AmnioExcel® Amniotic Allograft Membrane is a human placental-based tissue product processed using a proprietary method. The membrane acts as protective covering when placed over the wound, providing the key components found in human amnion including an intact extracellular matrix (ECM), growth factors, and cytokines. AmnioExcel easily molds and conforms to the wound, and helps provide an environment to repair, reconstruct, and replace tissue.
**Why Amniotic Tissue?**

Human amniotic membrane has been used to treat a variety of wounds for over 100 years. Research has shown that placental tissues can promote angiogenesis and new tissue formation, reduce scar tissue formation, modulate inflammation and pain and may have anti-microbial effects.

The amnion membrane is composed of:

- Collagen, elastin, fibronectin and proteoglycans that provide a three-dimensional architecture to promote reconstruction of damaged tissue
- Regenerative growth factors, such as PDGF, VEGF, TGF-β, FGF and IGF, as well as other proteins, anti-inflammatory cytokines and peptides that promote tissue repair

**The science behind AmnioExcel®**

Retains the structure of unprocessed human amniotic membrane including ECM

Laboratory analyses and assays demonstrated that DryFlex processing preserves continuous, intact epithelium, basement membrane, compact and fibroblast layers of the amniotic tissue, as illustrated in the histology section on the right. Other histological assessments demonstrate the presence of collagen and proteoglycans.

Retains key proteins of unprocessed human amniotic membrane

Laboratory analyses and assays demonstrated that the presence of cytokines and growth factors were maintained with particularly high quantities of EGF, PDGF, TGF-α, and TIMPs 1 and 2.

<table>
<thead>
<tr>
<th>Growth Factors</th>
<th>Interleukins</th>
<th>Tissue Inhibitors of metalloproteases</th>
</tr>
</thead>
<tbody>
<tr>
<td>bFGF</td>
<td>EGF</td>
<td>G-CSF</td>
</tr>
<tr>
<td>AmnioExcel</td>
<td>+</td>
<td>+</td>
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<tr>
<td>Native-human amnion</td>
<td>+</td>
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Multicenter RCT demonstrates AmnioExcel® + Standard of Care (SOC) significantly increases closure of chronic Diabetic Foot Ulcers (DFUs)\(^{16}\)

This prospective, multicenter, randomized, controlled clinical trial (RCT) with standardized ulcer care and off-loading incorporated a 2 week run-in period. Despite a short 6-week study period, AmnioExcel® + SOC achieved significantly greater (p=0.008) ulcer closure rates over SOC alone.

A Prospective, Randomized, Multicenter and Controlled Evaluation of the Use of Dehydrated Amnion Membrane Allograft (DAMA) compared to Standard of Care for the Closure of Chronic Diabetic Foot Ulcers.

Robert J. Snyder, DPM, MSc; Kenneth Shimozaki, DPM; Arthur Tallis, DPM; Michael Kerzner, DPM; Alexander Reyzelman, DPM; Dimitrios Lintzeris, DO; Desmond Bell, DPM; Randi L. Rutan; and Barry Rosenblum, DPM

*WOUNDS, March 2016*

**In this trial:**
- Stratified randomization yielded a statistically balanced demographic and wound characteristic distribution between groups
- Endpoint of complete ulcer closure objectively adjudicated with photographs and ulcer tracings
- Comparable adverse event profile between groups
- Both the Intent To Treat (all randomized subjects) and the Per Protocol (all completing the study) populations demonstrated statistically significantly greater ulcer closure rates with the addition of AmnioExcel® to the SOC regimen
AmnioExcel® Membrane Case Studies

Case 1

**WOUND TYPE: DFU**  
**PRODUCTS USED/APPLICATIONS:** AMNIOEXCEL® x 2  
**TIME TO CLOSE:** 8 WEEKS

**Post-Amputation Diabetic Foot Ulcer**

**Patient History:** 78-year-old male with diabetes, CAD, hyperlipidemia & HTN presented with post-amputation wound at his great left toe site measuring 4.0 x 3.3 x 0.6 cm.

**Challenges:** Diabetes and vascular insufficiency.

**Initial Assessment:** After 1 month of limited progress with standard wound care strategies and HBOT, he was treated with NPWT. Although he had previously been revascularized, his toe pressures had diminished to 25 mmHg, which is consistent with poor to lack of wound healing.

