
- Hemorrhage

- Myocardial infarction
- Prosthesis leaflet entrapment (Impingement)
- Prosthesis nonstructural dysfunction
- Prosthesis pannus
- Prosthesis perivalvular leak
- Prosthesis regurgitation
- Prosthesis structural deterioration
- Prosthesis thrombosis
- Stroke
- Thromboembolism

It is possible that these complications could lead to:

- Reoperation
- Explantation
- Permanent disability
- Death

For a patient/user/third party in the European Economic Area; if, during the using of this device or as a result of its use, a serious incident has occurred, please report it to the manufacturer and your national competent authority, which can be found at https://ec.europa.eu/growth/sectors/medical-devices/contacts_en

7.0 Clinical Studies

7.1 Pre-Approval Patient Cohort

Clinical data, available on 719 patients requiring isolated aortic valve replacement (AVR) with the Model 2700 Carpentier-Edwards pericardial bioprosthesis with mean follow-up of 3.9 years, indicate overall actuarial survival rate at 6 years of 73.7% ±2.0%. Clinical data, available on 70 patients requiring double valve replacement (DVR) with mean follow-up of 3.7 years, indicate overall actuarial survival rate at 6 years of 67.2% ±6.5%. This pre-approval patient cohort data was collected from the period between August 1981 to January 1989.

In the isolated AVR population, there were a total of 455 (63.3%) males and 264 (36.7%) females with a mean age at implant (± standard deviation) of 64 (±12.4) years and a range of 18 to 90 years. The indications for valve replacement were stenosis (63.4%), regurgitation (16.3%), mixed disease (15.3%) and previous prosthetic aortic valve dysfunction (5.0%).

In the DVR population, there were a total of 24 (34.3%) males and 46 (65.7%) females with a mean age (± standard deviation) of 62.9 (±12.7) years and a range of 31 to 94 years. The indications for valve replacement were stenosis (45.7%), regurgitation (25.7%), mixed disease (21.4%) and previous prosthetic aortic valve dysfunction (7.4%).

The follow-up methods used at each clinic included hospital visits, office visits and contact by telephone or letter with either the patient, the patient's family or local doctor.

Table 2 summarizes the operative and postoperative complication rates for the isolated AVR and DVR populations. The operative rates are based on 719 patients for the isolated AVR population and on 70 patients for the DVR population. The postoperative rates are based on 2767.9 and 255.8 years of follow-up occurring >30 days after implant for the isolated AVR and DVR populations respectively.

Table 3 presents, by valve size, the mean gradients reported in echocardiograms performed on patients in this study population.

Information on preoperative and postoperative NYHA Functional Class was gathered for the isolated AVR population. In 220 patients the NYHA was not reported (171 patients expired and 49 patients not available). Of the 499 patients with reported preoperative and postoperative NYHA Functional Class at the last available follow up, 10 patients (2.0%) got worse, 59 patients (11.8%) remained the same and 430 patients (86.2%) improved.

Table 4 presents data comparing preoperative NYHA Functional Class to postoperative NYHA Functional Class at the last available follow up.

7.2 Post-Approval Patient Cohort

Edwards continues to follow a post-approval cohort of 267 patients with isolated valve replacements (AVR) (Model 2700) from four centers of the original clinical trial for the Carpentier-Edwards PERIMOUNT pericardial bioprosthesis since November 1981. The population is comprised of 171 (64%) males and 96 (36%) females. The mean age (± standard deviation) of these patients at the time of implant was 64.9 ±11.8 years and ranged from 21 to 86 years. A total of 140 deaths occurred between 1981 and 1994. Thirty-one (22.1%) of the 140 deaths were determined to be valve-related. The actuarial valve-related survival is 83% at 12 years. In the postoperative period, 16 patients required valve explants. One event occurred as a result of perivalvular leak, two due to endocarditis/sepsis and 13 were due to valve dysfunction. The actuarial explant-free rate is 90% at 12 years.

The follow-up methods used at each clinic included hospital visits, office visits, and contact by telephone or letter with either the patient, the patient's family, or local doctor.

Table 5 summarizes operative (<30 days) and postoperative (≥30 days) valve-related complication rates. The postoperative linearized complication rates are based on 2131.5 patient years of follow-up. The Carpentier-Edwards PERIMOUNT pericardial bioprosthesis was implanted in this cohort from September 1981 through December 1983 with a mean follow-up of 8.1 years. The 267 patients in the cohort have a total of 2152 patient years of follow-up. Of the 127 patients eligible for follow-up (not considered dead or explanted prior to the 1994 update) 17 (13.4%) patients are considered lost to follow-up. In the operative period, there were eight thromboembolic events, four hemorrhagic anticoagulation complications (HAC), one perivalvular leak and one valve dysfunction. In the postoperative period there were 31 thromboembolic events, eight hemorrhagic anticoagulation complications, four perivalvular leaks, two incidences of hemolysis, seven cases of endocarditis and 53 incidents of valve dysfunction in 38 patients. Valve dysfunction included 23 patients with hemodynamic valve dysfunction, 13 required reoperation/explant, and valve dysfunction was the cause of death in two patients.

While overall patient survival is 45% at 12 years, freedom from valve related deaths is 83%. These results suggest a patient population which presents with morbidity from many **non-valve** related disorders. In addition, 12-year complication rates for freedom from explants, thromboembolism, endocarditis and HAC were above 80%. The 12-year freedom from valve dysfunction is 78%. This rate includes all forms of dysfunction, including PV leak, regurgitation, stenosis, leaflet disruption, calcification and unspecified dysfunction.

Improvement in NYHA functional classification has also been demonstrated postoperatively. Forty-five percent of the patients are in NYHA Functional Class I at 12 years post implant with the Carpentier-Edwards pericardial valve.

This data was compiled as of July 1994 from a multi-center clinical trial conducted by Edwards Lifesciences. Follow-up on this post-approval cohort is

continuing, and periodic updates will be available by contacting Edwards Lifesciences LLC, Cardiovascular Surgery Marketing Department, One Edwards Way, Irvine, CA 92614.

8.0 Individualization of Treatment

It is recommended that prophylactic antibiotic therapy be given to patients undergoing dental or other procedures, which are potentially bacteremic in order to minimize the risk of endocarditis.

Some medical professional societies recommend anticoagulant therapy unless contraindicated, during the first 3 months after bioprosthetic aortic valve implantation. Such postoperative anticoagulant therapy should be determined on an individual basis.

Long-term low dose aspirin, unless contraindicated, is recommended for all patients with bioprosthetic valves. Long-term anticoagulant therapy, unless contraindicated, is recommended for all patients with bioprosthetic valves who have risk factors for thromboembolism.

Careful and continuous medical follow-up is advised so that valve related complications can be diagnosed and properly managed.

The decision to use a tissue valve must ultimately be made by the physician on an individual basis after a careful evaluation of the short-term and long-term risks and benefits to the patient and consideration of alternative methods of treatment.

In the presence of conditions affecting calcium metabolism or when calcium containing chronic drug therapies are used, the use of a mechanical prosthesis as an alternative should be considered. This is also true in patients on a high calcium diet, and in patients who are on maintenance hemodialysis.

8.1 Specific Patient Populations

The safety and effectiveness of the PERIMOUNT Magna Ease aortic bioprosthesis has not been established for the following specific populations because it has not been studied in these populations:

- patients who are pregnant or lactating;
- patients with chronic renal impairment or calcium metabolism disorders;
- patients with active endocarditis or myocarditis;
- patients with aneurysmal aortic degenerative conditions (e.g., cystic medial necrosis, Marfan's syndrome);
- children or adolescents.

9.0 Patient Counseling Information

Careful and continued medical follow up (at least by an annual visit to the physician) is advised so that bioprosthesis-related complications, particularly those related to material failure, can be diagnosed and properly managed.

Patients with bioprostheses 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 Implantation Data Card at all times and to inform their healthcare providers that they have an implant when seeking care.

10.0 How Supplied

10.1 Available Models and Sizes

The Magna Ease aortic bioprosthesis is available in labeled sizes 19, 21, 23, 25, 27, and 29 mm (reference Table 1 for nominal specifications).

10.2 Packaging

The Magna Ease aortic bioprosthesis is provided sterile and nonpyrogenic packaged in glutaraldehyde, in a plastic jar to which a seal has been applied. Each bioprosthesis 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 which have been exposed to transient temperature extremes. Please refer to the Storage section for product storage conditions. Upon receipt of the bioprosthesis, 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 bioprosthesis and contact the local supplier or Edwards Lifesciences representative to make arrangements for return authorization and replacement. Any bioprosthesis returned to Edwards Lifesciences must be shipped in the original packaging in which it was received.

WARNING: The bioprosthesis must be carefully inspected before implantation for evidence of extreme temperature exposure or other damage.

Due to the biological nature of this bioprosthesis and its sensitivity to physical handling and environmental conditions, it cannot be returned, except as noted above.

Note: Products found to have been subjected to freezing or excessive heat later than 3 days following receipt will be considered to have resulted from environmental conditions within the control of the customer, and subject to replacement at customer's expense.

10.3 Storage

The Magna Ease aortic bioprosthesis should be stored at 10 °C to 25 °C (50 °F–77 °F). Stock inspection and rotation at regular intervals are recommended to ensure that the bioprostheses are used before the expiration date stamped on the package label.

CAUTION: Do not freeze. Always store bioprostheses in a dry, contamination-free area. Any bioprosthesis that has been frozen, or is suspected of having been frozen, should not be used for human implantation.

11.0 Directions for Use

11.1 Physician Training

No special training is required to implant the Magna Ease aortic bioprosthesis. The techniques for implanting this bioprosthesis are similar to those used for supra-annular or intra-annular placement of any stented aortic bioprostheses.

11.2 Handling and Preparation Instructions

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 glutaraldehyde, or missing intact seals must not be used for human implantation.

CAUTION: It is strongly recommended that a Magna Ease aortic bioprosthesis not be opened unless implantation is certain. This is necessary to reduce the risk of contamination, because it has been established that glutaraldehyde alone is not a 100% effective sterilant against all possible contaminants. No attempt should be made to resterilize a Magna Ease aortic bioprosthesis.

CAUTION: The bioprosthesis and glutaraldehyde storage solution are sterile. The outside of the jar is not sterile and must not be placed in the sterile field.

Remove the seal and screw-lid from the jar. The jar should contain enough buffered glutaraldehyde storage solution to cover the prosthesis. The contents of the jar should be handled in an aseptic manner to prevent contamination.

Using gloved hand, attach the handle to the bioprosthesis holder while the bioprosthesis is still in the container. To do this, align the handle with the threaded hole in the bioprosthesis holder and turn clockwise until a positive resistance is felt. Aligning the handle will ensure a proper and secure attachment. Using handle remove clip and bioprosthesis from jar. Using gloved hand grasp clip and continue to rotate the handle until fully engaged as shown in Figure 1. **Do not grasp the bioprosthesis**. Be careful not to exert too much pressure while turning so as to push the bioprosthesis off the clip and damage the bioprosthesis.

Once the handle has been attached, it should not be removed from the holder until after implantation has been completed and the handle/holder assembly has been detached as a unit and removed from the operating field.

Note: The model 1111 or model 1126 (single use) handle is recommended for use with the aortic bioprosthesis.

Remove the clip by grasping the clip edge and slide off parallel to bioprosthesis (Figure 2). Discard the clip.

