INSTRUCTIONS FOR USE
VIVERE BOVINE PERICARDIUM BIOLOGICAL VALVULAR PROSTHESIS

Rev. 01 (03/07/2023)
Cód. 610963 D-2

1.PRODUCT DESCRIPTION

The VIVERE low profile bovine pericardium biological valve prosthesis is manufactured with bovine pericardium (PB), obtained from slaughterhouses immediately after the animal is slaughtered, and inspected by the Federal Inspection Service. After transportation, cleaning, and selection, the bovine pericardium is processed by immersion in a glutaraldehyde solution in order to implement its physical properties. The processing includes the REALOG process, which consists of treating the PB with a natural amino acid (glutamic acid), followed by oxidation (hydrogen peroxide) to reduce the GA polymeric bonds and blocking the free residual aldehydic groups, involved directly with thepost-implant local and systemic calcification and toxicity. Before manufacturing the bioprosthesis, the processed bovine pericardium is stored in a formaldehyde conservative solution, submitted to quality control (thickness, mechanical properties, and shrinking temperature), and after approval, released to manufacturing the prostheses.

After the material is released, it is assembled on a Polyacetal support ring containing a 316L stainless steel ring, inserted externally to reinforce the ring base and identify the position of the prosthesis post-implant by means of radiological examination. Before assembling the cusps on the support ring, the ring is coated with bovine pericardium also processed with glutaraldehyde and fixed with a polyester tab. The important structural characteristic is that the cusps are manufactured from a single pericardium patch, which provides the bioprosthesis with more homogeneous behaviors regarding hemodynamics, resistance to wear, and functional fatigue resulting from higher collagen and elastic fiber orientation homogeneity. The thickness of the processed pericardium used maintains is directly related to the prosthesis diameter. Hemodynamics performance tests, conducted according to ANSI/AAMI/ISO 5840:2021. Cardiovascular Implants - Cardiac ValveProstheses, show that the products fully meet the requirements (Table I) regarding the Effective Orifice Area (AEO) and Regurgitation Fraction. The prosthesis maintains its integrity, suggesting the high level of preservation of the tissue components, mainly collagen and elastic fibers that, as the most important structural elements due to the mechanical properties, ensure the quality and uniform performance under mechanical and hydrodynamic stress conditions.

Table I: Hydrodynamic performance indexes of the VIVERE valve in respect to the requirements established by ISO5840:2021. Cardiovascular Implant - Cardiac Valve Prostheses.

Parameter	Standard			VIVERE Bioprostheses*		
	Aortic/Mitral Positions			Aortic/Mitral Positions		
Prostheses Diameter (mm)	19	27	35	19	27	35
EOA (cm^2)	≥ 0,85	≥ 1,70/1.45	≥ 2,15	1.71±0,01	2,74±0,01/2.36±0.01	3,95±0,01
Regurgitation Fraction (%)	≤ 10	≤ 15	≤ 20	6.90±1,01	8.72±1,88/4.58±0.94	11.35±3,85

***** Measurements under the experimental conditions: beat rate 70 bpm and cardiac output 5.0 ± 0.2 l/min.

As a routine, before being released, the prostheses are evaluated regarding the general aspect, coaptation of the cusps, stem finishing, absence of wrinkles, and surface irregularities.

1.1. Technical Specifications (Figure 1 and Table II)

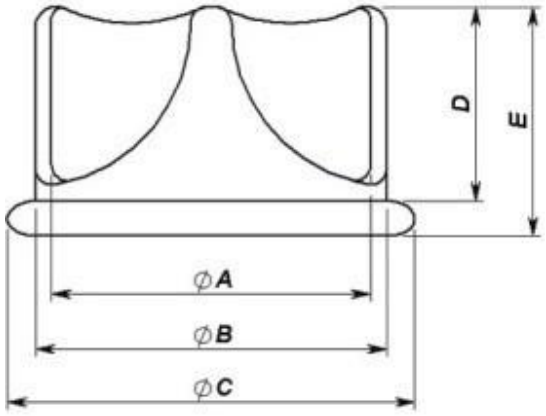


Figure 1: Schematic drawing of the technical specifications: VIVERE valve dimensions. ØA = internal diameter; ØB = external diameter; ØC = external diameter of thesuture ring; D = height of the stem; E = total profile height.

