MEDICAL POLICY

POLICY TITLE	BIO-ENGINEERED SKIN AND SOFT TISSUE SUBSTITUTES
POLICY NUMBER	MP- 1.017

Effective Date:	1/1/2024

I. POLICY

Breast reconstructive surgery using allogeneic acellular dermal matrix products* (including each of the following: AlloDerm® (Q4116), AlloMend® (Q4100), Cortiva® [AlloMax™] (Q4100), DermACELL™ (Q4122), DermaMatrix™ (Q4100), FlexHD® (Q4128), FlexHD® Pliable™, Graftjacket® (Q4107); see Policy Guidelines) may be considered **medically necessary**:

- When there is insufficient tissue expander or implant coverage by the pectoralis major muscle and additional coverage is required,
- When there is viable but compromised or thin postmastectomy skin flaps that are at risk of dehiscence or necrosis; **or**
- The inframammary fold and lateral mammary folds have been undermined during mastectomy and reestablishment of these landmarks is needed.

Treatment of chronic, noninfected, full-thickness diabetic lower-extremity ulcers using the following tissue engineered skin substitutes may be considered **medically necessary:**

- AlloPatch® (Q4128)*
- Apligraf® (Q4101)**
- Dermagraft® (Q4106)**
- Integra® Omnigraft™ Dermal Regeneration Matrix (Q4105)
- Integra Flowable Wound Matrix (Q4114)
- Celera Dual Layer™ (Q4259)*
- Signature APatch (Q4260)*

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:**

- Apligraf® (Q4101)**
- Oasis™ Wound Matrix (Q4102)***
- Signature APatch (Q4260)*

Treatment of dystrophic epidermolysis bullosa using the following tissue-engineered skin substitutes may be considered **medically necessary:**

- OrCel™ (for the treatment of mitten-hand deformity when standard wound therapy has failed and when provided in accordance with the humanitarian device exemption (HDE) specifications of the U.S. Food and Drug Administration [FDA]) (Q4100)****

Treatment of second- and third-degree burns using the following tissue-engineered skin substitutes may be considered **medically necessary:**

- Epicel® (for the treatment of deep dermal or full-thickness burns comprising a total body surface area ≥30% when provided in accordance with the HDE specifications of the FDA) (Q4100)****
- Integra Dermal Regeneration Template™ (Q4105)**

* Banked human tissue.
** FDA premarket approval.
*** FDA 510(k) cleared.
**** FDA-approved under an HDE.

All other uses of the bioengineered skin and soft tissue substitutes listed above are considered **investigational.** There is insufficient evidence to support a conclusion concerning the health outcomes or benefits associated with these procedures.

All other skin and soft tissue substitutes not listed above are considered **investigational,** including, but not limited to:

- ACell® UBM Hydrated /Lyophilized Wound Dressing (Q4100)
- AlloSkin™ (Q4115)
- AlloSkin™ RT (Q4123)
- AlloSkin AC (Q4141)
- Aongen™ Collagen Matrix (Q4100)
- Apis (A2010)
- Architect® ECM, PX, FX (Q4147)
- ArthroFlex™ (Flex Graft) (Q4125)
- Atlas Wound Matrix (Q4100)
- Avagen Wound Dressing (Q4100)
- AxoGuard® Nerve Protector (AxoGen) (Q4100)
- BellaCell HD or Surederm (Q4220)
- Biobrane®/Biobrane-L (Q4100, A2003)
- Bio-ConneKt (Q4161)
- Cocoon membrane (Q4264)
- CollaCare® (Q4100)
- CollaCare® Dental (Q4100)
- Collagen Wound Dressing (Oasis Research) (Q4100)
- CollaGUARD® (Q4100)
- CollaMend™ (Q4100)
- CollaWound™ (Q4100)