CAUTION: Unprotected forceps must never be used in handling these bioprostheses. The leaflet tissue should never be handled.

CAUTION: Avoid contact of the leaflet tissue or the rinse solution with towels, linens, or other sources of lint and particulate matter that may be transferred to the leaflet tissue.

To rinse the bioprosthesis, place the bioprosthesis in a minimum of 500 ml of sterile physiological saline solution. Be sure the saline solution completely covers the bioprosthesis and holder. Do not rinse with the clip/retainer attached. With the bioprosthesis and holder submerged, slowly agitate the basin (or use the attached handle to gently swirl the valve back and forth for a minimum of 1 minute). Discard the rinse solution. Repeat this process once using new saline solution for a minimum of 1 minute. The valve should be left in the final rinse solution until needed to prevent the tissue from drying.

CAUTION: Do not allow the tissue to come in contact with the bottom or sides of the rinse basin during agitation or swirling of the bioprosthesis. Care must be taken to ensure that the I.D. tag does not come in contact with the tissue and injure it. No other objects should be placed in the rinse basin.

Inspect the bioprosthesis and remove the serial number tag just prior to implantation.

11.3 Device Implantation

Because of the complexity and variation in the surgical procedure of cardiac valve replacement, the choice of surgical technique, appropriately modified in accordance with the previously described **Warnings, Precautions, and Techniques**, is left to the discretion of the individual surgeon. In general, the following steps should be used:

Step	Procedure
1	Surgically remove the diseased or damaged valve leaflets and all associated structures deemed necessary by the surgeon.
2	Surgically remove any calcium from the annulus to ensure proper seating of the sewing ring.
3	Measure the size of the annulus using only Carpentier-Edwards sizers, model 1133 aortic (Figures 4-6). The model 1133 sizers can be used to measure for either supra-annular or intra-annular placement, depending on surgeon preference. **Supra-annular sizing and implantation:** Using supra-annular technique, the sewing ring of the valve is placed above the annulus, maximizing valve orifice area. A larger valve size can often be implanted using a supra-annular technique compared to an intra-annular technique. This increase in prosthetic valve size provides improved hemodynamic performance. For optimal implantation of the valve in the supra-annular position, the sizer should be parallel with the plane of the annulus and the following sizing technique should be used: a) Using the model 1133 sizer, select the cylindrical end of the largest diameter sizer that comfortably fits in the patient's annulus (Figure 7). b) Once you have verified the appropriate cylindrical end, use the replica end of the same sizer to verify that the sewing ring will fit comfortably on top of the annulus (Figure 8). c) Determine if upsizing of the valve is possible by using the replica end of the **next larger sizer** (Figure 9). Ensure that the coronary ostia are not obstructed and that the valve stent posts do not interfere with the aortic wall at the sinotubular junction (Figure 10). If this larger size replica end fits comfortably, implant this size of the Magna Ease aortic bioprosthesis. If this larger size replica end does not fit comfortably, implant the valve size identified by Sub-Step b. A suture technique resulting in supra-annular placement of the valve, such as a horizontal mattress technique, should be employed. **Intra-annular sizing and implantation:** Using intra-annular technique, the entire valve including the sewing ring is placed inside the annulus. Either the cylindrical or valve replica end of the model 1133 sizer can be used for intra-annular sizing. For proper sizing, the sizer should be parallel with the plane of the annulus and the entire sizer, including the simulated sewing ring portion, should pass through the annulus (Figure 11-13). A suture technique resulting in intra-annular placement of the valve, such as an everting mattress technique, should be employed.
4	Suture the valve in place using an appropriate suture technique that avoids the potential problems noted under **5.0 Precautions**.

WARNING: Because of the intense temperature and lighting conditions in the operating field, the bioprosthesis should be irrigated frequently (every 1 to 2 minutes is recommended) on both sides with sterile physiological saline to keep the bioprosthesis moist during the implant procedure.

CAUTION: Examine sizers and handles for signs of wear, such as dullness, cracking or crazing. Replace sizer/handle if any deterioration is observed.

WARNING: Fragments of the sizers/handles cannot be located by means of an external imaging device.

11.3.1 Handle/Holder Removal

The integral holder and attached handle are removed as a unit at the completion of the suturing procedure in the following manner (see Figure 3):

Step	Procedure
1	Using a scalpel or scissors as shown, cut each of the three exposed sutures that are on the top of the holder. **CAUTION: Avoid cutting or damaging the stent or delicate leaflet tissue when cutting the sutures.**
2	When all three attaching sutures have been properly cut, remove the handle/holder assembly, along with the attaching sutures, from the bioprosthesis as a unit.
3	Following surgery, remove the holder from the handle and discard the holder. If using model 1111 handle clean and sterilize the handle before each use.

11.4 Accessories

Sizers

The use of a sizing instrument facilitates selection of the correct size valve for implantation. Model 1133 sizers are designed to permit direct observation of their fit within the annulus. The model 1133 sizer was developed to facilitate accurate sizing of the Magna Ease aortic bioprosthesis in a wide range of patients. Each sizer consists of a handle with a different sizer configuration at each end (Figure 4). On one side of the handle is a cylindrical end with an integrated lip that reflects the valve sewing ring geometry (Figure 5). On the other side of the handle is a valve replica end that reflects the valve sewing ring geometry as well as the height and location of the stent posts (Figure 6). A sizer is available for each size of the Magna Ease aortic bioprosthesis (19, 21, 23, 25, 27, and 29 mm).

CAUTION: Do not use other manufacturers' valve sizers, or sizers for other Edwards Lifesciences valve prostheses, to size the aortic bioprosthesis.

Valve Holder and Handle

The handle/holder assembly consists of two components: an integral disposable part that is physically mounted to the valve by the manufacturer, and a **malleable** handle (reusable model 1111 or disposable model 1126 for single use) that is attached to the holder at the time of surgery.

CAUTION: The model 1126 disposable handle is supplied sterile for single use and must not be resterilized.

11.5 Accessories Cleaning and Sterilization Instructions

Refer to the Instructions for Use supplied with the reusable accessories for cleaning and sterilization instructions.

The model 1111 handle and the model 1133 sizers are supplied nonsterile and must be sterilized before using. The handles and sizers must be cleaned and resterilized prior to each use.

CAUTION: Examine sizers and handles for signs of wear, such as dullness, cracking or crazing. Replace sizer/handle if any deterioration is observed.

11.6 Return of Explanted Bioprostheses

Edwards Lifesciences is extremely interested in obtaining recovered clinical specimens of Magna Ease aortic bioprostheses for analysis. Please contact your local bioprosthesis specialist for return of recovered bioprostheses. The explanted bioprostheses 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.

12.0 Patient Information

12.1 Registration Information

An Implantation Data Card is included in each device package for patient registration. After implantation, please complete all requested information. The bioprosthesis serial number is listed on the bioprosthesis packaging and on the identification tag attached to the bioprosthesis, and is pre-printed on the Implantation Data Card. Return the pre-addressed portion of the card to our Implant Patient Registry. The remaining portions of the card are provided for hospital and surgeon records. Upon receipt by our Implant Patient Registry, a wallet-sized identification card will be produced for the patient. This card allows patients to inform healthcare providers what type of implant they have when they seek care. When a bioprosthesis is discarded or a previous Edwards Lifesciences device is replaced, report this information to our Implant Patient Registry.

12.2 Patient Manual

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

12.3 Safety in the Magnetic Resonance (MR) Environment

MR Conditional

Non-clinical testing has demonstrated that the Carpentier-Edwards PERIMOUNT Magna Ease pericardial aortic bioprosthesis, model 3300TFX is MR Conditional. A patient with the valve can be scanned safely, in an MR system meeting the following conditions:

- Static magnetic field of 3 tesla or less
- Spatial magnetic gradient field of less than 3000 gauss/cm
- Maximum MR system reported, whole-body-averaged specific absorption rate (SAR) of 2.0 W/kg in the normal operating mode

Under the scan conditions defined above the Carpentier-Edwards PERIMOUNT Magna Ease pericardial aortic bioprosthesis, model 3300TFX is expected to produce a maximum temperature rise of 2.3 °C after 15 minutes of continuous scanning. In non-clinical testing, the image artifact caused by the device extends approximately as far as 25.5 mm from the Carpentier-Edwards PERIMOUNT Magna Ease pericardial aortic bioprosthesis when imaged with a gradient echo pulse sequence and approximately as far as 12.5 mm from the device when imaged with a spin echo pulse sequence and a 3 T MRI system. The lumen is partially to fully obscured under these conditions.

Prices subject to change without notice.

This product is manufactured and sold under at least one or more of the following U.S. Patents: US-Patent Nos. 6,413,275; 6,416,547; 8,202,314; 8,366,769; 8,632,608; and 9,439,762; and corresponding foreign patents. Likewise, additional patents pending.

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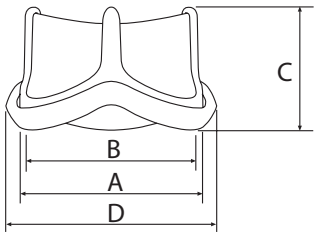
Table 1: Nominal Specifications (mm)

Carpentier-Edwards PERIMOUNT Magna Ease Aortic Pericardial Bioprosthesis, Model 3300TFX



Size	19 mm	21 mm	23 mm	25 mm	27 mm	29 mm
A. Stent Diameter (Wireform)	19	21	23	25	27	29
B. Internal Diameter (Stent I.D.)	18	20	22	24	26	28
C. Profile Height	13	14	15	16	17	18
D. External Sewing Ring Diameter	24	26	28	30	32	34
– Tissue Annulus Diameter	19	21	23	25	27	29

Note: For sizing, see surgical procedure recommendations.