Table II: Technical specifications - VIVERE valve size (according to the external diameter): ØA = internal diameter; ØB = external diameter; ØC = external diameter of the suture ring; D = height of the stem; E = total profile height.

	Valve Prosthesis Specifications (mm)				
Size	**ØA** (±0,5)	**ØB** (±0,5)	**ØC** (±1,0)	**D** (±0,5)	**E** (±0,5)
19	14	19	23	7	10
21	16	21	25	8	11
23	18	23	27	9	12
25	20	25	29	10	13
27	22	27	31	11	14
29	24	29	33	12	15
31	26	31	35	13	16
33	28	33	37	13	16

2. PRESENTATION

The Vivere Bovine Pericardium Biological Valve Prosthesis is sterile and apyrogenic, supported by a polyacetal frame whose position determines the atrioventricular or outflow tract implant position. The prosthesis is stored in a hermetic polycarbonate pot filled with a 4% formaldehyde solution (primary packaging). The pot is closed with a security seal. The primary packaging is stored in a polystyrene box (EPS) package that includes a temperature indicator to control the storage and transportation conditions. The latter is placed inside a cardboard box together with the instruction manual and implant record form. Each package contains one valve, and describes the respective position and size.

The instruction manual is provided with the product. The product is available in the following sizes:

Aortic Position: 19, 21, 23, 25, 27, and 29 mm.

Mitral Position: 25, 27, 29, 31 and 33 mm.

SINGLE USE PRODUCT - STERILE - REPROCESSING PROHIBITED

3. INDICATION

The Vivere Bovine Pericardium Biological Valve Prosthesis is indicated for patients that require replacement of the aortic and/or mitral valves, damaged in consequence of a contracted or congenital disease, or for previous replacement of an implanted prosthesis

4. INTENDED PURPOSE

The Bovine Pericardium Biological Valvular Prosthesis has the purpose of regulating blood flow in replacement of a native heart valve damaged as a result of contracted or congenital valve disease, or to replace a dysfunctional prosthesis previously implanted.

5. CONTRAINDICATIONS

The prosthesis should not be used in patients with alternative indications of surgical methods of reconstruction or other procedures, whilst its use is at the physicist's criterion. The product should not be used in patients who are sensitive to products of animal origin.

6. CLINICAL BENEFITS

The clinical benefits that the Bovine Pericardium Organic Biological Valvular Prosthesis can provide are stable hemodynamic performance, durability, low rates of fatal complications, and higher patient survival rates.

7. ADVERSE EVENTS

The use of this medical device may cause: bacteremia, endocarditis, acute and chronic inflammatory reactions, immune sensitization, embolization, stenosis, neurological complications, hemorrhagic or ischemic stroke, symptomatic infectious aneurysms; brain abscess, meningitis, toxic encephalopathy, seizures, hemolytic anemia, thrombosis, thromboembolism, bleeding, acute and severe heart failure, glomerulonephritis, thrombocytopenia, death.

8. INTENDED PATIENT POPULATION

The prosthesis can be use in adult patients, who have a medical indication for replacement of one or more heart valves. The valves should not be used in patients who have congenital bicuspid anatomy or other forms of abnormal geometry aortic root geometry. Is contraindicate in patients with alternative indications of surgical methods of reconstruction or other procedures, whilst its use is at the physician´s criterion.