- Coll-e-Derm (Q4193)
- Collexa® (Q4100)
- Collieva® (Q4100)
- Conexa™ (Q4100)
- Corecyte (Q4240)
- Coreleader Colla-Pad (Q4100)
- CorMatrix® (Q4100)
- Cryo-cord (Q4237)
- Cymetra™ (Micronized AlloDerm™) (Q4112)
- Cytal™ (previously MatriStem®) (Q4118, Q4166)
- Dermadapt™ Wound Dressing (Q4100)
- Derma-Gide (Q4203)
- DermaPure™ (Q4152)
- DermaSpan™ (Q4126)
- Derm-maxx (Q4238)
- DressSkin™ (Q4100)
- Durepair Regeneration Matrix® (Q4100)
- Endoform Dermal Template™ (Q4100)
- *ENDURA*Gen™ (Q4100)
- Excellagen® (Q4149)
- ExpressGraft™ (Q4100)
- E-Z Derm™ (Q4136)
- FlexiGraft® (Q4100)
- FlowerDerm™ (Q4179)
- GammaGraft (Q4111)
- Geistlich Derma-Gide™ (Q4203)
- Graftjacket® Xpress, injectable (Q4113)
- Helicoll™ (Q4164)
- HMatrix® (Q4134)
- Hyalomatrix® (Q4117)
- Hyalomatrix® PA (Q4117)
- Integra™ Bilayer Wound Matrix (C9363, Q4104)
- Integra® Matrix Wound Dressing (previously Avagen) (Q4108)
- Innovaburn (A2022)
- InnovaMatrix™ Innovamatrix fx (A2001, A2013)
- InnovMatrix pd (A2023)
- IntéguPly® (Q4126)
- Keramatrix® or kerasorbQ4165)
- Kerecis™ Omega3 (Q4158)
- Keroxx (Q4202)
- MariGen™/Kerecis™ Omega3™ (Q4158)
- MatriDerm® (Q4100)
- MatriStem Micromatrix (Q4118)

- Matrix HD™ (Q4100)
- Mediskin® (Q4135)
- MemoDerm™ (Q4126)
- Microderm® biologic wound matrix (Q4175)
- Microlyte® Matrix (A2005) Mirragen® Advanced Wound Matrix (A2002)
- Miro3d (A2025)
- Mucograft® (Q4203)
- MyOwn Skin (Q4226)
- NeoForm™ (Q4100)
- Novasorb® BTM (A2006)
- NuCel (Q4100)
- Nudyn dl (Q4285)
- Oasis® Burn Matrix (Q4103)
- Oasis® Ultra (Q4124)
- Ologen™ Collagen Matrix (Q4100)
- Omega3 Wound (Q4100)
- Omeza® Collagen Matrix (A2014)
- Pelvicol®/PelviSoft® (Q4100)
- PermeaDerm® b (A2016)
- PermeaDerm® Glove (A2017)
- PermeaDerm® C (A2018)
- Permacol™ (C9364)
- Phoenix® Wound Matrix (A2015)
- PriMatrix™ (Q4110)
- PriMatrix™ Dermal Repair Scaffold (Q4110)
- ProgenaMatrix (Q4222)
- Puracol® and Puracol® Plus Collagen Wound Dressings (Q4100)
- PuraPly™ Wound Matrix (previously FortaDerm™) (Q4195)
- PuraPly™ AM (Antimicrobial Wound Matrix) (Q4196)
- PuraPly™ XT (Q4197)
- Puros® Dermis (Q4100)
- RegenePro™ (Q4100)
- Repliform® (Q4100)
- Repriza™ (Q4143)
- Resolve (A2024)
- Restrata (A2007)
- SkinTE™ (Q4200)
- StrataGraft® (Q4130)
- Strattice TM (xenograft) (Q4130)
- Suprathel® (A2012)Supra sdrm (A2011)
- SurgiMend® (C9358, C9360)
- Symphony (A2009)
- Tag (Q4261)

- Talymed® (Q4127)
- TenoGlide™ (C9356, Q4100)
- TenSIX™ Acellular Dermal Matrix (Q4146)
- TissueMend (Q4100)
- TheraForm™ Standard/Sheet (Q4100)
- Theragensis (A2008)
- TheraSkin® (Q4121)
- TransCyte™ (Q4182)
- TranZgraft (Q4126)
- TruSkin™ (Q4167)
- Veritas® Collagen Matrix (C9354)
- Xcellerate (Q4234)
- Xcellistem (A2004)
- XCM Biologic® Tissue Matrix (Q4142)
- XenMatrix™ AB (Q4100)

There is insufficient evidence to support a conclusion concerning the health outcomes or benefits associated with these procedures.

POLICY GUIDELINES

Note that amniotic membrane and amniotic fluid products are reviewed in MP-4.042, Amniotic Membrane, and Amniotic Fluid Injections.