Table 2: Summary of Complication Rates, Model 2700

	Isolated AVR Population			DVR Population		
Complication	**Operative % of Pts.**	**Post-Operative % Per Pt. Yr.**	**% Event-Free at Six Years (Standard Error)**	**Operative % of Pts.**	**Post-Operative % Per Pt. Yr.**	**% Event-Free at Six Years (Standard Error)**
Death	4.7	4.6	73.5 (2.0)	12.9	4.2	67.2 (6.5)
Explant	0	0.3	98.5 (1.0)	0	0.8	NA*
Valve Related Reoperation	0.7	0.1	99.8 (0.4)	0	0	NA*
All Reoperation	22.4	1.8	75.4 (1.8)	34.3	2.3	NA*
Valve Related Thromboembolism	3.1	1.5	91.4 (1.1)	1.4	5.1	NA*
All Thromboembolism	5.0	2.4	84.9 (1.6)	5.7	6.6	NA*
Endocarditis	0.6	0.8	95.8 (0.9)	1.4	1.5	NA*
Valve Dysfunction	0.1	0.7	96.0 (1.1)	0	0.4	NA*
Perivalvular Leak	0.1	0.3	98.8 (0.5)	0	1.2	NA*
Hemorrhagic Anticoagulation Complication	1.4	0.4	96.4 (1.1)	4.3	2.3	NA*
Hemolysis	0	0.2	99.1 (0.4)	0	0.4	NA*
Valve Thrombosis	0	0	100.0 (0)	0	0.4	NA*

* NA = Not Applicable

Table 3: Postoperative Echocardiography Results, Model 2700

	Valve Size						
	19 mm	**21 mm**	**23 mm**	**25 mm**	**27 mm**	**29 mm**	**Total**
Total N	12	22	15	8	3	3	63
Avg. Months Postoperative	28.6 ± 7.2	34.9 ± 8.6	36.9 ± 9.2	39.9 ± 7.6	31.4 ± 15.9	15.3 ± 12.2	34.6 ± 9.2
Velocity (M/sec) mean ± S.D.	2.80 ± 0.49	2.56 ± 0.46	2.36 ± 0.42	2.15 ± 0.56	2.09 ± 0.27	2.08 ± 0.1	2.46 ± 0.50
n =	12	21	15	7	3	3	61
range	1.90 - 3.60	1.90 - 3.90	1.39 - 2.86	1.00 - 2.60	1.90 - 2.40	2.05 - 2.10	1.00 - 3.90
Peak Instantaneous							
Gradient (mmHg) mean ± S.D.	32.22 ± 11.08	27.04 ± 10.49	23.00 ± 7.30	19.50 ± 8.16	17.60 ± 4.70	14.4 ± 0.58	25.67 ± 10.14
n =	12	21	15	7	3	3	61
range	14.40 - 51.80	14.40 - 60.80	7.70 - 32.70	4.00 - 27.00	14.40 - 23.00	13.95 - 15.06	4.00 - 60.80

Table 4: Effectiveness Outcomes, Functional NYHA, Model 2700

Preoperative NYHA Functional Class	Postoperative NYHA Functional Class					
	I	II	III	IV	Expiration	Not Available
I	18	19			9	
II	140	37			35	15
III	181	48	4	1	72	24
IV	43	16	2		53	2
Not Available	5	1			2	2

Table 5: Summary of all Valve-Related Complication Rates (N = 267), Model 2700

	Operative Period (<30 Days) % of Pts.		Postoperative Period (≥30 Days) % Per Pt. Year	
Complication	**No. of Incidences**	**%**	**No. of Incidences**	**%**
Thromboembolism / Thrombus	8	3.0	31	1.45
Endocarditis	0	0	7	0.33
Valve Dysfunction	1	0.37	34	1.60
Perivalvular Leak	1	0.37	4	0.19
Hemorrhagic Anticoagulation Complication	4	1.50	8	0.38
Hemolysis	0	0	2	0.09
Reoperation / Explant	0	0	16	0.75
Reoperation - Other	3	1.12	1	0.05
Expiration	1	0.37	30	1.41
Totals	**18**		**133**	

Srpski

Carpentier-Edwards PERIMOUNT

Perikardna bioproteza Magna Ease

model 3300TFX, aortna

PERI zalistak

Isključivo za jednokratnu upotrebu

1.0 Opis medicinskog sredstva

Aortna perikardna bioproteza Edwards Carpentier-Edwards PERIMOUNT Magna Ease, model 3300TFX (takođe navedena pod nazivom aortna bioproteza Magna Ease) je trolisna bioproteza koja se sastoji od goveđeg perikarda koji je konzervisan u puferisanom rastvoru glutaraldehida i postavljen na fleksibilni okvir. Bioproteza je obrađena u skladu s postupkom Edwards ThermaFix u kom se koristi toplotna obrada tkiva u glutaraldehidu i u kom se koristi etanol i polisorbat-80 (surfaktant). Bioproteza je zapakovana i sterilisana u ambalaži u glutaraldehidu. Dokazano je da glutaraldehid smanjuje antigenost bioproteza ksenografta tkiva i povećava stabilnost tkiva (Reference 10 i 12). Nije dokazano da sam glutaraldehid utiče na ili smanjuje brzinu kalcifikacije bioproteze.

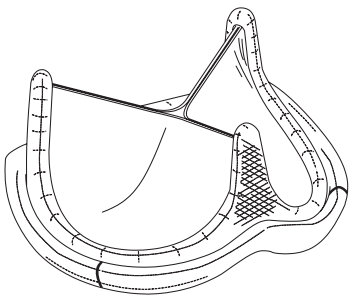
Okvir je dizajniran tako da bude rastegljiv na otvoru i na komisurama. Rastegljivost oslonaca komisura je predviđena za smanjenje šoka opterećenja na komisurama zaliska i slobodnim ivicama listića (Ref. 42). Rastegljivost otvora je predviđena za smanjenje opterećenja na listiću. Koncept rastegljivog otvora je zasnovan na fiziologiji i mehanici prirodnih srčanih zalistaka i objavljenog iskustva u implantaciji homograftova bez stenta (Reference 5 i 7).

Lagani žičani okvir je izrađen od legure Elgiloy koja je otporna na koroziju i koja je izabrana zbog svoje efikasne elastičnosti i svojstava otpornosti na zamor materijala i prekriven je pletenim poliesterskim materijalom.

Tanka laminirana traka od legure Elgiloy i poliestera je obavijena oko žičanog okvira i pruža strukturalnu potporu za otvor. Za ovaj okvir je pričvršćen meki prsten za zašivanje od silikonske gume koji je prekriven poroznim politetrafluoretilenskim platnom bez šavova koji olakšava urastanje i enkapsulaciju tkiva. Aortni prsten za zašivanje je nazubljen kako bi odgovarao prirodnom korenu aorte. Fleksibilna priroda prstena za zašivanje olakšava koaptaciju između bioproteze i često nepravilnog ili kalcifikovanog korita tkiva.

Integralni držač zaliska je pričvršćen za zalistak pomoću šavova kako bi se olakšalo rukovanje i zašivanje zaliska tokom implantacije. Hirurg može lako da skine držač (pogledajte odeljak **11.2 Uputstva za rukovanje i pripremu**).

Prečnik prstena za zašivanje i visina profila aortne bioproteze Magna Ease je smanjena kako bi se omogućila implantacija kod pacijenata sa manjim korenom aorte. Prsten za zašivanje ima tri markera na jednakom rastojanju koji pomažu u orijentaciji.



Aortna bioproteza PERIMOUNT Magna Ease, Model 3300TFX

2.0 Indikacije za upotrebu

Perikardni zalisci su indikovani za upotrebu kod pacijenata koji boluju od bolesti srčanih zalistaka. Aortno oboljenje srčanih zalistaka je oboljenje koje obuhvata: opstrukciju aortnog srčanog zaliska ili stenozu, curenje srčanog zaliska, odnosno regurgitaciju, nekompetenciju ili insuficijenciju ili kombinaciju nekompetencije i insuficijencije koja se naziva mešovitim oboljenjem ili kombinovanim lezijama.

Aortno oboljenje srčanih zalistaka mogu da izazovu brojni faktori kao što su kongenitalne abnormalnosti, infekcije različitim mikroorganizmima, degenerativna kalcifikacija i reumatsko oboljenje srca.

Perikardni zalisci se naročito koriste kod pacijenata kod kojih je kontraindikovana dugoročna antikoagulantna terapija ili kod kojih održavanje antikoagulantne terapije može biti otežano.

Aortna bioproteza Magna Ease je namenjena za upotrebu kod pacijenata kod kojih je aortno oboljenje srčanih zalistaka napredovalo u dovoljnoj meri da opravdava zamenu njihovog prirodnog zaliska protetičkim zaliskom. Takođe je namenjena za upotrebu kod pacijenata s ranije implantiranim protetičkim aortnim zaliskom koji više ne funkcioniše na odgovarajući način i zahteva zamenu. U tom slučaju, ranije implantirana proteza se hirurški uklanja i zamenjuje se zamenskom protezom. Bioproteza se može implantirati u supraanularnom ili intraanularnom položaju.

3.0 Kontraindikacije

Nemojte koristiti ako hirurg smatra da bi upotreba medicinskog sredstva bila suprotna najboljim interesima pacijenta. Konačnu odluku o korišćenju ili nekorišćenju ove bioproteze mora da donese hirurg koji može da proceni sve različite uključene rizike, uključujući anatomiju i patologiju koje su primećene prilikom operacije.

4.0 Upozorenja

ISKLJUČIVO ZA JEDNOKRATNU UPOTREBU Ovo medicinsko sredstvo je dizajnirano, namenjeno i distribuira se **ISKLJUČIVO ZA JEDNOKRATNU UPOTREBU. NEMOJTE PONOVO STERILISATI ILI KORISTITI OVO MEDICINSKO SREDSTVO**. Ne postoje podaci koji bi podržali sterilnost, apirogenost i funkcionalnost ovog medicinskog sredstva nakon ponovne obrade. Izlaganje bioproteze ili posude zračenju, pari, etilen-oksidu ili drugim hemijskim sredstvima za sterilizaciju će učiniti bioprotezu neupotrebljivom. Takve radnje mogu da dovedu do oboljenja i neželjenih događaja zato što medicinsko sredstvo možda neće funkcionisati na predviđeni način.

NEMOJTE PONOVO STERILISATI BIOPROTEZU NIJEDNOM METODOM. Izlaganje bioproteze ili posude zračenju, pari, etilen-oksidu ili drugim hemijskim sredstvima za sterilizaciju će učiniti bioprotezu neupotrebljivom.

NEMOJTE ZAMRZAVATI NITI IZLAGATI BIOPROTEZU EKSTREMNOJ TOPLOTI. Izlaganje bioproteze ekstremnim temperaturama može dovesti do neupotrebljivosti medicinskog sredstva. Svaka bioproteza se nalazi u kutiji s indikatorom temperature koji je prikazan u otvoru

na bočnom panelu. Indikator temperature je namenjen za praćenje temperature kojoj je medicinsko sredstvo izloženo tokom prenosa i skladištenja. Ako indikator prikaže bilo koje očitavanje osim „OK", nemojte koristiti bioprotezu.

NEMOJTE KORISTITI bioprotezu ako je sigurnosna zaptivka oštećena.

NEMOJTE KORISTITI bioprotezu ako je rok upotrebe istekao. Ne postoje podaci koji bi podržali funkcionalnost i učinak ovog medicinskog sredstva nakon isteka roka trajanja.

NEMOJTE KORISTITI bioprotezu ako posuda curi, ako je oštećena ili ako rastvor glutaraldehida u potpunosti ne prekriva bioprotezu. Ako ne održite vlažnost tkiva, može doći do ugrožene sterilnosti i/ili oslabljenog funkcionisanja bioproteze.

NEMOJTE IZLAGATI bioprotezu nikakvim rastvorima, hemikalijama, antibioticima itd., osim skladišnim rastvorima ili sterilnim fiziološkim slanim rastvorom zato što može doći do nepopravljivog oštećenja tkiva listića koje se ne može uočiti prilikom vizuelne provere.

NE DOZVOLITE da se bioproteza osuši. Mora da bude vlažna u svakom trenutku. Održavajte vlažnost tkiva ispiranjem sterilnim fiziološkim rastvorom na obe strane tkiva listića. Ako ne održite vlažnost tkiva, može doći do oslabljenog funkcionisanja bioproteze.

NEMOJTE SPROVODITI KATETERE, vodove za transvenski pejsing niti bilo koje druge hirurške instrumente preko bioproteze, osim hirurškog ogledala koje se koristi za proveru položaja šava. Druga hirurška sredstva mogu dovesti do oštećenja tkiva.

NEMOJTE KORISTITI bioprotezu ako je ispuštena, oštećena ili ako je došlo do pogrešnog rukovanja bioprotezom na bilo koji način. Ako dođe do oštećenja bioproteze tokom ugradnje, nemojte pokušavati popravku. Takve radnje mogu da dovedu do oboljenja i neželjenih događaja zato što medicinsko sredstvo možda neće funkcionisati na predviđeni način.