9. WARNINGS

- Read the instruction manual before using it.
- Product intended for SINGLE USE, WITH REPROCESSING FORBIDDEN, including re-sterilization, under the risk of causing permanent damages to it.
- The product should not be used in patients who are sensitive to products of animal origin.
- Do not use the product in case of leakage of conserving solution.
- Do not use the product in case the seal is broken, including when there is not leakage of conserving solution.
- Do not use the product in case it is not completely covered with conserving liquid.
- Do not use solutions with antimycotics because they could change the profile of original crosslinking resulting from the processing with the glutaraldehyde. The consequence would be alterations of the chemical, physical and biological properties of the product.
- Do not use the product in case it falls to the floor or is damaged, presenting clear signs of improper manipulation or presenting signs of deterioration.
- The product should be preferably stored at a temperature ranging from 10°C (50°F) to 30°C (86°F). It should not be used in case the temperature meter available on its external package is with its color altered, indicating that the product was submitted to extreme temperatures that can compromise its stability (≤0 (32°F) and ≥45°C (113°F), rendering the prosthesis unfit for use.
- Use aseptic techniques for all procedures.
- The product should not, under any circumstance, be submitted to any type of sterilization, under risk of causing permanent damages to it.
- Return the product immediately to the manufacturer in case it has some alteration.
- The product should not be used after the due date printed in its package.
- The clinical indication of Vivere Biological Valve Prosthesis of Bovine Pericardium, as well as the choice of its size, is the sole responsibility of the physician.

- The implantation of prosthesis with improper size can cause the deformation of the polyoxymethylene support, alteration in the performance of the prosthesis and damages to the adjacent tissues.
- The sale and use of this product are restricted to the use of the physician.
- The calcification which can happen after the implant in products manufactured with bovine pericardium processed with glutaraldehyde, results in structural deterioration of the prosthesis, a reaction that tends to be more significant in patients with high calcium metabolism, such as:
  - ✓ Pregnant and lactating women;
  - ✓ Children and young adults;
  - ✓ Patients with metabolic disorders of calcium, such as the patients with hyperthyroidism, chronic kidney problems and other pathologies;
  - ✓ Patients under regimen of hemodialysis;
  - ✓ Patients under aneurysmatic aortic degenerative conditions, with cystic medialnecrosis or Marfan's syndrome;
  - ✓ Patients with endocarditis.
- The implant of a valve prosthesis, although the countless clinical studies available in respect of its duration, is not exempt from adverse events which can include its replacement or death.

10. PRECAUTIONS AND SPECIAL CARE

- As the external portion of the package is not sterile, never place it on the instrumentation bench.
- The use of anticoagulant after the implant of valve bioprosthesis is recommended.
- The use of catheter and pacemaker electrode through the prosthesis should be carried at discretion of the physician in charge.
- The prosthesis should not be exposed to other solutions, except the formaldehyde contained in the package and sterile isotonic saline solutions used during the procedure of valve washing or irrigation.
- Vapors of formaldehyde are toxic and its contact with the skin or through respiratory tract should be avoided. In case of contact, wash the affected area thoroughly with water and seek medical care for appropriate treatment.
- Important: the prosthesis cannot be implanted without previous wash with sterile isotonic saline solutions due to cytotoxic effects of formaldehyde which is used in the conserving solution. The prosthesis should be washed as indicated in the guidelines for product handling before the implant.
- The use of antibiotics in any stage of prosthesis handling after its removal from sterile package is forbidden.
- Do not let the prosthesis dry after its removal from the conserving solution of sterile formaldehyde. The prosthesis should be continuously irrigated with its sterile isotonic saline solution during its implant.
- For definition of the best diameter and implantation of Vivere Valve Prosthesis, only the kit of meters and holder cable manufactured by Braile, should be used so as to ensure the security and effectiveness of the product. However, the users are reminded that the kit of meters and holder cable are not supplied in a sterile condition and should be cleaned and sterilized before every use, as per its instruction manual. They should be used in accordance with the appropriate techniques for their intended purpose and its use is the sole responsibility of the surgeon in charge of the procedure.
- The product is safe with Magnetic Resonance imaging studies until 3 Tesla (T), being

considered MR Conditional. The medical literature with 3T shows that there are not clinically significant interactions of the magnetic field which could compromise the safety of patients with heart valve bioprosthesis implanted, both with respect to thermal effects and to dehiscence of bioprosthesis (changes in the position of the implant).

