GRAFIX PL◇PRIME

Lyopreserved Placental Membrane

DESCRIPTION

GrafixPL PRIME (lyopreserved placental membrane) is a lyopreserved amnion matrix retaining the extracellular matrix, growth factors, and endogenous neonatal mesenchymal stem cells, fibroblasts and epithelial cells of the native tissue. GrafixPL PRIME is a Human Cells, Tissues, and Cellular Tissue Based Product (HCT/P) as defined in 21 CFR part 1271 and Section 361 of the Public Health Service Act.

GrafixPL PRIME is processed from donated human placental tissue that has been generously donated by healthy mothers who have undergone full term pregnancies and delivered healthy infants. GrafixPL PRIME allografts are processed aseptically in a controlled clean room environment using methods designated to prevent contamination and cross-contamination of the product, following rigorous quality assurance standards, and then stored and distributed for use in accordance with the regulations in 21 CFR 1271, the standards of the American Association of Tissue Banks (AATB) and applicable state regulations.

INDICATIONS AND USAGE

GrafixPL PRIME may be used to repair acute and chronic wounds, including but not limited to diabetic foot ulcers, venous leg ulcers, pressure ulcers, dehisced surgical wounds, burns, acute surgical wounds, pyoderma gangrenosum, and epidermolysis bullosa. The HCT/P is limited to homologous use as a wound cover and may be used for acute and chronic wounds encompassing both upper extremity and lower extremity. GrafixPL PRIME naturally conforms to complex anatomies and may be used over exposed bone, tendon, joint capsule, muscle and hardware.

Limitations of Use:

- Intended for use in one patient, on a single occasion only.
- The tissue is intended for use by qualified healthcare specialists such as physicians, podiatrists, or other appropriate healthcare professionals.

DOSAGE

The quantity and size of product used will vary based upon wound size and physician recommendation. Application of GrafixPL PRIME is recommended weekly for up to 12 weeks or until the wound is closed.

DONOR ELIGIBILITY - 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 disseminated in 21 CFR 1271, current AATB standards, and state/local regulations as required.

GrafixPL PRIME was deemed suitable for transplantation. The Medical Director or physician designee, has determined that the donor of the tissue contained in this product is eligible to donate tissue for transplantation based on meeting the following criteria: (1) The results of donor screening indicated that the donor was free from risk factors for, and clinical evidence of, infection due to relevant communicable disease agents and diseases, and is neither a xenotransplantation recipient nor a close contact of a xenotransplantation recipient, and (2) the results of donor testing by the following methodologies are negative or nonreactive:

Human Immunodeficiency Virus Type 1 Antibody (HIV)
Human Immunodeficiency Virus Type 2 Antibody (HIV)
Hepatitis C Virus Antibody (HCV)
Hepatitis B Surface Antigen (HBV)
Hepatitis B Core Antibody (HBV)
Syphilis Rapid Plasma Reagin (RPR) or Treponemal Specific Assay
Human T-Cell Lymphotropic Virus Type I Antibody (HTLV)
Human T-Cell Lymphotropic Virus Type II Antibody (HTLV)
HIV/HCV/HBV Nucleic Acid Test (NAT)
West Nile Virus (WNV) Nucleic Acid Test (NAT)

Communicable disease testing was performed by a laboratory registered with FDA to perform donor testing and certified to perform such testing on human specimens in accordance with the Clinical Laboratory Improvement Amendments of 1988 (CLIA) and 42 CFR part 493, or that has met equivalent requirements as determined by the Centers for Medicare and Medicaid Services (CMS). The testing was conducted using the appropriate FDA-licensed, approved or cleared donor screening tests for living donors following manufacturers' instructions for these tests. The records of this testing are maintained at Smith+Nephew at the address on this document.

QUALITY CONTROL TESTING

1. Asepsis – Representative product from each lot undergoes destructive microbiological verification testing per USP <71> Sterility Tests. The results must show "No Growth" after 14 days incubation in growth promoting media.
2. Representative product from each lot undergoes residual moisture content analysis per USP <921> Water Determination. The results must demonstrate less than or equal to 10% moisture from each lot.
3. Custom in vitro assays are performed to determine the presence of Epidermal Growth Factor and the presence of viable cells across ≥ 70% of the tissue tested.

CONTRAINDICATIONS

There are no known contraindications for this product.