NEMOJTE HVATATI tkivo listića bioproteze instrumentima i nemojte oštećivati tkivo bioproteze. Čak i najmanja perforacija tkiva se vremenom može povećati i značajno smanjiti funkcionalnost bioproteze.

NEMOJTE KORISTITI PREVELIKU VELIČINU. Korišćenje prevelike veličine može da izazove oštećenje bioproteze ili da dovede do lokalizovanih mehaničkih opterećenja koja mogu dovesti do povrede srca ili otkazivanja tkiva listića, distorcije stenta i regurgitacije zaliska.

Klinički podaci kojima se uspostavljaju bezbednost i efikasnost upotrebe bioproteze kod pacijenata mlađih od 20 godina nisu dostupni. Zato preporučujemo pažljivo razmatranje upotrebe bioproteze kod mlađih pacijenata.

Konačnu odluku o tome da se koristi tkivni zalistak mora da donese lekar na individualnom nivou nakon pažljive procene kratkoročnih i dugoročnih rizika i koristi za pacijenta u poređenju sa alternativnim metodama lečenja. Nije utvrđena dugoročna trajnost bioproteza.

Kao i kod svih implantiranih medicinskih sredstava, postoji mogućnost imunološke reakcije. Neke komponente modela 3300TFX su izrađene od legure metala koja sadrži kobalt, hrom, nikl, molibden, mangan, ugljenik, berilijum i gvožđe. Potrebno je primeniti posebnu pažnju kod pacijenata koji su hipersenzitivni na ove materijale. Ovo medicinsko sredstvo ne sadrži lateks od prirodne gume, ali postoji mogućnost da je proizvedeno u okruženju koje sadrži lateks.

Ozbiljni neželjeni događaji, koji u nekim slučajevima dovode do zamene bioproteze i/ili smrtnog ishoda, mogu da budu povezani s upotrebom protetičkih zalistaka (pogledajte odeljak **6.0 Neželjeni događaji**). Svakom potencijalnom pacijentu je potrebno dati potpuno objašnjenje koristi i rizika pre operacije.

Napomena: Bioproteze je potrebno pažljivo koristiti u prisustvu ozbiljne sistemske hipertenzije ili kada je očekivani životni vek pacijenta duži od poznatog životnog veka proteze (pogledajte odeljak 7.0 Kliničke studije).

Neophodno je pažljivo i kontinuirano medicinsko praćenje (najmanje jedna godišnja poseta lekaru) da bi se komplikacije povezane sa bioprotezom, naročito one povezane s problemima s materijalom, dijagnostikovale i pravilno kontrolisale.

Primaoci protetičkih srčanih zalistaka koji se podvrgavaju stomatološkim procedurama treba da prime profilaktičku terapiju antibioticima radi maksimalnog smanjenja mogućnosti protetičke infekcije.

Primaoci bioprotetičkih srčanih zalistaka treba da budu na antikoagulantnoj terapiji (osim u slučaju kontraindikacije) tokom prvih faza lečenja nakon implantacije u periodu od oko 2 do 3 meseca. Antikoagulantnu terapiju je zatim potrebno prekinuti na 10 dana, osim kod pacijenata kod kojih je indikovana neograničena antikoagulantna zaštita, tj. u slučaju nedostatka sinusnog ritma i kod pacijenata s dilatiranom levom srčanom pretkomorom, kalcifikacijom zida pretkomore ili istorijom prethodnog atrijalnog tromba. Međutim, odgovarajuću antikoagulantnu terapiju mora da odredi lekar na individualnoj bazi (Ref. 1).

Odgovarajuće ispiranje fiziološkim rastvorom koje je opisano u odeljku Tehnika je obavezno pre implantacije da bi se smanjila koncentracija glutaraldehida. Drugi rastvori, lekovi, hemikalije, antibiotici itd. se nikada ne smeju dodavati rastvorima glutaraldehida ili rastvorima za ispiranje zato što mogu dovesti do nepovratnog oštećenja tkiva listića koje možda neće biti primetno prilikom vizuelne provere.

5.0 Mere predostrožnosti

- Spoljašnjost posude nije sterilna i ne sme se stavljati u sterilno polje.
- Potrebno je obaviti odgovarajuće ispiranje fiziološkim rastvorom pre implantacije da bi se smanjila koncentracija glutaraldehida.
- Potrebno je obaviti odgovarajuće uklanjanje naslaga kalcijuma iz anulusa pacijenta pre implantacije kako bi se izbeglo oštećivanje osetljivog tkiva listića protetičkog zaliska usled kontakta sa naslagama kalcijuma.
- Glutaraldehid može da izazove iritaciju kože, očiju, nosa i grla. Izbegavajte produženo ili stalno izlaganje rastvoru ili njegovo udisanje. Koristite samo s adekvatnom ventilacijom. Ako dođe do kontakta s kožom, odmah isperite zahvaćenu oblast vodom. U slučaju kontakta s očima, odmah zatražite medicinsku pomoć. Više informacija o izloženosti glutaraldehidu potražite u bezbednosnom listu MSDI0424 koji je dostupan kod kompanije Edwards Lifesciences.
- Aortna bioproteza Magna Ease se odlikuje jedinstvenom konfiguracijom koja je dizajnirana za postavljanje iznad anulusa ili unutar anulusa pacijenta. Hirurg mora da bude upoznat sa preporukama za pravilno određivanje veličine u supraanularnoj ili intraanularnoj poziciji. Detaljne informacije potražite u odeljku Implantacija medicinskog sredstva (11.3).
- Rukujte bioprotezom isključivo uz pomoć dodatne opreme kompanije Edwards Lifesciences. Prilikom izbora veličine bioproteze, smeju se koristiti isključivo merači veličine kompanije Edwards. Upotreba merača veličine drugih proizvođača može dovesti do neodgovarajućeg izbora bioproteze.
- **Kada birate bioprotezu za određenog pacijenta, morate uzeti u obzir veličinu, uzrast i fizičko stanje pacijenta u odnosu na veličinu**

proteze da biste smanjili mogućnost dobijanja neodgovarajućeg hemodinamskog rezultata. Međutim, konačan izbor bioproteze mora da donese lekar na individualnoj osnovi i nakon pažljivog razmatranja svih rizika i koristi za pacijenta.

- Zbog relativne fleksibilnosti okvira, **potrebno je da budete pažljivi kako biste sprečili savijanje ili deformaciju stenta** koja može da dovede do regurgitacije, izmenjene hemodinamike i/ili rascepa listića koji će dovesti do nekompetencije bioproteze. Zbog toga se mora izbegavati primena prevelike veličine.
- Rastojanje šavova u ostatku valvularnog otvora i prsten za zašivanje proteze moraju pažljivo da se uklope kako bi se izbeglo sklapanje listića ili distorzija otvora. Kompanija Edwards Lifesciences je primila izveštaje o tome da su pojedinačni povratni šavovi, na udaljenosti od 10 do 15 mm, kreirali efekat duvankese i izazivali stezanje otvora zaliska.
- Kada koristite pojedinačne šavove, važno je da isečete šavove u blizini čvorova i da osigurate da izloženi krajevi šavova ne dođu u kontakt sa tkivom listića. Prijavljivani su slučajevi ozbiljne regurgitacije bioproteza koje su morale da budu zamenjene usled habanja koje je nastalo prilikom kontakta sa šavovima (Ref. 2).
- Za razliku od čvrstih mehaničkih zalistaka, zid stenta je mekan i neće sprečavati penetraciju igle. Shodno tome, mora se obratiti izuzetna pažnja prilikom postavljanja šavova kroz ivicu za zašivanje kako bi se izbegla penetracija u bočni zid stenta i moguća laceracija tkiva listića.
- Kao i kod svih proteza koje imaju otvorene kaveze, slobodne oslonce ili oslonce komisure, morate paziti da izbegnete omotavanje ili kačenje šava oko komisure što može dovesti do ometanja pravilnog funkcionisanja zaliska.
- Stent aortne bioproteze je simetričan i podupirači komisure (oslonci) su podjednako udaljeni. Oslonci treba da odgovaraju ostacima prirodnih komisura kako ne bi blokirali ostijume koronarnih arterija.
- Oznaka sa serijskim brojem je pričvršćena za prsten za zašivanje svake bioproteze pomoću šava. Ovaj serijski broj je potrebno proveriti u odnosu na broj na posudi i na kartici sa podacima o implantaciji. Ako primetite bilo kakvu razliku, potrebno je da vratite bioprotezu u nekorišćenom stanju. Ovu oznaku ne treba skidati sa bioproteze do neposredno pre ugradnje implanta. Treba voditi računa da se izbegne sečenje ili cepanje platna prstena za zašivanje tokom uklanjanja.
- Neophodno je pažljivo rukovanje kod svih implantabilnih medicinskih sredstava. Ako ispustite, oštetite ili na bilo koji način pogrešno rukujete bioprotezom, bioproteza se ne sme koristiti za humanu implantaciju.
- Na osnovu izveštaja iz literature o tkivnim zaliscima (Reference 3, 18, 23, 26, 48, 49 i 54), čini se da postoji povećana incidenca kalcifikacije listića kod pacijenata mlađih od 20 godina. Kada je to moguće, potrebno je izbegavati često davanje intravenskih injekcija koje sadrže kalcijum tokom postoperativnog perioda i potrebno je izbegavati prekomerno konzumiranje mleka ili mlečnih proizvoda kod dece. U istraživačkim studijama na životinjama (Ref. 11) je dokazano da visoka sistemska koncentracija kalcijuma može dovesti do rane kalcifikacije.

6.0 Neželjeni događaji

6.1 Primećeni neželjeni događaji

Kao i kod svih protetičkih srčanih zalistaka, ozbiljni neželjeni događaji koji u nekim slučajevima mogu dovesti do smrtnog ishoda mogu da budu povezani s upotrebom tkivnih zalistaka. Osim toga, neželjeni događaji usled reakcija pojedinačnih pacijenata na implantirano sredstvo ili fizičke ili hemijske promene komponenata, naročito onih koji su biološkog porekla, mogu da se javljaju u varirajućim intervalima (na nekoliko sati ili dana) i mogu da zahtevaju ponovnu operaciju i zamenu protetičkog sredstva.

Neželjeni događaji koji su povezani s upotrebom perikardnih bioproteza Carpentier-Edwards PERIMOUNT koji su sakupljeni iz literature i izveštaja dobijenih putem sistema za praćenje proizvoda u skladu s uredbama Sjedinjenih Država (na federalnom nivou) kojima se uspostavljaju dobre proizvođačke prakse, odeljak 820.198, obuhvataju stenozu, regurgitaciju u oslabljenom zalisku, perivalvularno curenje, endokarditis, hemolizu, tromboemoboliju, trombotsku opstrukciju, dispoziciju za krvarenje koja je povezana s antikoagulantnom terapijom i insuficijenciju zaliska usled distorzije na implantu, frakture Elgiloy žičanog okvira ili fizičkog ili hemijskog propadanja komponenata zaliska. Tipovi oštećenja tkiva obuhvataju infekciju, kalcifikaciju, zadebljanje, perforaciju, degeneraciju, abraziju šava, traumu od instrumenta i odvajanje listića sa podupirača stenta zaliska. Ove komplikacije klinički mogu da se manifestuju kao abnormalan šum na srcu, nedostatak daha, intolerancija na vežbanje, dispnea, ortopneja, anemija, groznica, aritmija, krvarenje, prolazni ishemijski napad, šlog, paraliza, mali minutni volumen srca, plućni edem, kongestivna srčana insuficijencija, srčana insuficijencija i infarkt miokarda.