- The product does not have restrictions regarding the exposure in other environmental conditions.
- Take care to avoid damage to the cuspids when stitching the site of implantation. If this is the case, then the product should be replaced.
- The leaflets which form part of the prosthesis should never be touched, under risk of being damaged.
- In case of damages during the handling, do not try to repair the prosthesis regardless the type of damage. If this is the case, it should not be used.
- Do not use cutting appliances and do not handle the prosthesis with pointed instruments, since there could be structural damages to it.
- The selection of valve diameter is responsibility of the surgeon and based on anatomic geometry of the receiving area of the prosthesis. The implantation of prostheses with improper size can cause the deformation of the polyoxymethylene support, alteration in the performance of the prosthesis and damages to the adjacent tissues. This is why the indication of using only Braille heart valve meters.
- In case of an intermediate anatomic diameter, always use a prosthesis with a smaller diameter. The implant of prostheses with greater diameters could result in difficulties of technical-surgical nature, structural damages and could even create mechanical stresses, which would cause the separation of pillar leaflets of the valve ring, causing regurgitation.
- The prosthesis is supplied in a sterile condition in a conserving solution of buffered formaldehyde contained in a sealed container with screw cap and after its removal, the prosthesis should be always handled under antiseptic conditions so as to avoid its contamination.

Warning: the prosthesis cannot be implanted without first being washed thoroughly with a sterile physiological saline solution.

11. SIDE EFFECTS

Valve implants manufactured with biological tissue are not exempt from side effects that may occur with higher or lower intensity, such as:

- Angina;
- Hemolytic anemia;
- Cardiac arrhythmia;
- Cardiac dysfunction;
- Heart attack;
- Cerebrovascular accident;
- Valve thrombosis;
- Thromboembolism;
- Hemolysis;

- Structural deterioration (calcification, leaflet laceration, or other);
- Nonstructural disorder (ventricular perforation with the ring stem, ring fracture, suture, inappropriate size, or other);
- Endocarditis;
- Stenosis;
- Regurgitation;
- Bleeding related to the use of anticoagulants/antiplatelet medications;
- Infective endocarditis;
- Valve or transvalvar leakage;

These events may lead to complications that include reoperation, prosthesis removal,permanent disability, and even death.

12. PACKAGING, STORAGE AND TRANSPORTATION

The prosthesis is supplied in a hermetic polycarbonate pot containing 4% formaldehyde solution and fixed to a holder by means of suture stitches.
In the original package, the product must be preferably conserved in a clean, dry environment protected from weather and with temperature between 10°C and 30°C. During transportation, the product shall never be refrigerated, frozen, or exposed to temperatures above 45°C.

13. VALIDITY

Four (4) years from the manufacturing date, as long as there are no visible signs of violationof the packaging or seal that ensure sterility.

14. USAGE INSTRUCTIONS

14.1. Procedure to remove the product from the packaging

Use only the set of meters and holder cable appropriate for the VIVERE valve. The use of other prosthesis meters may result in incorrect information to define the prosthesis dimensions.

- The prosthesis must be removed from the container by hand (Figures 2A and 3A)
- Using your hands, unscrew the holder support by turning it counterclockwise (Figures 2B and 3B).
- Fix the cable in the holder by turning it clockwise until the thread is complete (Figures 2C and 3C) to facilitate the positioning of the prosthesis in the implant site.
- Pass the suture threads through the valve prosthesis ring, suture the prosthesis, cut the three holder fixation points (Figures 2D and 3D), and remove the holder along with the cable.

