PrimeWest HEALTH
A greater Minnesota health plan™

3905 Dakota St
Alexandria, MN 56308
1-888-588-4420 • 1-320-763-4135
Fax 1-320-762-8750 • www.primewest.org

**Topic:** **Bioengineered Skin and Soft Tissue Substitutes and Amniotic Membrane and Amniotic Fluid**

**Effective Date: December 12, 2023**
**Last Reviewed Date: December 11, 2025**

**Procedure codes:**

**For Bioengineered Skin and Soft Tissue Substitutes:** A2001 A2002 A2004 A2005 A2006 A2007 A2008 A2009 A201 Q4100 Q4101 Q4102 Q4103 Q4104 Q4105 Q4106 Q4107 Q4110 Q4111 Q4112 Q4113 Q4114 Q4115 Q4116 Q4117 Q4118 Q4121 Q4122 Q4123 Q4124 Q4125 Q4126 Q4127 Q4128 Q4130 Q4134 Q4135 Q4136 Q4141 Q4142 Q4143 Q4146 Q4147 Q4149 Q4152 Q4158 Q4164 Q4165 Q4166 Q4167 Q4179 Q4182 Q4195 Q4196 Q4197 Q4200 Q4202 Q4203 Q4220 Q4222 Q4226 Q4238

**For Amniotic Membrane and Amniotic Fluid:** Q4100 Q4132 Q4133 Q4137 Q4138 Q4139 Q4140 Q4145 Q4148 Q4150 Q4151 Q4153 Q4154 Q4155 Q4156 Q4157 Q4159 Q4160 Q4162 Q4163 Q4168 Q4169 Q4170 Q4171 Q4173 Q4174 Q4175 Q4176 Q4178 Q4180 Q4181 Q4183 Q4184 Q4185 Q4186 Q4187 Q4188 Q4189 Q4190 Q4191 Q4192 Q4194 Q4198 Q4199 Q4201 Q4204 Q4205 Q4206 Q4208 Q4209 Q4210 Q4211 Q4212 Q4213 Q4214 Q4215 Q4216 Q4217 Q4218 Q4219 Q4221 Q4227 Q4229 Q4230 Q4231 Q4232 Q4233 Q4234 Q4235 Q4237 Q4239 Q4240 Q4241 Q4242 Q4244 Q4245 Q4246 Q4248 Q4249 Q4250 Q4251 Q4253 Q4254 Q4255 Q4259 Q4260 Q4261

## Bioengineered Skin and Soft Tissue Substitutes

Bioengineered skin and soft tissue substitutes may be derived from human tissue (autologous or allogeneic), nonhuman tissue (xenographic), synthetic materials, or a composite of these materials. Bioengineered skin and soft tissue substitutes are being evaluated for a variety of conditions including breast reconstruction, tendon repair, healing lower-extremity ulcers and treatment of severe burns.

Regulatory status of bioengineered skin and soft tissue substitutes by the U.S. Food and Drug Administration (FDA) varies depending on the materials used and intended function of the tissue. Acellular dermal matrix (ADM) products derived from donated human skin tissue are supplied by tissue banks compliant with standards of the American Association of Tissue Banks (AATB) and FDA guidelines. The processing removes the cellular components (i.e., epidermis, all viable dermal cells) that can lead to rejection and infection. ADM products from human skin tissue are regarded as minimally processed and not significantly changed in structure from the natural material; FDA classifies ADM products as banked human tissue and therefore, not requiring FDA approval. Products in this category include but are not limited to AlloDerm®, Cortiva® (formerly AlloMax™), AlloMend®, AlloPatch®, DermACELL™, DermaPure™, and Graftjacket® Regenerative Tissue Matrix.

Products that utilize xenogenic materials, such as porcine tissue, to provide scaffolding for healing are subject to the 510(k) marketing clearance process. These include but are not limited to Cytal™, Biodesign Anal Fistula Plug, Oasis™ Wound Matrix, Permacol™, PriMatrix™, SIS Fistula Plug, Suprathel®, SurgiMend®, and Surgisis® rectal and vaginal fistula plugs.