Napomena: Na osnovu izveštaja iz literature o tkivnim zaliscima (Reference 3, 18, 23, 26, 36, 48, 49 i 54), čini se da postoji povećana incidenca kalcifikacije listića kod pacijenata mlađih od 20 godina. U tom pogledu, u istraživačkim studijama na životinjama (Ref. 11) je dokazano da visoka sistemska koncentracija kalcijuma može dovesti do rane kalcifikacije. Pored toga, u najmanje jednom objavljenom izveštaju je opisana potencijalna veza između svakodnevnog konzumiranja suplemenata kalcijuma i rane kalcifikacije listića kod odraslih (Ref. 34). Kada je to moguće, potrebno je izbegavati često davanje intravenskih injekcija koje sadrže kalcijum tokom postoperativnog perioda i potrebno je izbegavati prekomerno konzumiranje mleka ili mlečnih proizvoda kod dece. Trenutno nisu dostupni klinički podaci koji dokazuju povećanu otpornost aortnih bioproteza Magna Ease na kalcifikaciju u odnosu na druge komercijalno dostupne bioproteze.

6.2 Potencijalni neželjeni događaji

Neželjeni događaji koji su potencijalno povezani s upotrebom bioprotetičkih srčanih zalistaka obuhvataju:

- Angina
- Srčane aritmije
- Endokarditis
- Lokalna i/ili sistemska infekcija
- Srčana insuficijencija
- Hemoliza
- Hemolitička anemija
- Krvarenje
- Infarkt miokarda
- Zarobljavanje listića proteze (udaranje)
- Nestrukturalna disfunkcija proteze
- Panus proteze
- Perivalvularno curenje proteze
- Regurgitacija kroz protezu

- Strukturalno propadanje proteze
- Tromboza proteze
- Moždani udar
- Tromboembolija

Ove komplikacije mogu da dovedu do sledećih događaja:

- Ponovna operacija
- Eksplantacija
- Trajni invaliditet
- Smrt

Za pacijente/korisnike/treća lica u Evropskom ekonomskom prostoru: ako dođe do ozbiljnog incidenta tokom upotrebe medicinskog sredstva ili usled upotrebe medicinskog sredstva, prijavite incident proizvođaču i nadležnom organu u vašoj zemlji kog možete pronaći na veb-sajtu https://ec.europa.eu/growth/sectors/medical-devices/contacts_en

7.0 Kliničke studije

7.1 Kohorta pacijenata pre odobrenja medicinskog sredstva

Klinički podaci, koji su dostupni o 719 pacijenata kod kojih je bila potrebna izolovana zamena aortnog zaliska (AVR) modelom 2700 Carpentier-Edwards perikardne bioproteze sa srednjim vremenom kontrole od 3,9 godina, ukazuju na ukupnu akturijalnu stopu preživljavanja na 6 godina od 73,7 % ±2,0 %. Klinički podaci, koji su dostupni o 70 pacijenata kod kojih je bila potrebna zamena mitralnog i aortnog zaliska (DVR) sa srednjim vremenom kontrole od 3,7 godina, ukazuju na ukupnu akturijalnu stopu preživljavanja na 6 godina od 67,2 % ±6,5 %. Ovi podaci o kohorti pacijenata pre odobrenja medicinskog sredstva su sakupljeni u periodu od avgusta 1981. do januara 1989. godine.

U populaciji sa izolovanom zamenom aortnog zaliska (AVR) bilo je ukupno 455 (63,3 %) muškaraca i 264 (36,7 %) žena srednje starosti u trenutku implantacije (± standardna devijacija) od 64 (±12,4) godine i rasponom od 18 do 90 godina. Indikacije za zamenu zaliska su bile stenoza (63,4 %), regurgitacija (16,3 %), mešovito oboljenje (15,3 %) i ranija disfunkcija protetičkog aortnog zaliska (5,0 %).

U populaciji sa zamenom mitralnog i aortnog zaliska (DVR) bilo je ukupno 24 (34,3 %) muškaraca i 46 (65,7 %) žena srednje starosti (± standardna devijacija) od 62,9 (±12,7) godina i rasponom od 31 do 94 godine. Indikacije za zamenu zaliska su bile stenoza (45,7 %), regurgitacija (25,7 %), mešovito oboljenje (21,4 %) i ranija disfunkcija protetičkog aortnog zaliska (7,4 %).

Metode kontrole koje su korišćene na svakoj klinici su obuhvatale bolničke posete, posete ordinaciji i kontakt telefonskim ili pisanim putem sa pacijentom ili porodičnim lekarom pacijenta ili sa lokalnim lekarom.

U Tabeli 2 su navedeni sažeci operativnih i postoperativnih stopa komplikacija za izolovane populacije sa zamenom aortnog zaliska (AVR) i zamenom mitralnog i aortnog zaliska (DVR). Operativne stope su zasnovane na 719 pacijenata za izolovanu populaciju sa zamenom aortnog zaliska (AVR) i na 70 pacijenata sa zamenom mitralnog i aortnog zaliska (DVR). Postoperativne stope su zasnovane na 2767,9 i 255,8 godina kontrole koje su vršene >30 dana nakon implantacije za izolovane populacije sa zamenom aortnog zaliska (AVR) i zamenom mitralnog i aortnog zaliska (DVR).

U Tabeli 3 su navedeni, po veličini zaliska, srednji gradijenti dobijeni iz ehokardiograma koji su obavljeni na pacijentima u ovoj studijskoj populaciji.

Informacije o preoperativnoj i postoperativnoj funkcionalnoj klasi NYHA su sakupljeni za izolovanu populaciju sa zamenom aortnog zaliska (AVR).

Funkcionalna klasa NYHA nije navedena za 220 pacijenata (za 171 pacijenta je istekao rok a 49 pacijenata nije bilo dostupno). Od 499 pacijenata sa izdatom preoperativnom i postoperativnom funkcionalnom klasom NYHA prilikom poslednje dostupne kontrole, kod 10 pacijenata (2,0 %) stanje se pogoršalo, kod 59 pacijenata (11,8 %) je stanje ostalo isto i kod 430 pacijenata (86,2 %) se stanje popravilo.

U Tabeli 4 su navedeni podaci u kojima se upoređuje preoperativna funkcionalna klasa NYHA sa postoperativnom funkcionalnom klasom NYHA prilikom poslednje dostupne kontrole.

7.2 Kohorta pacijenata nakon odobrenja medicinskog sredstva

Kompanija Edwards nastavlja da prati kohortu od 267 pacijenata s izolovanom zamenom aortnog zaliska (AVR) (Model 2700) iz četiri studijska centra u kojima je vršeno originalno kliničko ispitivanje Carpentier-Edwards PERIMOUNT perikardnih bioproteza od novembra 1981. godine. Populaciju čini 171 (64 %) muškaraca i 96 (36 %) žena. Srednja starost (± standardna devijacija) ovih pacijenata u trenutku implantacije je bila 64,9 ±11,8 godina i bila je u rasponu od 21 do 86 godina. Bilo je ukupno 140 smrtnih ishoda od 1981. do 1994. godine. Za trideset i jedan (22,1 %) od 140 smrtnih ishoda je utvrđeno da su povezani sa zaliskom. Akturijalno preživljavanje povezano sa zaliskom je 83 % na 12 godina. U postoperativnom periodu su eksplantati zaliska bili neophodni kod 16 pacijenata. Do jednog događaja je došlo usled perivalvularnog curenja, do dva usled endokarditisa/sepse i do 13 usled disfunkcije zaliska. Akturijalna stopa bez eksplantata je 90 % na 12 godina.

Metode kontrole koje su korišćene na svakoj klinici su obuhvatale bolničke posete, posete ordinaciji i kontakt telefonskim ili pisanim putem sa pacijentom ili porodičnim lekarom pacijenta ili sa lokalnim lekarom.

U tabeli 5 su navedeni sažeci operativnih (<30 dana) i postoperativnih (≥30 dana) stopa komplikacija koje su povezane sa zaliskom. Linearizovane postoperativne stope komplikacije su zasnovane na praćenju od 2131,5 godina pacijenata. Perikardna bioproteza Carpentier-Edwards PERIMOUNT je implantirana pacijentima iz ove kohorte od septembra 1981. do decembra 1983. sa srednjim vremenom kontrole od 8,1 godine. 267 pacijenata u kohorti imaju ukupno 2152 godina praćenja pacijenata. Od 127 pacijenata koji su smatrani kvalifikovanim za praćenje (koji nisu smatrani mrtvim ili eksplantiranim pre 1994. godine) 17 (13,4 %) pacijenata se smatra izgubljenim za praćenje. U operativnom periodu je bilo osam tromboembolijskih događaja, četiri hemoragične komplikacije antikoagulantne terapije (HAC), jedno perivalvularno curenje i jedna disfunkcija zaliska. U postoperativnom periodu je došlo do 31 tromboembolijskog događaja, osam hemoragičnih komplikacija antikoagulantne terapije, četiri perivalvularna curenja, dve incidence hemolize, sedam slučajeva endokarditisa i 53 incidenta disfunkcije zaliska kod 38 pacijenata. Disfunkcija zaliska je obuhvatila 23 pacijenta sa hemodinamskom disfunkcijom zaliska, kod 13 je bila neophodna ponovna operacija/eksplantat, a disfunkcija zaliska je bila uzrok smrtnog ishoda kod dva pacijenta.

Dok je ukupno preživljavanje pacijenata 45 % na 12 godina, smrtnih ishoda koji su povezani sa zaliskom nema kod 83 %. Ovi rezultati ukazuju na populaciju pacijenata sa morbiditetom od više oboljenja koja **nisu povezana sa zaliscima**. Pored toga, stope komplikacija na 12 godina za nedostatak eksplantata, tromboembolije, endokarditisa i hemoragične komplikacije antikoagulantne terapije (HAC) su bili viši od 80 %. Izostanak disfunkcije zaliska na 12 godina je 78 %. Ova stopa obuhvata sve oblike disfunkcije kao što su perivalvularno curenje, regurgitacija, stenoza, rascep listića, kalcifikacija i neodređena disfunkcija.

Poboljšanje funkcionalne klasifikacije NYHA je takođe dokazano postoperativno. Četrdeset pet procenata pacijenata su u funkcionalnoj klasi I NYHA 12 godina nakon implantacije Carpentier-Edwards perikardnog zaliska.

Ovi podaci su sakupljeni do jula 1994. godine iz multicentričnog kliničkog ispitivanja koje je vodila kompanija Edwards Lifesciences. Praćenje ove kohorte nakon odobrenja medicinskog sredstva se nastavlja i periodična obaveštenja su dostupna putem kontakta sa odeljenjem marketinga za kardiovaskularnu hirurgiju kompanije Edwards Lifesciences LLC, One Edwards Way, Irvine, CA 92614.

8.0 Individualizacija terapije

Preporučuje se davanje profilaktičke terapije antibioticima pacijentima koji se podvrgavaju stomatološkim i drugim procedurama koje su potencijalno bakteremijske kako bi se smanjio rizik od endokarditisa.

