LifeNet Health®
Saving Lives. Restoring Health. Giving Hope.

CARDIOGRAFT® CRYOPRESERVED CARDIAC ALLOGRAFT BIO-IMPLANT
(Aortic and Pulmonary Heart Valves)

Read this entire package insert carefully prior to use.

Federal law (U.S.A.) restricts this allograft bio-implant for use by a licensed clinician only.

DESCRIPTION

This allograft bio-implant was processed from donated human tissue, resulting from the generous gift of an individual or his/her family. Processing involves dissection, antibiotic disinfection and cryopreservation.

Aortic heart valves consist of the donor's ascending aortic conduit, aortic heart valve, myocardial sewing skirt, and intact anterior mitral leaflet. It should also be noted that the coronary arteries are ligated using medical grade sutures.

Pulmonary heart valves consist of the donor's pulmonary artery branch, pulmonary heart valve, and myocardial sewing skirt.

INDICATIONS FOR USE

This allograft bio-implant is intended for the replacement or reconstruction of diseased, damaged, malformed or malfunctioning native or prosthetic heart valves.

CONTRAINDICATIONS

The contraindications include, but are not limited to:

- Use in any patient who has a known or suspected allergy to any of the antibiotics and/or processing reagents listed in this package insert.

WARNINGS AND PRECAUTIONS

The same medical/surgical conditions or complications that apply to any surgical procedure may occur during or following implantation. The surgeon is responsible for informing the patient of the risks associated with their treatment and the possibility of complications or adverse reactions. As with any allograft bio-implant, the potential for transmission of infectious agents exists.

This bio-implant may contain residuals of antibiotics (Ciprofloxacin, Gentamicin, Lincomycin, Mefoxitin, Meropenem, Polymyxin B Sulfate, and/or Vancomycin), Anidulafungin and dimethylsulfoxide (DMSO). The concentration of DMSO in the final packaging is approximately 10%. Following the thaw and dilution instructions in this insert will result in a residual DMSO of approximately 2%. Caution should be exercised if the patient has a known sensitivity to any of these antibiotics and/or reagents.

This bio-implant and its packaging materials are latex-free.

STORAGE REQUIREMENTS

The distributor, intermediary and/or end-user clinician or facility is responsible for storing this allograft bio-implant under appropriate conditions prior to further distribution or implantation. Bio-implants must be stored as listed in the table below. Storage conditions are also stated on the label.

Preservation Method	Storage Temperature	Special Conditions
Cryopreserved	Store at liquid nitrogen vapor phase temperature (-120°C or below).	Store in its original cardboard box.
		Store in liquid nitrogen vapor phase freezers or equivalent, or maintain in the cryoshipper until removed for thawing and dilution.
		Do not submerge directly into liquid nitrogen.

If a cryopreserved bio-implant is accidentally immersed in liquid nitrogen, contact LifeNet Health immediately. The circumstances surrounding accidental immersion must be reviewed prior to the potential use of the bio-implant.

DONOR SCREENING AND TESTING

All donors have been screened and tissues recovered, processed, stored, tested and distributed in accordance with current U.S. federal regulations as promulgated in 21 CFR 1270 and 1271, current *Standards for Tissue Banking* set forth by the American Association of Tissue Banks (AATB) and international laws and regulations as required.

This allograft bio-implant was deemed suitable for implantation by LifeNet Health. A physician medical director evaluated the following donor variables to determine donor suitability: infectious disease test results, current donor medical history, behavioral risk assessment interview, physical assessment, relevant medical records, including previous medical history, laboratory test results, and autopsy or coroner reports (if performed).

All donors are tested for relevant infectious diseases. Testing is performed by laboratories that are registered with the U.S. Food and Drug Administration (FDA) and certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA) and 42 CFR 493. Test methods that are FDA-licensed, approved, or cleared for donor screening are used as available. The following test criteria were met for the donor of this allograft bio-implant:

REQUIRED INFECTIOUS DISEASE TESTING	
TEST	**ACCEPTANCE CRITERIA**
HBcAb: Hepatitis B Total Core Antibody	NEGATIVE/NON-REACTIVE
HBsAg: Hepatitis B Surface Antigen	NEGATIVE/NON-REACTIVE
HCV NAT: Hepatitis C Virus Nucleic Acid Test	NEGATIVE/NON-REACTIVE
HCVAb: Hepatitis C Antibody	NEGATIVE/NON-REACTIVE
HIV-1 NAT: Human Immunodeficiency Virus Type 1 Nucleic Acid Test	NEGATIVE/NON-REACTIVE
HIV 1/2 Ab: Human Immunodeficiency Virus Types 1/2 Antibody	NEGATIVE/NON-REACTIVE
RPR/STS or Equivalent: Syphilis	CONFIRMATORY NEGATIVE/NON-REACTIVE
HTLV I/II Ab: Human T-Lymphotropic Virus Types I/II Antibody*	NEGATIVE/NON-REACTIVE

* *Not required for donors recovered after March 31, 2010. Performed as required by international laws and regulations.*

POTENTIAL ADVERSE EVENTS

Potential adverse events or outcomes include, but are not limited to, infection, allograft tissue rejection, allergic reaction to residual processing reagents, fibrocalcification, stenosis, hemorrhage, thromboembolism, loss of bio-implant structural integrity, bio-implant rupture, aneurysm, reoperation and/or death.