Interactive wound and burn dressings, including those with living cells and biosynthetic products, are approved under the FDA PMA process as class III devices. These include but are not limited to Apligraf®, Dermagraft®, Epicel®, OrCel™ and TheraSkin®.

Two bioengineered skin substitutes have received FDA approval under a humanitarian device exemption (HDE), which is reserved for those medical devices (known as humanitarian use devices) intended to benefit patients in the treatment or diagnosis of a disease or condition that affects or is manifested in not more than 8,000 individuals in the United States per year. An HDE is exempt from the effectiveness requirements of other FDA approval processes and is subject to certain profit and use restrictions. These include Epicel®, which has received an HDE approval from the FDA for the treatment of deep dermal or full-thickness burns comprising a total body surface area of 30% or more, and OrCel™, which received an HDE approval for use in patients with recessive dystrophic epidermolysis bullosa undergoing hand reconstruction surgery to close and heal wounds created by the surgery, including those at donor sites.

*This policy is designed to address medical guidelines that are appropriate for the majority of individuals with a particular disease, illness, or condition. Each person's unique clinical circumstances may warrant individual consideration, based on review of applicable medical records.*

**Policy Position** *Coverage is subject to the specific terms of the member's benefit plan.*

**I.** Breast reconstructive surgery following mastectomy using allogeneic acellular dermal matrix products, including but not limited to the following, is considered **MEDICALLY NECESSARY AND APPROPRIATE**:

- AlloDerm®
- AlloMend®
- Cortiva® (AlloMax™)
- DermACELL™
- DermaMatrix™
- FlexHD®
- Graftjacket®

**II.** Treatment of chronic, noninfected, full-thickness diabetic lower-extremity ulcers using the following tissue engineered skin substitutes may be considered **MEDICALLY NECESSARY AND APPROPRIATE**:

- AlloPatch®
- Apligraf®
- Dermagraft®
- Integra® Omnigraft Dermal Regeneration Matrix (also known as Omnigraft)

**III.** Treatment of chronic, noninfected, partial- or full-thickness lower-extremity skin ulcers due to venous insufficiency, which have not adequately responded following a 1-month period of conventional ulcer therapy, using the following tissue-engineered skin substitutes may be considered **MEDICALLY NECESSARY AND APPROPRIATE**:

- Apligraf®

- Oasis™ Wound Matrix

**IV.** Treatment of second- and third-degree burns using the following tissue-engineered skin substitutes may be considered **MEDICALLY NECESSARY AND APPROPRIATE**:

- Epicel® for the treatment of deep dermal or full-thickness burns comprising a total body surface area ≥30%
- Integra Dermal Regeneration Template™

**V.** Treatment of dystrophic epidermolysis bullosa using OrCel™ for mitten-hand deformity when standard wound therapy has failed may be considered **MEDICALLY NECESSARY AND APPROPRIATE.**

**VI.** All other uses of the bioengineered skin and soft tissue substitutes listed above are considered **EXPERIMENTAL/INVESTIGATIVE** for all other indications due to a lack of clinical evidence demonstrating an impact on improved health outcomes.

**VII.** All other skin and soft tissue substitutes not listed above are considered **EXPERIMENTAL/INVESTIGATIVE** for all indications due to a lack of clinical evidence demonstrating an impact on improved health outcomes including, but not limited to:

- ACell® UBM Hydrated/Lyophilized Wound Dressing
- AlloSkin™
- AlloSkin™ RT
- Aongen™ Collagen Matrix
- Architect® ECM, PX, FX
- ArthroFlex™ (Flex Graft)
- Atlas Wound Matrix
- Avagen Wound Dressing
- AxoGuard® Nerve Protector
- BellaCell HD
- Biodesign Anal Fistula Plug
- CollaCare®
- CollaCare® Dental
- Collagen Wound Dressing (Oasis Research)
- CollaGUARD®
- CollaMend™
- CollaWound™
- Collexa®
- Collieva®
- Conexa™
- Coreleader Colla-Pad
- CorMatrix®
- Cymetra™ (Micronized AlloDerm™)
- Cytal™ (previously MatriStem®)
- Dermadapt™ Wound Dressing
- Derma-Gide®
- Derm-Maxx
- DermaPure™
- DermaSpan™