Neka profesionalna lekarska udruženja preporučuju antikoagulantnu terapiju – osim kada je kontraindikovana – tokom prva 3 meseca nakon implantacije aortnog zaliska. Takvu postoperativnu antikoagulantnu terapiju je potrebno odrediti na individualnoj bazi.

Dugoročna terapija manjim dozama aspirina, osim u slučajevima kada je kontraindikovana, se preporučuje svim pacijentima s bioprotetičkim zaliscima. Dugoročna antikoagulantna terapija, osim u slučajevima kontraindikacije, se preporučuje svim pacijentima sa bioprotetičkim zaliscima kod kojih postoji faktor rizika za tromboemboliju.

Preporučuje se pažljivo i kontinuirano medicinsko praćenje da bi se komplikacije povezane sa zaliskom dijagnostikovale i pravilno kontrolisale.

Konačnu odluku o tome da se koristi tkivni zalistak mora da donese lekar na individualnom nivou nakon pažljive procene kratkoročnih i dugoročnih rizika i koristi za pacijenta u poređenju sa alternativnim metodama lečenja.

Kada postoje stanja koja utiču na metabolizam kalcijuma ili kada se koriste hronične terapije lekovima koji sadrže kalcijum, potrebno je razmotriti upotrebu mehaničke proteze kao alternative. Ovo se odnosi i na pacijente čija je ishrana bogata kalcijumom i na pacijente koji su na održavanju hemodijalizom.

8.1 Određene populacije pacijenata

Bezbednost i efikasnost aortne bioproteze PERIMOUNT Magna Ease nije utvrđena za sledeće populacije pacijenata zato što nisu vršena ispitivanja kod ovih populacija:

- pacijentkinje koje su trudne ili doje;
- pacijenti sa hroničnim oštećenjem bubrega ili poremećajima u metabolizmu kalcijuma;
- pacijenti s aktivnim endokarditisom ili miokarditisom;
- pacijenti s aneurizmalnim aortnim degenerativnim oboljenjima (npr. cističnom nekrozom medije, Marfanovim sindromom);
- deca ili adolescenti.

9.0 Informacije o savetovanju pacijenata

Neophodno je pažljivo i kontinuirano medicinsko praćenje (najmanje jedna godišnja poseta lekaru) da bi se komplikacije povezane sa bioprotezom, naročito one povezane s problemima s materijalom, dijagnostikovale i pravilno kontrolisale.

Pacijenti koji imaju bioproteze su pod rizikom od bakteremije (npr. usled stomatoloških procedura) i potrebno im je pružiti informacije o profilaktičkoj terapiji antibioticima.

Pacijente treba posavetovati da uvek sa sobom nose karticu sa podacima o implantaciji i da obaveste svoje lekare da imaju implant kada traže lekarsku pomoć.

10.0 Kako se isporučuje

10.1 Dostupni modeli i veličine

Aortna bioproteza Magna Ease je dostupna u označenim veličinama od 19, 21, 23, 25, 27 i 29 mm (nominalne specifikacije pogledajte u Tabeli 1).

10.2 Pakovanje

Aortna bioproteza Magna Ease se isporučuje u sterilnom i apirogenom stanju, u glutaraldehidu, u plastičnoj zaptivenoj posudi. Svaka bioproteza se nalazi u kutiji s indikatorom temperature koji je prikazan u otvoru na bočnom panelu. Indikator temperature je predviđen za identifikovanje proizvoda koji su izloženi prolaznim ekstremnim temperaturama. Informacije o uslovima skladištenja proizvoda pogledajte u odeljku Čuvanje. Kada primite bioprotezu, odmah proverite indikator i pogledajte oznaku na kutiji da biste potvrdili stanje „Use“ (za upotrebu). Ako stanje „Use“ (za upotrebu) nije očigledno, nemojte koristite bioprotezu i obratite se lokalnom dobavljaču ili predstavniku kompanije Edwards Lifesciences da biste organizovali vraćanje radi provere i zamene. Sve bioproteze koje se vraćaju kompaniji Edwards Lifesciences moraju da se pošalju u originalnoj ambalaži u kojoj su primljene.

UPOZORENJE: Potrebno je pažljivo proveriti da li na bioprotezi ima tragova izloženosti ekstremnim temperaturama ili drugih oštećenja pre implantacije.

Zbog biološke prirode ove bioproteze i njene osetljivosti na fizičko rukovanje i uslove životne sredine, vraćanje nije moguće, osim u slučaju koji je ranije naveden.

Napomena: Proizvodi za koje se utvrdi da su bili izloženi zamrzavanju ili prekomernoj toploti kasnije od 3 dana nakon primanja će se smatrati oštećenim dejstvom uslova životne sredine pod nadzorom kupca i moći će da se zamene o trošku kupca.

10.3 Čuvanje

Aortnu bioprotezu Magna Ease je potrebno čuvati na temperaturi od 10 °C do 25 °C (50 °F–77 °F). Preporučuju se provera i rotiranje zaliha u redovnim intervalima kako bi se osiguralo da se bioproteze koriste pre datuma isteka roka trajanja koji je odštampan na nalepnici na pakovanju.

OPREZ: Ne zamrzavati. Uvek čuvajte bioproteze na suvom mestu bez kontaminacije. Nijedna bioproteza koja je zamrznuta ili za koju se smatra da je bila zamrznuta se ne sme koristiti za humanu implantaciju.

11.0 Uputstvo za upotrebu

11.1 Obuka lekara

Nije potrebna posebna obuka za implantaciju aortne bioproteze Magna Ease. Tehnike implantacije bioproteze su slične tehnikama koje se koriste za supraanularnu ili intraanularnu implataciju bilo koje aortne bioproteze sa stentom.

11.2 Uputstva za rukovanje i pripremu

Bioproteza se isporučuje u sterilnoj plastičnoj posudi sa navojnim zatvaračem i zaptivkom. Pre otvaranja pažljivo proverite da li na posudi ima tragova oštećenja (npr. naprslina na posudi ili poklopcu), curenja, oštećenih ili nedostajućih zaptivki.

OPREZ: Bioproteze iz posuda koje su oštećene, cure, ne sadrže odgovarajuću količinu glutaraldehida ili koje nemaju netaknute zaptivke se ne smeju koristiti za humanu implantaciju.

OPREZ: Otvaranje aortne bioproteze Magna Ease se ne preporučuje, osim u slučaju kada je implantacija izvesna. Ovo je neophodno kako

bi se smanjio rizik od kontaminacije zato što je utvrđeno da sam glutaraldehid nije 100 % efikasan sterilant protiv svih mogućih kontaminata. Ne smete da pokušavate ponovnu sterilizaciju aortne bioproteze Magna Ease.

OPREZ: Bioproteza i skladišni rastvor glutaraldehida su sterilni. Spoljašnjost posude nije sterilna i ne sme se stavljati u sterilno polje.

Uklonite zaptivku i navojni poklopac sa posude. Posuda mora da sadrži dovoljnu količinu skladišnog rastvora puferisanog glutaraldehida koja pokriva protezu. Sadržajem posude treba da rukujete na aseptični način kako biste sprečili kontaminaciju.

Stavite rukavice i pričvrstite dršku za držač bioproteze dok se bioproteza još uvek nalazi u posudi. Da biste to učinili, poravnajte dršku sa navojnim otvorom u držaču bioproteze i okrenite je u smeru kazaljke na satu dok ne osetite pozitivan otpor. Poravnanjem drške ćete obezbediti pravilno i bezbedno pričvršćivanje. Izvadite spojnicu i bioprotezu iz posude pomoću ručke. Stavite rukavice, uhvatite spojnicu i nastavite da okrećete dršku dok ne bude u potpunosti postavljena kao što je prikazano na slici 1. **Nemojte hvatati bioprotezu**. Budite pažljivi i nemojte primenjivati prekomerni pritisak prilikom okretanja da ne biste odvojili bioprotezu sa spojnice i tako oštetili bioprotezu.

Kada pričvrstite dršku, ne smete da je uklanjate sa držača do nakon završetka implantacije i odvajanja i uklanjanja sklopa drške/držača kao jedne jedinice iz operacionog polja.

Napomena: Ručka modela 1111 ili modela 1126 (za jednokratnu upotrebu) se preporučuje za korišćenje s aortnom bioprotezom.

Uklonite spojnicu tako što ćete uhvatiti ivicu spojnice i prevući je paralelno u odnosu na bioprotezu (slika 2). Odložite spojnicu u otpad.

OPREZ: Za rukovanje ovim bioprotezama se nikada ne sme koristiti nezaštićeni forceps. Tkivom listića nikada ne smete da rukujete.

OPREZ: Izbegavajte kontakt tkiva listića ili rastvora za ispiranje sa ubrusima, platnom ili drugim izvorima dlačica i čestica koje se mogu preneti na tkivo listića.

Stavite bioprotezu u najmanje 500 ml sterilnog fiziološkog slanog rastvora da biste isprali bioprotezu. Postarajte se da fiziološki rastvor u potpunosti potopi bioprotezu i držač. Nemojte ispirati sa pričvršćenom spojnicom/osiguračem. Dok su bioproteza i držač potopljeni, polako promešajte tečnost u posudi (ili koristite pričvršćenu dršku i nežno pomerajte zalistak unapred i unazad najmanje 1 minut). Odložite rastvor za ispiranje u otpad. Još jednom ponovite ovaj proces sa novim fiziološkim rastvorom i u trajanju od najmanje 1 minuta. Zalistak je potrebno ostaviti u finalnom rastvoru za ispiranje onoliko koliko je potrebno da se spreči sušenje tkiva.

OPREZ: Ne dozvolite da tkivo dođe u kontakt sa dnom ili zidovima posude za ispiranje tokom mešanja ili pomeranja bioproteze. Potrebno je da pazite da identifikaciona oznaka ne dođe u kontakt s tkivom i ne povredi ga. Nije dozvoljeno stavljanje drugih predmeta u posudu za ispiranje.

Proverite bioprotezu i uklonite oznaku sa serijskim brojem neposredno pre implantacije.