Cross-reference:

MP 1.103 Reconstructive Breast Surgery/Management of Breast Implants
MP 2.033 Recombinant and Autologous Platelet-Derived Growth Factors as a Treatment of Wound Healing and Other Conditions
MP 4.042 Amniotic Membrane and Amniotic Fluid Injections
MP 4.028 Wound and Burn Care and Specialized Treatment Centers

II. PRODUCT VARIATIONS

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This policy is only applicable to certain programs and products administered by Capital Blue Cross please see additional information below, and subject to benefit variations as discussed in Section VI below.

FEP PPO:
FEP PPO - Refer to FEP Medical Policy Manual. The FEP Medical Policy manual can be found at:
https://www.fepblue.org/benefit-plans/medical-policies-and-utilization-management-guidelines/medical-policies .

III. DESCRIPTION/BACKGROUND

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Skin and Soft Tissue Substitutes

Bioengineered skin and soft tissue substitutes may be either acellular or cellular. Acellular products (e.g., dermis with cellular material removed) contain a matrix or scaffold composed of materials such as collagen, hyaluronic acid, and fibronectin. Acellular dermal matrix (ADM) products can differ in a number of ways, including as species source (human, bovine, porcine), tissue source (e.g., dermis, pericardium, intestinal mucosa), additives (e.g., antibiotics, surfactants), hydration (wet, freeze-dried), and required preparation (multiple rinses, rehydration).

Cellular products contain living cells such as fibroblasts and keratinocytes within a matrix. The cells contained within the matrix may be autologous, allogeneic, or derived from other species (e.g., bovine, porcine). Skin substitutes may also be composed of dermal cells, epidermal cells, or a combination of dermal and epidermal cells, and may provide growth factors to stimulate healing. Bioengineered skin substitutes can be used as either temporary or permanent wound coverings.

Applications

There are a large number of potential applications for artificial skin and soft tissue products. One large category is nonhealing wounds, which potentially encompasses diabetic neuropathic ulcers, vascular insufficiency ulcers, and pressure ulcers. A substantial minority of such wounds do not heal adequately with standard wound care, leading to prolonged morbidity and increased risk of mortality. For example, nonhealing lower-extremity wounds represent an ongoing risk for infection, sepsis, limb amputation, and death. Bioengineered skin and soft tissue substitutes have the potential to improve rates of healing and reduce secondary complications.

Other situations in which bioengineered skin products might substitute for living skin grafts include certain postsurgical states (e.g., breast reconstruction) in which skin coverage is inadequate for the procedure performed, or for surgical wounds in patients with compromised ability to heal. Second- and third-degree burns are another indication in which artificial skin products may substitute for auto- or allografts. Certain primary dermatologic conditions that involve large areas of skin breakdown (e.g., bullous diseases) may also be conditions in which artificial skin products can be considered as substitutes for skin grafts. ADM products are also being evaluated in the repair of other soft tissues including rotator cuff repair, following oral and facial surgery, hernias, and other conditions.

Regulatory Status

A large number of artificial skin and soft-tissue products are commercially available or in development. The following section summarizes commercially available skin and soft tissue substitutes that have substantial relevant evidence on efficacy. Information on additional

products is available in a 2020 Technical Brief on skin substitutes for treating chronic wounds that was commissioned by the Agency for Healthcare Research and Quality[1.]

ADM Products
Allograft ADM products derived from donated cadaveric human skin tissue are supplied by tissue banks compliant with standards of the American Association of Tissue Banks and U.S. Food and Drug Administration (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 for homologous use.

In 2017, FDA published a clarification of what is considered minimal manipulation and homologous use for human cells, tissues, and cellular and tissue-based products (HCT/Ps) [two].

HCT/Ps are defined as human cells or tissues that are intended for implantation, transplantation, infusion, or transfer into a human recipient. If an HCT/P does not meet the criteria below and does not qualify for any of the stated exceptions, the HCT/P will be regulated as a drug, device, and/or biological product, and applicable regulations and premarket review will be required.