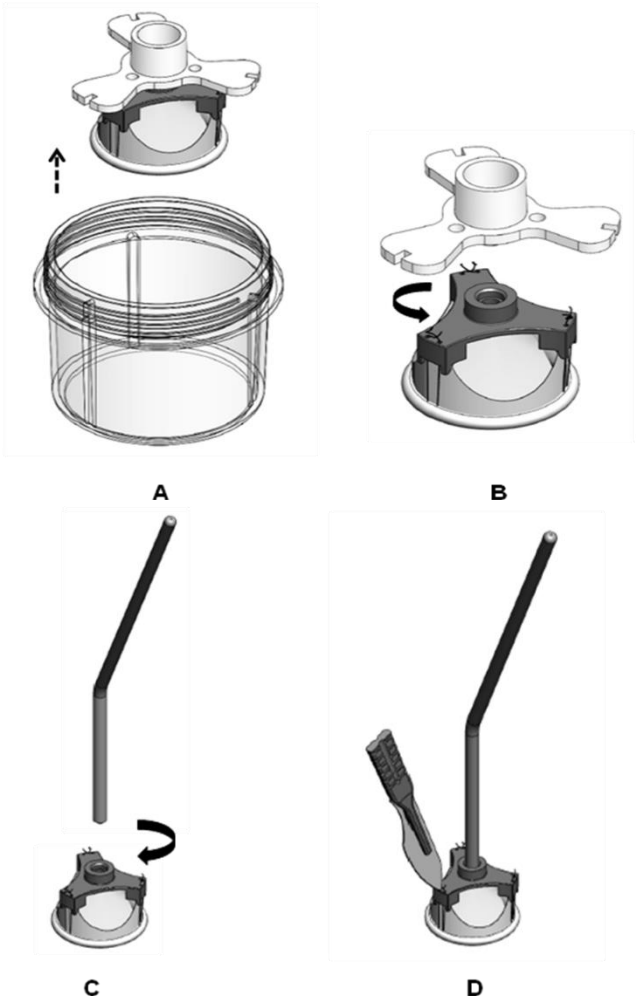


Figure 2: Schematic representation for removing the holder and prosthesis set from the packaging (A and B), attachment of cable to holder (C) and cut the holder fixation points (D) in aortic position.

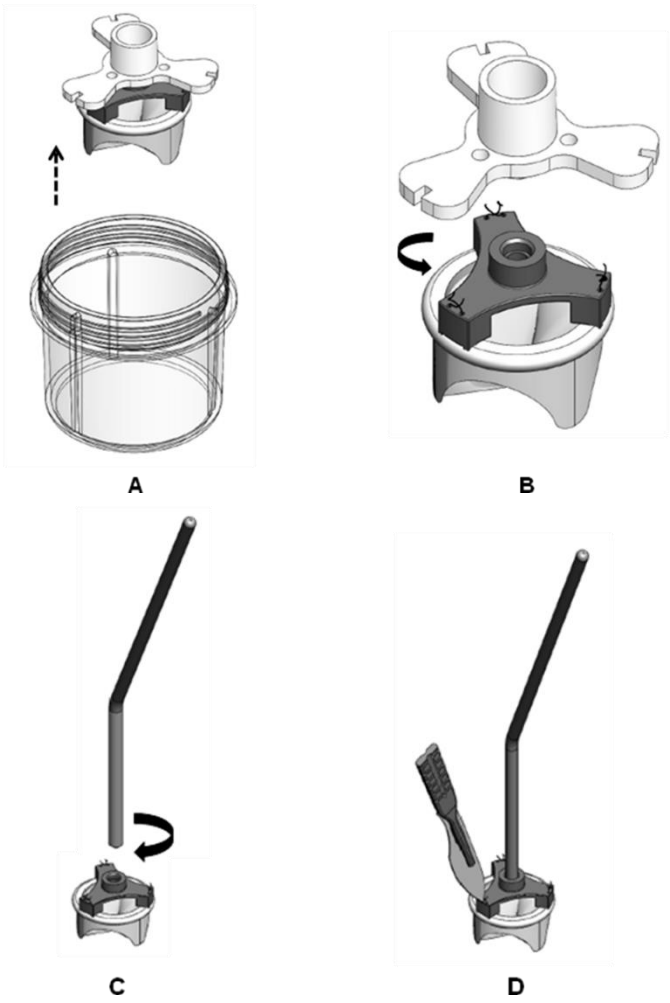


Figure 3: Schematic representation for removing the holder and prosthesis set from the packaging (A and B), attachment of cable to holder (C) and cut the holder fixation points (D) in mitral position.