- DressSkin
- Durepair Regeneration Matrix®
- Endoform Dermal Template™
- *ENDURA*Gen™
- Excellagen
- ExpressGraft™
- E-Z Derm™
- FlexiGraft®
- FlowerDerm™
- GammaGraft
- Geistlich Derma-Gide®
- Graftjacket® Xpress, injectable
- Helicoll™
- Hyalomatrix®
- Hyalomatrix® PA
- hMatrix®
- InnovaMatrix FS®
- Integra™ Flowable Wound Matrix
- Integra™ Bilayer Wound Matrix
- Keramatrix®/Kerasorb
- Keroxx®
- MariGen™/Kerecis™ Omega3™
- MatriDerm®
- MatriStem™
- Matrix HD™
- Mediskin®
- MemoDerm™
- Microderm® biologic wound matrix
- MicroMatrix®
- MyOwnSkin™
- NeoForm™
- NuCel
- Oasis® Burn Matrix
- Oasis® Ultra
- Pelvicol®/PelviSoft®
- Permacol™
- PriMatrix™
- PriMatrix™ Dermal Repair Scaffold
- ProgenaMatrix™
- PuraPly™ Wound Matrix (previously FortaDerm™)
- PuraPly™ AM (Antimicrobial Wound Matrix)
- PuraPly™xt
- Puros® Dermis
- Recell®
- RegenePro™
- Repliform®
- Repriza™
- Supra SDRM®
- SureDerm®
- SIS Fistula Plug
- SkinTE™
- StrataGraft®

- Strattice™ (xenograft)
- Suprathel®
- SurgiMend®
- Surgisis® (including Surgisis® AFP™ Anal Fistula Plug, Surgisis® Gold™ Hernia Repair Grafts, and Surgisis® RVP™ Recto-Vaginal Fistula Plug)
- Talymed®
- TenoGlide™
- TenSIX™ Acellular Dermal Matrix
- TissueMend
- TheraForm™ Standard/Sheet
- TheraSkin®
- TransCyte™
- TruSkin™
- Veritas® Collagen Matrix
- XCM Biologic® Tissue Matrix
- XenMatrix™ AB

## Amniotic Membrane and Amniotic Fluid

Human amniotic membrane consists of 2 conjoined layers, the amnion and chorion, and forms the innermost lining of the amniotic sac or placenta. When prepared for use as an allograft, the membrane is harvested immediately after birth, cleaned, sterilized, and either cryopreserved or dehydrated. Many products available using amnion, chorion, amniotic fluid, and umbilical cord are being studied for the treatment of a variety of conditions, including chronic full-thickness diabetic lower-extremity ulcers, venous ulcers, knee osteoarthritis, plantar fasciitis, and ophthalmic conditions. The products are formulated either as patches, which can be applied as wound covers, or as suspensions or particulates, or connective tissue extractions, which can be injected or applied topically.

Amniotic fluid surrounds the fetus during pregnancy and provides protection and nourishment. In the second half of gestation, most of the fluid is a result of micturition and secretion from the respiratory tract and gastrointestinal tract of the fetus, along with urea. The fluid contains proteins, carbohydrates, peptides, fats, amino acids, enzymes, hormones, pigments, and fetal cells. Amniotic fluid has been compared with synovial fluid, containing hyaluronan, cholesterol, and cytokines. Injection of amniotic fluid or amniotic fluid-derived cells is currently being evaluated for the treatment of osteoarthritis and plantar fasciitis.