**Treatment Strategy:** Due to the slow rate of wound progression and failed therapies, AmnioExcel® Membrane was initiated at week 13 (Figure 1). AmnioExcel® Membrane was applied every 2 weeks with a total of 4 applications (Figure 2).

**Wound Progress:** Within 2 weeks, the wound was more granular (95%) and decreased in size.

**Outcome:** Wound closed 8 weeks after initial application of AmnioExcel® Membrane (Figure 3).

Case provided by Dimitrios Lintzeris, DO, CWS  
Medical Director, Wayne Memorial Hospital  
Clinical Preceptor, Campbell University Jerry M. Wallace School of Osteopathic Medicine  
Goldsboro, NC

Case 2

**WOUND TYPE: DFU**  
**PRODUCTS USED/APPLICATIONS:** AMNIOEXCEL® x 4 AND TCC-EZ®  
**TIME TO CLOSE:** 6 WEEKS

**Diabetic Foot Ulcer with Vascular Insufficiency**

**Patient History:** 91 year old male with CVA, diabetes, ABI 0.49, DFU with exposed tendon following failed vascular intervention.

**Challenges:** Diabetes and vascular insufficiency.

**Initial Assessment:** Wound measured 1.2 x 1.2 x 0.7 cm (Figure 1). Patient was ambulatory with a brace.

**Treatment Strategy:** AmnioExcel® was applied every 2 weeks.

**Wound Progress:** Wound progressively decreased in size as new granulation tissue formed (Figure 2).

**Outcome:** The wound closed at week 6 following 2 applications of AmnioExcel® (Figure 3). As of week 9, the patient tolerated independent ambulation and resumed wearing diabetic footwear with inserts.

Case provided by Margaret Doucette, DO, FABPM, CWSP  
Chief, Physical Medicine and Rehabilitation, Medical Director;  
Amputee/Wound Care/High Risk Foot, Boise VAMC  
Boise, ID
Indications For Use

AmnioExcel® Membrane is intended for use in wounds. This placental-derived allograft tissue is intended for homologous use for the repair, reconstruction and replacement of skin at the discretion of a physician.

- Clinical Applications to Repair, Reconstruct, and Replace for:
  - Chronic and acute wounds
  - Diabetic ulcers
  - Venous & arterial ulcers
  - Pressure ulcers
  - Traumatic injuries
  - Burns
  - Surgical wounds

FDA Regulation

AmnioExcel® Membrane is regulated as a Human Cellular and Tissue-Based Product (HCT/P) under Section 361 of the Public Health Service Act and is governed by the FDA Center for Biologics Evaluation and Research (CBER).

AmnioExcel® Membrane Advantages

- Helps provide an environment to repair, reconstruct, and replace wound tissue
- AmnioExcel® is one of the only dehydrated amniotic allograft to have published, Level 1 clinical evidence supporting its use on DFUs (16) and is supported by numerous peer-reviewed papers (16, 17, 19-21)
- DryFlex® Processing
  - Preserve the inherent ECM, growth factors, and cytokines
  - Excellent handling and non-side specific application
  - Molds and conforms upon application fully integrating into the wound over time
  - Stored at room temperature with a 5 year shelf life

“Dehydrated Amniotic Membrane Allograft (AmnioExcel®), in combination with SOC ...is more likely to lead to complete wound closure, to accelerate the rate of wound closure and presents no additional safety risks when compared to SOC alone in the treatment of DFUs.”
Integra LifeSciences Corporation intends to use reasonable efforts to provide accurate coding information, but this information should not be construed as providing clinical advice, dictating reimbursement policy or substituting for the judgment of a practitioner. It is always the Provider's responsibility to determine and submit appropriate codes, charges and modifiers for services that are rendered. Integra LifeSciences Corporation assumes no responsibilities or liabilities for the timeliness, accuracy and completeness of the information contained herein. Since reimbursement laws, regulations and payer policies change frequently, it is recommended that providers consult with their payors, coding specialists and/or legal counsel regarding coverage, coding and payment issues.

References:

Availability of these products might vary from a given country or region to another, as a result of specific local regulatory approval or clearance requirements for sale in such country or region.

- Non contractual document. The manufacturer reserves the right, without prior notice, to modify the products in order to improve their quality.
- Warning: Applicable laws restrict these products to sale by or on the order of a physician.
- Consult product labels and inserts for any indication, contraindications, hazards, warnings, precautions, and instructions for use.

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