14.2. Washing Procedure to Remove the Residual Formaldehyde

- After fixing the cable in the holder with the prosthesis, the assembly (prosthesis and holder) must be submerged for three (3) minutes in a container with approximately 500 ml of sterile saline solution and washed by moving gently to help remove the residual formaldehyde.
- After three minutes, the solution must be discarded and the prosthesis shall be submerged in new sterile saline solution for another three (3) minutes and again moved gently.
- This process must be repeated another three (3) times to completely remove the formaldehyde. This pre-implant washing process for biological bovine pericardial prostheses is validated and, provided it is carried out as described above, guarantees that the residual concentration of formaldehyde in the bioprostheses after the washing process is less than 0.1% by mass (m/m). This percentage, according to the requirements of (EU) 2017/745 Medical Devices Regulation, indicates that this concentration level of formaldehyde is considered a non-CMR substance, and does not offer any risk to the patient post-implantation.

ATTENTION: do not let the prosthesis dry during this stage, under the risk of causing irreversible damage to the structure of the cusps.

14.3. Implantation Technique

- The surgeon is responsible for choosing the surgical technique to implant the prosthesis.
- The size of the valve annulus must be measured exclusively with the set of meters supplied by Braile , taking care to sterilize the equipment before use.
- In order to identify the diameter of the prosthesis to be used, the meter must be introduced easily without valve annulus resistance.
- The decision to have an intra-annular or supra-annular implant rests exclusively with the surgeon responsible for the surgery.

  Intra annular: To implant the aortic valve prosthesis in the intra-annular position, it is necessary to perform the measurement using Braile aortic valve meters. For this type of implant with the patient's aortic valve cusps properly removed along with the calcifications, the meter must fit inside the aortic annulus. The cylinder that replicates the valve prosthesis sealing ring must be comfortably positioned inside the patient's aortic valve annulus. At this point, ensure that there is no obstruction of the coronary ostia and that the valve prosthesis posts will not interfere with the wall of the aorta or the sinotubular junction. When you obtain a meter that fits comfortably in the aortic valve annulus and does not obstruct the coronary ostia, nor in the aortic wall or in the sinotubular junction, opt for this size of the aortic valve prosthesis.

  Supra annular: When implanting the Braile aortic valve prosthesis in a supra-annular position, it will be possible to use larger valves than in the intra-annular implant. Therefore, it is possible to have better hemodynamic results with a larger effective orifice area.
- To perform this implant, it is necessary to use the Braile aortic valve prosthesis meters.
- With the patient's aortic valve cusps removed along with the calcifications, position the meter over the aortic annulus, using the cylindrical part of the meter that replicates the valve prosthesis' sealing ring. Therefore, ensure that there is no obstruction of the coronary ostia and observe the relationship between the height of the valve and the wall of the aorta and the sinotubular junction.
- Carry out an attempt to measure with a meter a larger number than the previous one with it resting on the aortic annulus (supra-annular) and confirm that there is no obstruction of the coronary ostia or interference with the height of the valve posts in the wall of the aorta or the sinotubular junction. If this larger meter is not comfortably accommodated above the aortic annulus or interferes with the coronary ostia, opt for the smaller prosthesis as explained initially.
- If there is probable interference of the valve post in the aortic wall or sinotubular junction, evaluate the possibility of enlarging the aortic root with a bovine pericardium patch at the surgeon's discretion, or if not, implant the smaller valve.
- When suturing the valve, care must be taken to avoid damaging the leaflet that is part of the structure.
- During the procedure, do not let the valve dry to avoid irreversible damage to its structure.
- All patients that are submitted to valve prosthesis implants must be evaluated by means of echocardiography after release or after thirty–days (30) and between six (6) to twelve (12) months after the surgery, in order to assess the performance of the prosthesis, including morphology and mobility or thickening of the leaflets.
- The examination is recommended every five (5) years after the implant as a routine or at any time due to clinical suspicion of any valve prosthesis disorder.
- The surgeon is responsible for choosing the use of transthoracic echocardiography, transesophageal echocardiography, or other imaging technologies.