Promptly report any adverse event(s) or outcome(s) potentially attributable to the allograft bio-implant (See COMPLAINTS AND RETURNS section).

TRACEABILITY

It is the responsibility of the end-user to maintain recipient records for the purpose of tracking tissue post-implantation. LifeNet Health has enclosed an Implant Registration Card. Please refer to the enclosed card for additional instructions.

Please See Back for Thawing and Dilution Instructions

INSTRUCTIONS FOR USE

⚠ It is important to read and understand the following instructions prior to clinical use. Improper preparation technique may adversely affect handling properties and/or performance.

GENERAL INSTRUCTIONS

- Use on a single occasion for a single patient only.
- Once the packaging is opened, the bio-implant must be used for the current procedure or discarded.
- Inspect the bio-implant, inner and outer packaging, and labels carefully:
  - Do not use past the expiration date as indicated on the label.
  - Do not use if the bio-implant is damaged or the packaging integrity is compromised.
  - Do not use if there are discrepancies in label information.
  - If using more than one bio-implant in the same procedure, ensure to maintain proper identification of each bio-implant type after it is removed from its outer packaging.
- Use aseptic technique at all times.
- Do not sterilize.
- Keep the bio-implant stored according to recommended storage instructions until preparing it for implantation.
- Thaw and dilute each bio-implant individually.
- Once the bio-implant is thawed, it must be used for the current procedure or discarded.
- Do not refreeze the bio-implant after thawing has begun.
- Dropping or jarring may compromise the integrity and/or functionality of the bio-implant.

PREPARATIONS FOR USE:

Supplies Needed:

- 2 major basins (≥ 5000 ml capacity)
- Non-toothed clamp
- Scissors
- Smooth forceps
- 1000 ml room temperature D5LR sterile solution
- 2000 ml warm 0.9% (normal) sterile saline
- Thermometer

Note: *Additional warm or room temperature sterile saline may be required to maintain thawing temperature or utilize a sterile warmer that can be maintained at 37°C – 42°C.*

⚠ **This thawing process helps minimize damage to the bio-implant by controlling the melting of ice crystals and considerably diluting the cryoprotectant, DMSO. Failure to follow these instructions could result in failure of the bio-implant and be detrimental to patient safety. Please coordinate the timing of this procedure with the surgeon.**

Opening and Thawing Instructions:

1. **Non-Sterile Team Member:** Using insulated gloves, retrieve the packaged bio-implant from the appropriate storage location. Open the box lid and **place at room temperature for 7 minutes on a stable surface**. While the bio-implant is thawing, pour a minimum of 2000 ml warmed sterile saline solution into the first sterile major basin. Add enough room temperature sterile saline to maintain a temperature at 37°C – 42°C.

2. After the 7 minutes has elapsed, remove the bio-implant from its box, open the outer peel pack and present the inner pouch to the **Sterile Team Member.**

3. **Sterile Team Member:** Using a non-toothed clamp, firmly grasp the inner pouch by the sealed edge and remove from outer peel pack.

4. Slowly lower inner pouch into the pre-filled major basin. **The saline must maintain a temperature at 37°C to 42°C throughout the entire thawing process.** To monitor the temperature, use a sterile thermometer or a sterile warmer that can be set to a temperature at **37°C to 42°C.** If using a thermometer, add warm or room temperature sterile saline as appropriate to maintain the required temperature range. **Do not exceed 42°C. Exceeding 42°C may damage the bio-implant.** Do not pour saline directly onto the pouch; pour into surrounding saline bath.

5. Gently agitate pouch periodically for 5-7 minutes until ice is melted. Do not manipulate the bio-implant.

6. Once the bio-implant has thawed, dry the outside of the pouch thoroughly. Open with scissors.

Dilution Instructions:

7. **Non-Sterile Team Member:** Pour 1000 ml of room temperature D5LR into the second sterile major basin.

8. **Sterile Team Member:** Gently remove the bio-implant from the pouch with smooth forceps and carefully place into the basin containing the D5LR. Allow the bio-implant to passively rinse in this solution for a minimum of 5 minutes.

⚠ ***Do not allow the bio-implant to dry. If implantation is delayed, cover basin with sterile towel and place basin in larger basin of sterile slush.***

COMPLAINTS AND RETURNS

For further information on returns or to report a complaint or adverse event, please contact your authorized distributor or LifeNet Health Client Services (available 24 hours a day) at 1-888-847-7831 (inside the U.S.) or 00+1-757-464-4761 ext. 2000 (outside the U.S.) and have the bio-implant's identification number available (see label).

Cryoshipper Return: Please refer to CardioGraft Tissue Receiving & Cryoshipper Return Instructions. This document accompanies each cryoshipper.

WARRANTY STATEMENT

Due to the inherent variability of allograft tissue, biological and biomechanical properties cannot be guaranteed by LifeNet Health.

Source Establishment: LifeNet Health CTO #100038

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1864 Concert Drive | Virginia Beach, VA 23453, USA
1-888-847-7831 (inside the U.S.) | 00+1-757-464-4761 ext. 2000 (outside the U.S.)
www.lifenethealth.org