The U.S. Food and Drug Administration (FDA) regulates human cells and tissues intended for implantation, transplantation, or infusion through the Center for Biologics Evaluation and Research, under Code of Federal Regulation (CFR) title 21, parts 1270 and 1271. Human amniotic membrane products and amniotic fluid products are included in these regulations. In 2003, ProKera™ was cleared for marketing by FDA through the 510(k) process for the ophthalmic conformer that incorporates amniotic membrane (K032104). The ProKera™ device is intended "for use in eyes in which the ocular surface cells have been damaged, or underlying stroma is inflamed and scarred."

*This policy is designed to address medical guidelines that are appropriate for the majority of individuals with a particular disease, illness, or condition. Each person's unique clinical circumstances may warrant individual consideration, based on review of applicable medical records.*

**Policy Position** *Coverage is subject to the specific terms of the member's benefit plan.*

### I. Human Amniotic Membrane Grafts for Ophthalmic Conditions

- Use of human amniotic membrane graft (i.e., Prokera®, AmbioDisk®, Ambio2, Ambio5, Artacent Ocular, and AmnioGraft®), may be considered **MEDICALLY NECESSARY AND APPROPRIATE** for treatment of the following ophthalmic conditions:
    - Neurotrophic keratitis with ocular surface damage and inflammation that does not respond to conservative therapy (e.g., 5 days of pressure patching, therapeutic contact lens, topical lubricants, and topical antibiotics);
    - Corneal ulcers and melts that do not respond to initial conservative therapy (e.g., 2 days of patching, therapeutic contact lens, and topical antibiotics;
    - Pterygium repair
    - Ocular damage related to moderate or severe Stevens-Johnson syndrome
    - Epithelial defects that have failed to close completely after 5 days of conservative treatment or have failed to demonstrate a decrease in size after 2 days of conservative treatment (e.g., topical lubricants, topical antibiotics, therapeutic contact lens, or patching)
    - Severe dry eye with ocular surface damage and inflammation that remains symptomatic after at least three conservative treatments (e.g., therapeutic contact lens, soft bandage lens, punctal occlusion, topical secretagogues, moisture chamber spectacles);
    - Moderate or severe acute ocular chemical burn;
    - Corneal perforation when corneal tissue is not immediately available.
- Use of human amniotic membrane grafts for all other ophthalmic conditions is considered **EXPERIMENTAL/INVESTIGATIVE** due to a lack of clinical evidence demonstrating an impact on improved health outcomes.

## II. Human Amniotic Membrane Grafts for Non-Ophthalmic Conditions

- Use of the following human amniotic membrane grafts for the treatment of diabetic lower-extremity ulcers may be considered **MEDICALLY NECESSARY AND APPROPRIATE** when decrease in wound area is less than 20% after standard wound care for at least 2 weeks:
    - Affinity®
    - AmnioBand® Membrane
    - Biovance®
    - EpiFix®
    - EpiCord®
    - GrafixCore®
    - GrafixPrime®
- Use of the human amniotic membrane grafts listed above is considered **EXPERIMENTAL/ INVESTIGATIVE** for all other conditions including but not limited to treatment of lower-extremity ulcers due to venous insufficiency, osteoarthritis, plantar fasciitis, or repair following Mohs micrographic surgery, due to a lack of clinical evidence demonstrating an impact on improved health outcomes.

## III. Experimental/Investigative Human Amniotic Membrane

- All other human amniotic membrane products are considered **EXPERIMENTAL/INVESTIGATIVE** for all conditions due to a lack of clinical evidence demonstrating an impact on improved health outcomes. Products include but are not limited to the following:
    - Allogen
    - AlloWrap™
    - AmbioDry5®
    - AmnioAMP-MP