An HCT/P is regulated solely under section 361 of the PHS Act and 21 CFR Part 1271 if it meets all of the following criteria:

1. The HCT/P is minimally manipulated;
2. The HCT/P is intended for homologous use only, as reflected by the labeling, advertising, or other indications of the manufacturer's objective intent;
3. The manufacture of the HCT/P does not involve the combination of the cells or tissues with another article, except for water, crystalloids, or a sterilizing, preserving, or storage agent, provided that the addition of water, crystalloids, or the sterilizing, preserving, or storage agent does not raise new clinical safety concerns with respect to the HCT/P; and
4. Either:
    a. The HCT/P does not have a systemic effect and is not dependent upon the metabolic activity of living cells for its primary function; or
    b. The HCT/P has a systemic effect or is dependent upon the metabolic activity of living cells for its primary function, and: a) Is for autologous use; b) Is for allogeneic use in a first-degree or second-degree blood relative; or c) Is for reproductive use."

- AlloDerm® (LifeCell Corp.) is an ADM (allograft) tissue-replacement product created from native human skin and processed so that the basement membrane and cellular matrix remain intact. Originally, AlloDerm® required refrigeration and rehydration before use. It is currently available in a ready-to-use product stored at

room temperature. An injectable micronized form of AlloDerm® (Cymetra) is available.
- Cortiva® (previously marketed as AlloMax™ Surgical Graft and before that NeoForm™) is an acellular non-cross-linked human dermis allograft.
- AlloPatch® (Musculoskeletal Transplant Foundation) is an acellular human dermis allograft derived from the reticular layer of the dermis and marketed for wound care. This product is also marketed as FlexHD® for postmastectomy breast reconstruction.
- FlexHD® and the newer formulation FlexHD® Pliable™ (Musculoskeletal Transplant Foundation) are acellularhydrated reticular dermis allograft derived from donated human skin.
- DermACELL™ (LifeNet Health) is an allogeneic ADM processed with proprietary technologies MATRACELL® and PRESERVON®.
- DermaMatrix™ (Synthes) is a freeze-dried ADM derived from donated human skin tissue. DermaMatrix Acellular Dermis is processed by the Musculoskeletal Transplant Foundation.
- DermaPure™ (Tissue Regenix Wound Care) is a single layer decellularized human dermal allograft for the treatment of acute and chronic wounds.
- Graftjacket® Regenerative Tissue Matrix (also called Graftjacket Skin Substitute; KCI) is an acellular regenerative tissue matrix that has been processed from human skin supplied from U.S. tissue banks. The allograft is minimally processed to remove the epidermal and dermal cells while preserving dermal structure. Graftjacket Xpress® is an injectable product.

Although frequently used by surgeons for breast reconstruction, FDA does not consider this homologous use and has not cleared or approved any surgical mesh device (synthetic, animal collagen-derived, or human collagen-derived) for use in breast surgery. The indication of surgical mesh for general use in “Plastic and reconstructive surgery” was cleared by the FDA before surgical mesh was described for breast reconstruction in 2005. FDA states that the specific use of surgical mesh in breast procedures represents a new intended use and that a substantial equivalence evaluation via 510(k) review is not appropriate and a pre-market approval evaluation is required.

FDA product codes: FTM, OXF.

Xenogenic Products

Cytal™ (previously called MatriStem®) Wound Matrix, Multilayer Wound Matrix, Pelvic Floor Matrix, MicroMatrix, and Burn Matrix (all manufactured by ACell) are composed of porcine-derived urinary bladder matrix.

Helicoll (Encol) is an acellular collagen matrix derived from bovine dermis. In 2004, it was cleared for marketing by FDA through the 510(k) process for topical wound management that includes partial and full-thickness wounds, pressure ulcers, venous ulcers, chronic vascular

ulcers, diabetic ulcers, trauma wounds (e.g., abrasions, lacerations, second-degree bums, skin tears), and surgical wounds including donor sites/grafts.

Keramatrix® (Keraplast Research) is an open-cell foam comprised of freeze-dried keratin that is derived from acellular animal protein. In 2009, it was cleared for marketing by FDA through the 510(k) process under the name of Keratec. The wound dressings are indicated in the management of the following types of dry, light, and moderately exudating partial and full-thickness wounds: pressure (stage I-IV) and venous stasis ulcers, ulcers caused by mixed vascular etiologies, diabetic ulcers, donor sites, and grafts.

Kerecis™ Omega3 Wound (Kerecis) is an ADM derived from fish skin. It has a high content of omega three fatty acids and is intended for use in burn wounds, chronic wounds, and other applications.

Permacol™ (Covidien) is xenogeneic and composed of cross-linked porcine dermal collagen. Cross-linking improves the tensile strength and long-term durability but decreases pliability.

