# GRAFIX PRIME◊

## Cryopreserved Placental Membrane

**DESCRIPTION**

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

Grafix 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. Grafix PRIME allografts are processed aseptically in a controlled clean room environment using methods designated to prevent contamination and cross-contamination of the HCT/P 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**

Grafix 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. Grafix 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 HCT/P is intended for use by qualified healthcare specialists such as physicians, podiatrists, or other appropriate healthcare professionals.

**DOSAGE**

The quantity and size of the graft used will vary based upon wound size and physician recommendation. Application of Grafix 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. Grafix PRIME was deemed suitable for transplantation. The Medical Director or physician designee has determined that the donor of the tissue contained in this HCT/P 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:

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| 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 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. Custom *in vitro* assays are performed to determine the presence of Epidermal Growth Factors.
3. Custom *in vitro* assay is performed to determine the presence of live cells across 70% of the membrane sampled.

**CONTRAINDICATIONS**

There are no known contraindications for this HCT/P.

**WARNINGS AND PRECAUTIONS**

1. Do not use if package integrity has been compromised. Once the user breaks the seal on the 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 that may remain on the HCT/P:
   - ***Cryopreservation Solution***: 5% v/v Dimethyl Sulfoxide (DMSO), 1% v/v Human Serum Albumin (25% solution) (HSA), 94% Sodium Chloride (0.9% solution)
   - ***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:*** Dulbecco's Phosphate Buffered Saline (DPBS), 11% Anticoagulant Citrate Dextrose Solution in Saline, Formula A (ACD-A)
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 HCT/P transplantation may occur, such as immune rejection of transplanted HCT/P or loss of function and/or integrity of HCT/P.
8. The HCT/P is shipped frozen on dry ice. Caution should be exercised when removing the HCT/P from the shipper and when disposing of the dry ice. Please follow your approved Environmental and Health Safety Policy and/or the instruction on the Safety Data Sheet (SDS) for dry ice (solid carbon dioxide).

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

(continued on page 2)

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**TRACEABILITY**

It is the responsibility of the tissue distribution intermediary, and/or end-user clinician to maintain HCT/Ps 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+Nepehw 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 HCT/P must be reported promptly to Smith+Nephew.

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

**HOW SUPPLIED**

Grafix PRIME is supplied frozen in sheet form and packaged within a sterile cryobag contained 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 Grafix PRIME under the appropriate conditions prior to further distribution or application. Grafix PRIME must be stored as listed in the table below.

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| Preservation Method | Cryopreservation |
| Storage Temperature | Store frozen at -75° C to -85° C (-103° F to -121° F) until ready for use. If onsite storage is not available, the HCT/P may be stored in the validated sealed shipper within the labeled validated shipper expiry.<br>Product quality is not impacted by short term freezer excursions [temperatures up to -65° C (-85° F) for a maximum of 15 minutes] due to cycling or opening and closing of freezer doors. |
| Special Conditions | Single Use<br>Do Not X-RAY<br>Do Not Refreeze<br>Do Not Refrigerate<br>Do Not Irradiate/Sterilize<br>Any unused product must be discarded in biohazard waste. |

**EXPIRATION DATING**

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| Shelf-Life | Refer to expiry date on labeled package. |
| Following Preparation | The graft can be held in the sterile rinse basin for up to 1 hour after thawing. Use graft within 1 hour of thawing. |

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**INSTRUCTIONS FOR USE**

**WARNING: Once the product is removed from -75° C to -85° C storage the application protocol below must be followed or the HCT/P must be discarded. The product cannot be refrozen.**

Grafix 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 technique. Sterile materials and reagents do not necessarily need to be used when thawing the graft but can be utilized. Proper aseptic technique should be followed when applying the graft.

**APPLICATION PROTOCOL**

**Preparation**: (Gather and set out)

- 2 basins (one large basin for thawing and one small sterile basin for rinsing the graft),
- Warm or room temperature water (this does not need to be sterile as it is used to thaw the graft),
- A bottle of sterile saline (to rinse the graft and may be used to thaw the graft instead of water),
- Scissors, forceps, and gloves.

**Thaw:**

1. Remove graft from the outer box.
2. Grafix PRIME is packaged in a sterile cryobag which is contained in a sterile chevron pouch. The outside of the chevron pouch is not sterile. Do not use if the package integrity has been compromised.
3. Grasp the chevron end of the pouch and pull the layers apart.
4. Gently drop the cryobag into the large thaw basin.
5. Add enough water or saline (sterile or non-sterile) to completely immerse the cryobag.

**Warning: Do not use water or saline at a temperature greater than 39°C (102°F).**

6. The graft is completely thawed when no ice crystals are present (approximately 2-3 minutes).

**Warning: Do not leave Grafix PRIME in the thaw basin for more than 15 minutes.**

7. Once thawed, remove the graft from the cryobag. Hold the cryobag with the port side down. With scissors, cut the top of the bag taking care not to cut near the graft. With sterile forceps remove the graft from the cryobag.
8. Place the graft into the small sterile rinse basin containing sterile saline.
9. Grafix PRIME is now ready for application and should be applied within one hour or the graft should be discarded.

**Application:**

1. Hold the plastic backing on the tab labeled PRIME and remove the smaller, solid plastic cover from the top of the graft.
2. Once the cover is off, slowly slide graft from the plastic backing onto the bed of the wound.
3. Gently maneuver the graft to ensure the entire wound bed is covered. Grafix PRIME does not require fixation (suturing, etc.), but these methods may be used by the physician or appropriate healthcare professional at his/her discretion.
4. Cover the wound with a non-adherent dressing. Apply the appropriate compressive or outer layer dressing dictated by wound type.

**REAPPLICATION PROTOCOL**

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

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