WARNINGS AND PRECAUTIONS

1. Do not use if package integrity has been compromised. Once the user breaks the seal on the foil pouch, the HCT/P must be transplanted or discarded.
2. The HCT/P may not be sterilized.
3. The same medical/surgical conditions or complications that apply to any medical/surgical procedure may occur during or following application.
4. The healthcare professional is responsible for informing the patient of the risks associated with his/her treatment and the possibility of complications or adverse reactions.
5. Caution should be exercised for patients with known sensitivities to the following reagents used for processing, disinfection, and storage and may remain on the HCT/P:
   - ***Lyopreservation Solution:*** 18.9% w/v Trehalose in Dulbecco's Phosphate Buffered Saline (DPBS)
   - ***Disinfection Solution:*** 0.5% v/v Gentamicin Sulfate, 0.1% v/v Vancomycin reconstituted in Water for Injection (WFI), 1% v/v Amphotericin B, 98.4% Dulbecco's Modified Eagle's Medium (DMEM)
   - ***Processing Solution:*** DMEM, DPBS, 11% Anticoagulant Citrate Dextrose Solution in Saline, Formula A (ACD-A), 1.7% w/v Trehalose in DPBS
6. Although the tissue has been tested and screened for human pathogens according to FDA and CDC guidelines, and processed under aseptic conditions, human derived tissue may still transmit infectious agents or diseases of known or unknown etiology including, but not limited to fungi, bacteria, or viruses [e.g. HIV or Zika Virus (ZIKV)].
7. Other complications of tissue transplantation may occur, such as immune rejection of transplanted HCT/P or loss of function and/or integrity of HCT/P.

Please promptly report adverse outcomes to Smith+Nephew at the address on page 2 of this document.

(continued on page 2)

GRAFIX PL® PRIME

Lyopreserved Placental Membrane

TRACEABILITY

It is the responsibility of the tissue distribution intermediary, and/or end-user clinician to maintain tissue intended for transplantation in appropriate storage conditions prior to further distribution or transplant and that recipient records must be maintained for the purpose of tracing tissue post-transplantation. Please record the distinct HCT/P identification code in your records and in the patient's files. As a courtesy to the end-user clinician or facility, a Tissue Tracking Form is enclosed to help facilitate proper tracking of this tissue; when completed and returned, this Form gives Smith+Nephew the ability to maintain records for the purpose of tracing the tissue post-transplant. Please complete the enclosed Tissue Tracking Form and fax to 443.552.4960 according to 21 CFR 1271.290(b) and Joint Commission Standards TS.03.02.01 and EP 7.

ADVERSE EVENTS, COMPLAINTS, AND RETURNS

To report an adverse event or complaint, please contact your sales representative, authorized distributor, or Smith+Nephew Customer Service at 888.674.9551. Adverse outcomes potentially attributed to the tissue must be reported promptly to Smith+Nephew.

Please contact your local sales representative, authorized distributor, or Smith+Nephew Customer Service for information on returns.

HOW SUPPLIED

GrafixPL PRIME is supplied in sheet form between two (2) mesh applicators and packaged within a heat-sealed pouch contained within a tertiary box. This packaging configuration allows for the introduction of the HCT/P into the sterile field. One reimbursable unit is $1cm^2$.

STORAGE CONDITIONS

The intermediary, end-user and/or clinician or facility is responsible for storing GrafixPL PRIME under appropriate conditions prior to further distribution or application. GrafixPL PRIME must be stored as listed in the table below.

Preservation Method	Lyopreservation
Storage Temperature	Room Temperature
Special Conditions	Single Use Do Not Freeze Do Not Refrigerate Do Not X-RAY Do Not Irradiate/Sterilize Any unused product must be discarded in biohazard waste.

EXPIRATION DATING

Shelf-Life	Refer to expiry date on labeled package.

INSTRUCTIONS FOR USE

WARNING: Open the pouch slowly to prevent mesh and graft from popping out of the pouch. Once the product is removed from the packaging, the application protocol below must be followed. Once the user breaks the seal on the foil pouch, the tissue graft must be transplanted or discarded.

GrafixPL PRIME can be applied in an office, hospital outpatient setting, or in an operating room. Always review and follow your facility's policy regarding sterile/aseptic/clean technique. Proper aseptic technique should be followed when applying the product.

APPLICATION PROTOCOL

For application of the product, follow one of the two below methods.

Method #1

1. Remove one mesh applicator from the graft.
2. Apply the graft side directly onto the wound bed.
3. Press and hold until product is rehydrated by wound fluid or the addition of sterile saline.
4. Remove the other mesh applicator. Do not leave mesh on wound.

Method #2

1. Remove the mesh applicators from both sides of graft. Discard the two mesh pieces.
2. Apply product directly onto the wound bed.
3. Press and hold until product is rehydrated by wound fluid or the addition of sterile saline.

Application Notes for Both Methods

- Ensure the graft is in direct contact with all surfaces of the wound bed.
- Apply sterile saline if needed to ensure the entire product is moistened and fold any excess product into the wound bed.

GrafixPL PRIME does not require fixation (suturing, etc.) but these methods may be used by the physician or the appropriate healthcare provider at his or her discretion.

Cover the applied graft in the wound with a non-adherent dressing followed by saline moistened gauze to fill but not pack the wound, or use another dressing as appropriate for the wound type.

REAPPLICATION PROTOCOL

GrafixPL PRIME should be reapplied weekly at the discretion of the responsible physician or healthcare professional for the duration of the treatment.

FDA Registration Number 3006638648
Patent pending

Osiris THERAPEUTICS, INC.
is now part of
Smith+Nephew

7015 Albert Einstein Drive
Columbia, MD 21046
888.674.9551
www.grafixpl.com