11.3 Implantacija medicinskog sredstva

Zbog složenosti i varijacija hirurških procedura zamene srčanog zaliska, izbor hirurške tehnike koja je na odgovarajući način izmenjena u skladu s ranije opisanim **Upozorenjima, merama predostrožnosti i tehnikama** se ostavlja svakom pojedinačnom hirurgu. Generalno je potrebno primeniti sledeće korake:

Korak	Procedura
1	Hirurško uklanjanje obolelih ili oštećenih listića zalistaka i svih povezanih struktura čije uklanjanje hirurg smatra neophodnim.
2	Hirurško uklanjanje kompletnog kalcijuma iz anulusa kako bi se osiguralo pravilno postavljanje prstena za zašivanje.
3	Merenje veličine anulusa pomoću Carpentier-Edwards merača veličine, model 1133 aortni (slike 4–6). Merači veličine modela 1133 se mogu koristiti za merenje supraanularnog ili intraanularnog postavljanja u zavisnosti od izbora hirurga. **Supraanularno određivanje veličine i implantacija:** U supraanularnoj tehnici se prsten za zašivanje zaliska postavlja iznad anulusa i tako povećava oblast otvora zaliska. Zalistak veće veličine se često može implantirati primenom supraanularne tehnike u odnosu na intraanularnu tehniku. Ovo povećanje veličine protetičkog zaliska pruža unapređene hemodinamske performanse. Za optimalnu implantaciju zaliska u supraanularnom položaju je potrebno postaviti merač veličine paralelno u odnosu na ravan anulusa i potrebno je koristiti sledeću tehniku za određivanje veličine: a) Pomoću merača veličine modela 1133 izaberite cilindrični kraj merača najvećeg prečnika koji komotno staje u anulus pacijenta (slika 7). b) Kada potvrdite odgovarajući cilindrični kraj, koristite kraj replike istog merača veličine da potvrdite da li prsten za zašivanje komotno staje na anulus (slika 8). c) Utvrdite da li je povećanje veličine zaliska moguće pomoću kraja s replikom **sledećeg najvećeg merača veličine** (slika 9). Postarajte se ostijumi koronarnih arterija ne budu blokirani i da podupirači stenta zaliska ne ometaju zid aorte na sinotubularnom spoju (slika 10). Ako se kraj ove replike veće veličine pravilno uklapa, implantirajte aortnu bioprotezu Magna Ease te veličine. Ako ovaj kraj s replikom veće veličine ne ulazi komotno, implantirajte veličinu zaliska koja je identifikovana u potkoraku b. Potrebno je primeniti tehniku zašivanja koja dovodi do supraanularnog postavljanja zaliska kao što je tehnika zašivanja horizontalnim povratnim šavovima. **Intraanularno određivanje veličine i implantacija:** Primenom intraanularne tehnike kompletan zalistak sa prstenom za zašivanje se postavlja u anulus. Za intraanularno određivanje veličine se može koristiti cilindrični kraj ili kraj s replikom zaliska merača veličine modela 1133. Za pravilno određivanje veličine je potrebno da merač veličine bude postavljen paralelno u odnosu na ravan anulusa i kompletan merač veličine, uključujući i simulirani deo s prstenom za zašivanje, treba da prođe kroz anulus (slika 11-13). Potrebno je primeniti tehniku zašivanja koja dovodi do intraanularnog postavljanja zaliska kao što je tehnika zašivanja izvrnutim povratnim šavovima.
4	Zašijte zalistak primenom odgovarajuće tehnike zašivanja kojom se izbegavaju potencijalni problemi koji su navedeni u odeljku **5.0 Mere predostrožnosti.**

UPOZORENJE: Zbog intenzivnih temperaturnih i svetlosnih uslova u operacionoj sali, bioprotezu je potrebno često ispirati (preporučuje na 1 do 2 minuta) na obe strane sterilnim fiziološkim rastvorom kako bi bioproteza ostala vlažna tokom procedure implantacije.

OPREZ: Pregledajte merače veličine i drške i uverite se da nema znakova habanja kao što su tupost, naprsline ili pukotine. Zamenite merač veličine/dršku ako uočite bilo koji znak propadanja.

UPOZORENJE: Fragmenti merača veličine/drški ne mogu da se pronađu pomoću spoljnog sredstva za snimanje.

11.3.1 Uklanjanje držača/drške

Integralni držač i dodatna drška se uklanjaju kao jedna jedinica nakon završetka procedure zašivanja na sledeći način (pogledajte sliku 3):

Korak	Procedura
1	Kao što je prikazano, skalpelom ili makazama isecite svaki od tri izložena šava na vrhu držača. **OPREZ: Izbegavajte sečenje ili oštećivanje stenta ili osetljivog tkiva listića prilikom sečenja šavova.**
2	Kada pravilno isečete sva tri pričvrsna šava, uklonite sklop držača/drške i pričvrsne šavove sa bioproteze kao jednu jedinicu.
3	Uklonite držač sa drške i odložite ga u otpad nakon operacije. Ako koristite dršku modela 1111, očistite i sterilišite dršku pre svake upotrebe.

11.4 Dodatna oprema

Merači veličine

Korišćenje instrumenata za određivanje veličine olakšava izbor odgovarajuće veličine zaliska za implantaciju. Merači veličine modela 1133 su dizajnirani tako da omogućavaju direktnu proveru uklapanja u anulus. Merač veličine modela 1133 je razvijen za precizno određivanje veličine aortne bioproteze Magna Ease kod različitih pacijenata. Svaki merač veličine ima ručku sa različitim konfiguracijama merača veličina na svakom kraju (slika 4). Na jednoj strani ručke je cilindrični kraj sa integrisanom ivicom koja odražava geometriju prstena za zašivanje zaliska (slika 5). Na drugoj strani ručke je kraj replike zaliska koji održava geometriju prstena za zašivanje zaliska, visinu i lokaciju podupirača stenta (slika 6). Merač veličine je dostupan za svaku veličinu aortne bioproteze Magna Ease (19, 21, 23, 25, 27 i 29 mm).

OPREZ: Nemojte koristiti merače veličine zaliska drugih proizvođača niti merače veličine za druge proteze zaliska kompanije Edwards Lifesciences za određivanje veličine aortne bioproteze.

Držač i drška zaliska

Sklop držača/drške se sastoji od dve komponente: integralnog jednokratnog dela koji proizvođač fizički montira na zalistak i **savitljive** ručke (za višekratnu upotrebu na modelu model 1111 ili za jednokratnu upotrebu na modelu 1126) koja se postavlja na držač prilikom operacije.

OPREZ: Jednokratna ručka modela 1126 se isporučuje u sterilnom stanju za jednokratnu upotrebu i ne sme se ponovo sterilisati.

11.5 Uputstva za čišćenje i sterilizaciju dodatne opreme

Uputstva za čišćenje sterilizaciju potražite u Uputstvima za upotrebu koja se isporučuju uz dodatnu opremu za višekratnu upotrebu.

Ručka modela 1111 i merači veličine modela 1133 se isporučuju nesterilni i moraju se sterilisati pre upotrebe. Ručke i merači veličine se moraju očistiti i ponovo sterilisati pre svake upotrebe.

OPREZ: Pregledajte merače veličine i drške i uverite se da nema znakova habanja kao što su tupost, naprsline ili pukotine. Zamenite merač veličine/dršku ako uočite bilo koji znak propadanja.

11.6 Vraćanje eksplantiranih bioproteza

Kompanija Edwards Lifesciences je izuzetno zainteresovana za pribavljanje izvađenih kliničkih primeraka aortnih bioproteza Magna Ease radi analize. Informacije o vraćanju eksplantiranih bioproteza zatražite od svog lokalnog specijaliste za bioproteze. Eksplantirane bioproteze je potrebno staviti u odgovarajući histološki fiksativ kao što je formalin od 10 % ili glutaraldehid od 2 % i vratiti kompaniji. Nije potrebno čuvanje u frižideru u ovim okolnostima.

12.0 Informacije o pacijentu

12.1 Informacije o registrovanju

Kartica sa podacima o implantaciji za registraciju pacijenta se isporučuje u svakom pakovanju medicinskog sredstva. Unesite sve tražene informacije nakon implantacije. Serijski broj bioproteze je naveden na pakovanju bioproteze i na identifikacionoj oznaci koja je zakačena za bioprotezu i odštampana je na kartici sa podacima o implantaciji. Vratite unapred adresirani deo kartice našem Registru pacijenata sa implantom. Preostali delovi kartice namenjeni su za evidenciju bolnice i hirurga. Po prijemu od strane našeg Registra pacijenata sa implantom, za pacijenta će se izdati identifikaciona kartica koja staje u novčanik. Ova kartica omogućava pacijentima da obaveste zdravstvene radnike o tome koji tip implanta imaju kada se jave na pregled. Prilikom odlaganja bioproteze u otpad ili menjana prethodnog medicinskog sredstva kompanije Edwards Lifesciences, o tome obavestite naš Registar pacijenata sa implantom.

12.2 Uputstvo za pacijenta

Materijali s informacijama za pacijente se mogu dobiti od kompanije Edwards ili specijaliste za prodaju kliničkih proizvoda kompanije Edwards.

12.3 Bezbednost u okruženju magnetne rezonance (MR)

Uslovno bezbedno za MR

U nekliničkom testiranju je dokazano da je perikardna aortna bioproteza Carpentier-Edwards PERIMOUNT Magna Ease, model 3300TFX, uslovno bezbedna za MR. Pacijent sa zaliskom može bezbedno da se snima u MR sistemu koji ispunjava sledeće uslove:

- Statičko magnetno polje od 3 T ili manje
- Prostorni gradijent magnetnog polja manji od 3000 G/cm
- Maksimalna specifična brzina apsorpcije (SAR) uprosečena za celo telo koju prijavljuje MR sistem od 2,0 W/kg u normalnom radnom režimu

Pod gorenavedenim uslovima skeniranja, očekuje se da perikardna aortna bioproteza Carpentier-Edwards PERIMOUNT Magna Ease, model 3300TFX, proizvede maksimalan porast temperature od 2,3 °C nakon 15 minuta neprekidnog snimanja. U nekliničkom testiranju je artefakt na snimku koji je izazvalo medicinsko sredstvo bio oko 25,5 mm od perikardne aortne bioproteze Carpentier-Edwards PERIMOUNT Magna Ease prilikom snimanja gradijent eho pulsnom sekvencom i oko 12,5 mm od medicinskog sredstva prilikom snimanja spin eho pulsnom sekvencom na MR sistemu od 3 T. Lumen je pod ovim uslovima delimično do potpuno zatamnjen.

Cene podležu promeni bez najave.

Ovaj proizvod se proizvodi i prodaje pod najmanje jednim ili više patenata u SAD: Brojevi patenata u SAD 6,413,275; 6,416,547; 8,202,314; 8,366,769; 8,632,608; i 9,439,762; i odgovarajućim stranim patentima. Pored toga, dodatni patenti su u procesu registracije.

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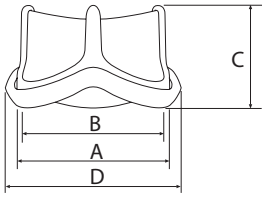
Tabela 1: Nominalne specifikacije (mm)

Aortna perikardna bioproteza Carpentier-Edwards PERIMOUNT Magna Ease, model 3300TFX



Veličina	19 mm	21 mm	23 mm	25 mm	27 mm	29 mm
A. Prečnik stenta (žičani okvir)	19	21	23	25	27	29
B. Unutrašnji prečnik stenta	18	20	22	24	26	28
C. Visina profila	13	14	15	16	17	18
D. Spoljni prečnik prstena za zašivanje	24	26	28	30	32	34
– Prečnik anulusa tkiva	19	21	23	25	27	29

Napomena: Prilikom određivanja veličine pratite preporuke za hiruršku proceduru.