14.4. Patient Records

- The form to record the implant, which is supplied together with the prosthesis, must be completed with all information requested and sent to the address indicated in the form.
- To ensure traceability, the surgeon or the surgical team shall fill in the product information in the patient's medical records.
- The product is supplied with traceability tags that shall be attached to the medical records.
- In case of any side effects, this traceability information is required by the manufacturer and shall be communicated to the competent bodies.
- In case of explant of newly implanted valve, Braile request that it be informed to collect the prosthesis and conduct further analysis. The explanted prosthesis must be stored in 10% formaldehyde solution.

14.5. Post-Implant Treatment Individualization

- Use of anticoagulants and/or antiplatelet medication: except in case of contraindication due to specific patient conditions, the general recommendation is that patients submitted to valve replacement shall be treated with these therapies for at least twelve (12) weeks after the implant. The surgeon is responsible for selecting the type of treatment, as well as the duration, based on the clinical conditions of the patient.
- Likewise, except in case of contraindication due to specific patient conditions, the use of low doses of aspirin is also indicated for patients submitted to valve replacement.
- Prophylaxis with antibiotics shall be considered as a possibility in case of patients undergoing dental treatment, due to the high bacteremic potential involved with procedures of such nature.

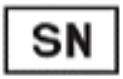
15. LIMITED WARRANTY

BRAILE INDÚSTRIA, COMÉRCIO E REPRESENTAÇÕES LTDA certifies that the product has been manufactured with due care, using quality materials, and is guaranteed against flaws and manufacturing defects according to the Brazilian Consumer Protection Code. The company also informs that, if unauthorized or unqualified persons violate the product, the warranty shall expire. The manufacturer establishes that no other warranty, express or implied by third parties, shall be considered valid. The use of the product is restricted to physicians or qualified and trained technicians under the supervision of the attending physician, who are familiarized with the product usage procedures, and who shall be responsible for the use of the respective products. The manufacturer shall not be responsible for any damages resulting from improper use of the product. BRAILE LTDA. also establishes that the provisions included in Article 26 of the Brazilian Consumer Protection Code (Law 8.078/90) shall rule the right of complaints regarding the product. No agent, employee, representative, or distributor of BRAILE LTDA. has the authority to change or amend this warranty, or assume or link BRAILE LTDA. to any other responsibility or warranty related to this product.

16. SYMBOLOGY DESCRIPTION


Consult instructions for use or consult eletronic instructions for use

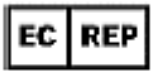
Catalogue number



Serial number

Batch code


Manufacturer



Authorized representative in the European Community/European Union

Date of manufacture


Use-by date


Do not re-use


Do not use if package is damaged and consult instructions for use


Do not resterilize

Sterile


Non-pyrogenic

MR Conditional

Contains biological material of animal origin

Medical Device

Unique device Identifier

Indicates that the product is in compliance with European legislation for medical devices


Temperature limit


Fragile, handle with care


This way up


Keep dry


Keep away from sunlight

Stacking limit by number


Recyclable packaging

17. LABEL TEMPLATE

Braile Indústria Comércio e Representações Ltda.
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EC REP

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E-Mail: info@marsmedical.de

Technical name: Biological Heart Valve Prosthesis

Commercial Name: Vivere Bovine Pericardium Biological Valvular Prosthesis

Commercial Model: XXXXXXX

Package contents: 01 Unit intended to medical application and 01 instructions for use.

REF SN LOT

BR YYYY/MM/DD YYYY/MM/DD

Single use product

Reprocessing Prohibited

Liquid Chemical Sterilization

STERILE STERILIZE MR BIO MD UDI CE 2797

braile.com.br/en/produtos/
cemarkproducts

Conditions for storage, conservation, and/or handling of the product / Instructions for correct and safe use of the product / Warnings and/or precautions: See Instructions for Use.

The product must be stored between 10 and 30ºC and must not be frozen or exposed to temperatures above 45ºC during transport.

30°C 10°C 5

ANVISA Registration nº 10159030026

Responsible Technician: Vladimir D. A. Ramirez – CRF-SP 09010