- AmnioArmor™
- AmnioBind™
- Amnion Bio
- AmnioClear™
- Amniocore
- Amniocyte plus
- AmnioExcel®
- AmnioFill®
- AmnioFix®
- Amnio-maxx or Amnio-maxx lite
- Amniorepair or altiply
- Amniotext
- Amniowound
- Amnio Wrap2™
- Amniply
- Artacent AC
- Artacent (R) Cord
- Artacent® Wound
- Arthrex Amnion Matrix
- Ascent
- AxoBioMembrane
- Axolotl Ambien or Axolotl Cryo
- Axolotl DualGraft™
- Axolotl Graft™
- Barrera™ DL
- Barrera™ SL
- BioDDryFlex®
- BioDExcel®
- BioDFactor®
- BioDfence™
- BioSkin (thin - 45 microns)
- BioSkin (thick - 200 microns)
- Biovance® 3L
- BioWound
- BioWound Plus™
- BioWound XPlus™
- CarePATCH
- celera™ Dual Layer
- celera™ Dual Membrane
- Cellesta™
- Cellesta™ Cord
- Cellesta™ Duo
- Cellesta™ Flowable
- Clarix®
- Cogenex
- Cogenex Flowable
- Cocoon Membrane
- Complete FT
- Complete SL
- Corecyte
- Corplex P
- Coretext

- Cryo-cord
- Cygnus
- Cygnus™ Dual
- Cygnus Max
- DermaBind SL™
- Dermacyte
- Dermavest™
- Dual Layer Impax™
- Enverse
- Epieffect®
- Esano™
- Esano™ AAA
- Esano™ AC
- Esano™ ACA
- Essence Viable Amnion Matrix
- Floweramniopatch
- Fluid Flow™
- Fluid GF
- Genesis Amniotic Membrane
- Human Health Factor 10 Amniotic Patch™(HHF10P™)
- Matrion
- Membrane Graft™
- Membrane Wrap™
- Miroderm Acellular Wound Matrix
- MLG-Complete
- NeoPatch
- NeoStim DL
- NeoStim Membrane
- NeoStim TL
- Neox® 100
- Neox® Cord
- Neox® Wound Allograft
- Novachor
- Novafix
- Novafix DL
- NuDyn
- NuShield™
- Orion
- PalinGen® Membrane
- Plurivest™
- Polycyte
- Procenta®
- Protext
- REGUaRD
- Relese
- Restorigin™
- Revita®
- Revitalon™
- Signature APatch
- Stravix Cryopreserved Placental Tissue
- Stravix PL
- Surfactor

- Surgicord
- SurGraft
- SurGraft FT
- SurGraft TL
- SurGraft XT
- SurgiGraft™
- SurgiGRAFTTM-DUAL
- TAG
- Therion
- VIM
- Vendaje
- WoundEx® (45 microns)
- WoundEx® (200 microns)
- WoundFix
- WoundFix Plus
- WoundFix XPlus
- WoundPlus™
- Xcell Amnio Matrix®
- XCellerate
- XWRAP
- ZenithTM Amniotic Membrane

## IV. Micronized or Particulated Human Amniotic Membrane

- Micronized or particulated human amniotic membrane products are considered **EXPERIMENTAL/ INVESTIGATIVE** for all conditions due to a lack of clinical evidence demonstrating an impact on improved health outcomes. Products include but are not limited to the following:
  - AmnioBand® Particulate
  - AmnioFill®
  - AmnioMatrix®
  - AmnioVisc™
  - Artacent AC Powder
  - BioDMatrix®
  - BioSkin® Flow
  - Clarix® Flo
  - EpiFix® injectable
  - Fluid Flow™
  - Fluid GF
  - Interfyl™
  - Neox® Flo
  - OrthoFlo™
  - PalinGen® Flow
  - PalinGen® SportFlow
  - ProMatrX™
  - ReNu™
  - WoundEx® Flow

## V. Injection of Amniotic Fluid

Injection of amniotic fluid is considered **EXPERIMENTAL/ INVESTIGATIVE** for all conditions due to a lack of clinical evidence demonstrating an impact on improved health outcomes.

**References:**

*A guide to Tissue-Engineered skin Substitutes*. (2018, January 1). PubMed. https://pubmed.ncbi.nlm.nih.gov/29320588/

*LCD - application of skin substitute grafts for treatment of DFU and VLU of lower extremities (L36377)*. (n.d.). https://www.cms.gov/medicare-coverage-database/view/lcd.aspx?lcdid=36377&ver=7&bc=0