Tabela 2: Sažetak stopa komplikacija, Model 2700

	Izolovana populacija sa zamenom aortnog zaliska (AVR)			Populacija sa zamenom mitralnog i aortnog zaliska (DVR)		
Komplikacije	**Operativni % pacijenata**	**Postoperativni % po pacijent-godini**	**% bez događaja na šest godina (standardna greška)**	**Operativni % pacijenata**	**Postoperativni % po pacijent-godini**	**% bez događaja na šest godina (standardna greška)**
Smrt	4,7	4,6	73,5 (2,0)	12,9	4,2	67,2 (6,5)
Eksplantat	0	0,3	98,5 (1,0)	0	0,8	NP*
Ponovna operacija povezana sa zaliskom	0,7	0,1	99,8 (0,4)	0	0	NP*
Sve ponovne operacije	22,4	1,8	75,4 (1,8)	34,3	2,3	NP*
Tromboembolija povezana sa zaliskom	3,1	1,5	91,4 (1,1)	1,4	5,1	NP*
Sve tromboembolije	5,0	2,4	84,9 (1,6)	5,7	6,6	NP*
Endokarditis	0,6	0,8	95,8 (0,9)	1,4	1,5	NP*
Disfunkcija zaliska	0,1	0,7	96,0 (1,1)	0	0,4	NP*
Perivalvularno curenje	0,1	0,3	98,8 (0,5)	0	1,2	NP*
Hemoragična komplikacija antikoagulantne terapije	1,4	0,4	96,4 (1,1)	4,3	2,3	NP*
Hemoliza	0	0,2	99,1 (0,4)	0	0,4	NP*
Tromboza zaliska	0	0	100,0 (0)	0	0,4	NP*

* NP = Nije primenljivo

Tabela 3: Rezultati postoperativne ehokardiografije, Model 2700

	Veličina zaliska						
	19 mm	**21 mm**	**23 mm**	**25 mm**	**27 mm**	**29 mm**	**Ukupno**
Ukupno N	12	22	15	8	3	3	63
Prosečno meseci nakon operacije	28,6 ±7,2	34,9 ±8,6	36,9 ±9,2	39,9 ±7,6	31,4 ±15,9	15,3 ±12,2	34,6 ±9,2
Brzina (M/sek.) srednja vrednost ± SD	2,80 ±0,49	2,56 ±0,46	2,36 ±0,42	2,15 ±0,56	2,09 ±0,27	2,08 ±0,1	2,46 ±0,50
n =	12	21	15	7	3	3	61
opseg	1,90–3,60	1,90–3,90	1,39–2,86	1,00–2,60	1,90–2,40	2,05–2,10	1,00–3,90
Trenutna vršna vrednost							
Gradijent (mmHg) srednja vrednost ± SD	32,22 ±11,08	27,04 ±10,49	23,00 ±7,30	19,50 ±8,16	17,60 ±4,70	14,4 ±0,58	25,67 ±10,14
n =	12	21	15	7	3	3	61
opseg	14,40–51,80	14,40–60,80	7,70–32,70	4,00–27,00	14,40–23,00	13,95–15,06	4,00–60,80

Tabela 4: Ishodi efikasnosti, funkcionalna klasifikacija NYHA, Model 2700

Preoperativna funkcionalna klasifikacija NYHA	Postoperativna funkcionalna klasifikacija NYHA					
	I	**II**	**III**	**IV**	**Rok trajanja**	**Nije dostupno**
I	18	19			9	
II	140	37			35	15
III	181	48	4	1	72	24
IV	43	16	2		53	2
Nije dostupno	5	1			2	2

Tabela 5: Sažetak svih stopa komplikacija povezanih sa zaliskom (N = 267), Model 2700

	Operativni period (<30 dana) % pacijenata		**Postoperativni period (≥30 dana) % po pacijent-godini**	
Komplikacije	**Br. incidenci**	**%**	**Br. incidenci**	**%**
Tromboembolija / Tromb	8	3,0	31	1,45
Endokarditis	0	0	7	0,33
Disfunkcija zaliska	1	0,37	34	1,60
Perivalvularno curenje	1	0,37	4	0,19
Hemoragična komplikacija antikoagulantne terapije	4	1,50	8	0,38
Hemoliza	0	0	2	0,09
Ponovna operacija / eksplantat	0	0	16	0,75
Ponovna operacija – Drugo	3	1,12	1	0,05
Rok trajanja	1	0,37	30	1,41
Ukupno	**18**		**133**	

Figures ■ Slike

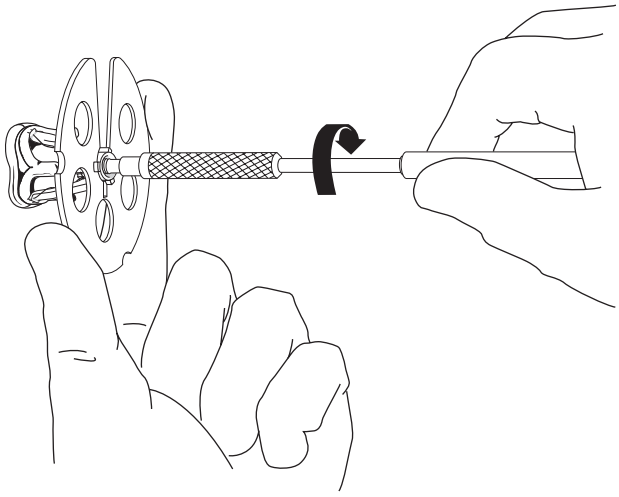


Figure 1: Aortic ■ Slika 1: Aortno

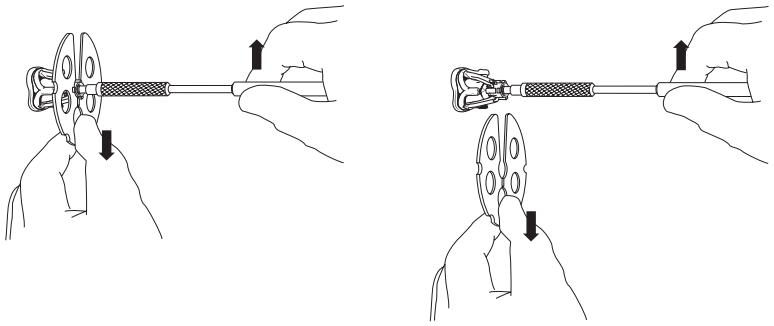


Figure 2: Aortic ■ Slika 2: Aortno

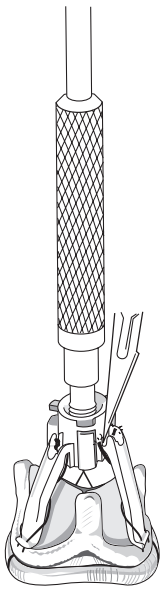


Figure 3: Aortic ■ Slika 3: Aortno

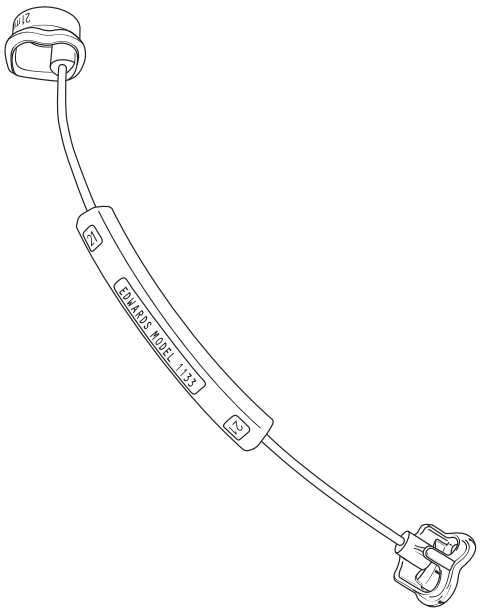


Figure 4: Aortic Sizer ■ Slika 4: Merač veličine aorte

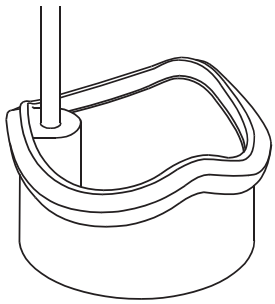


Figure 5: Cylindrical Sizer ■ Slika 5: Cilindrični merači veličine

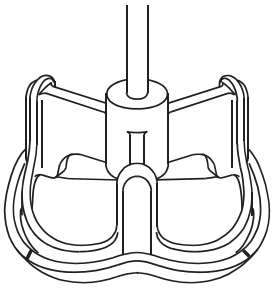


Figure 6: Replica Sizer ■ Slika 6: Merač veličine replike

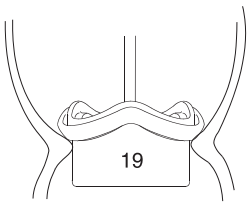


Figure 7: Supra-Annular Measurement ■ Slika 7: Supraanularno merenje

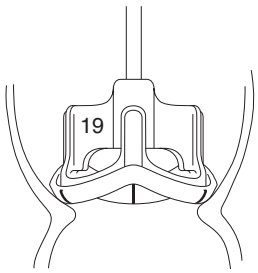


Figure 8: Supra-Annular Measurement ■ Slika 8: Supraanularno merenje

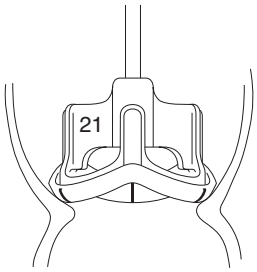


Figure 9: Supra-Annular Measurement ■ Slika 9: Supraanularno merenje

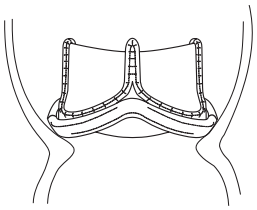


Figure 10: Supra-Annular Placement ■ Slika 10: Supraanularno postavljanje

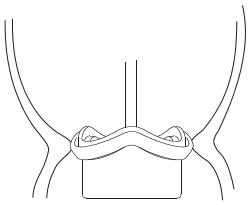


Figure 11: Intra-Annular Measurement ■ Slika 11: Intraanularno merenje

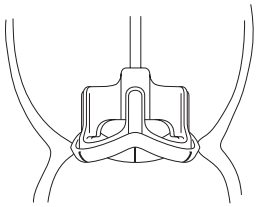


Figure 12: Intra-Annular Measurement ■ Slika 12: Intraanularno merenje

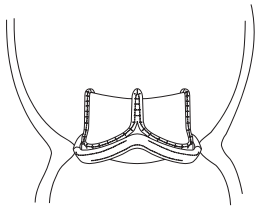


Figure 13: Intra-Annular Placement ■ Slika 13: Intraanularno postavljanje

Symbol Legend ■ Legenda sa simbolima

	English	Srpski
	Caution	Oprez
	Do Not Freeze - Store between 10 °C and 25 °C	Ne zamrzavati – čuvati na temperaturi između 10 °C i 25 °C
	Do not re-use	Ne koristiti ponovo
	Consult instructions for use	Pogledajte uputstvo za upotrebu
	Consult instructions for use on the website	Pogledajte uputstva za upotrebu na veb-sajtu
	Catalogue Number	Kataloški broj
	Date of manufacture	Datum proizvodnje
	Serial Number	Serijski broj
	Sterile	Sterilno
	Do not use if package is damaged	Ne koristite ako je pakovanje oštećeno

	English	Srpski
	Use-by date	Rok korišćenja
	Non-pyrogenic	Apirogeno
	Manufacturer	Proizvođač
	Quantity	Količina
	Size	Veličina
	Authorized representative in the European Community	Ovlašćeni predstavnik u Evropskoj zajednici
	MR Conditional	Uslovno bezbedno za MR
	Conformité Européenne (CE Mark)	Conformité Européenne (CE znak)
	Use product if indication is shown	Koristite proizvod ako je indikator prikazan
	Do not use product if indication is shown	Nemojte koristiti proizvod ako je prikazan indikator

Note: Not all symbols may be included in the labeling of this product. ■ **Napomena:** Na ambalaži proizvoda se možda ne nalaze svi simboli.

EC REP

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