PriMatrix™ (TEI Biosciences; a subsidiary of Integra Life Sciences) is a xenogeneic ADM processed from fetal bovine dermis. It was cleared for marketing by FDA through the 510(k) process for partial- and full-thickness wounds; diabetic, pressure, and venous stasis ulcers; surgical wounds; and tunneling, draining, and traumatic wounds. FDA product code: KGN.

SurgiMend® PRS (TEI Biosciences; a subsidiary of Integra Life Sciences) is a xenogeneic ADM processed from fetal and neonatal bovine dermis.

Strattice™ Reconstructive Tissue Matrix (LifeCell Corp.) is a xenogenic non-cross-linked porcine-derived ADM. There are pliable and firm versions, which are stored at room temperature and come fully hydrated.

Oasis™ Wound Matrix (Cook Biotech) is a collagen scaffold (extracellular matrix) derived from porcine small intestinal submucosa. In 2000, it was cleared for marketing by FDA through the 510(k) process for the management of partial- and full-thickness wounds, including pressure ulcers, venous ulcers, diabetic ulcers, chronic vascular ulcers, tunneled undermined wounds, surgical wounds, trauma wounds, and draining wounds. FDA Product code: KGN.

Living Cell Therapy

Apligraf® (Organogenesis) is a bilayered living cell therapy composed of an epidermal layer of living human keratinocytes and a dermal layer of living human fibroblasts. Apligraf® is supplied as needed, in one size, with a shelf-life of 10 days. In 1998, it was approved by FDA for use in conjunction with compression therapy for the treatment of noninfected, partial- and full-thickness skin ulcers due to venous insufficiency and in 2001 for full-thickness neuropathic diabetic lower-extremity ulcers nonresponsive to standard wound therapy. FDA product code: FTM.

Dermagraft® (Organogenesis) is composed of cryopreserved human-derived fibroblasts and collagen derived from newborn human foreskin and cultured on a bioabsorbable polyglactin mesh scaffold. Dermagraft has been approved by FDA for repair of diabetic foot ulcers. FDA product code: PFC.

TheraSkin® (Soluble Systems) is a cryopreserved split-thickness human skin allograft composed of living fibroblasts and keratinocytes and an extracellular matrix in epidermal and dermal layers. TheraSkin® is derived from human skin allograft supplied by tissue banks compliant with the American Association of Tissue Banks and FDA guidelines. It is considered a minimally processed human cell, tissue, and cellular- and tissue-based product by FDA.

Epicel® (Genzyme Biosurgery) is an epithelial autograft composed of a patient's own keratinocytes cultured ex vivo and is FDA-approved under a humanitarian device exemption for the treatment of deep dermal or full-thickness burns comprising a total body surface area of 30% or more. It may be used in conjunction with split-thickness autografts or alone in patients for whom split-thickness autografts may not be an option due to the severity and extent of their burns. FDA product code: OCE.

OrCel™ (Forticell Bioscience; formerly Composite Cultured Skin) is an absorbable allogeneic bilayered cellular matrix, made of bovine collagen, in which human dermal cells have been cultured. It was approved by FDA premarket approval for healing donor site wounds in burn victims and under a humanitarian device exemption (HDE) 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. FDA product code: ODS.

Biosynthetic Products

Biobrane®/Biobrane-L (Smith & Nephew) is a biosynthetic wound dressing constructed of a silicon film with a nylon fabric partially imbedded into the film. The fabric creates a complex 3-dimensional structure of trifilament thread, which chemically binds collagen. Blood/sera clot in the nylon matrix, adhering the dressing to the wound until epithelialization occurs. FDA product code: FRO.

Integra® Dermal Regeneration Template (also marketed as Omnigraft Dermal Regeneration Matrix; Integra LifeSciences) is a bovine, collagen/glycosaminoglycan dermal replacement covered by a silicone temporary epidermal substitute. It was approved by FDA for use in the post excisional treatment of life-threatening full-thickness or deep partial-thickness thermal injury where sufficient autograft is not available at the time of excision or not desirable because of the physiologic condition of the patient and for certain diabetic foot ulcers. Integra® Matrix Wound Dressing and Integra® Meshed Bilayer Wound Matrix are substantially equivalent skin substitutes and were cleared for marketing by FDA through the 510(k) process for other indications. Integra® Bilayer Matrix Wound Dressing (Integra LifeSciences) is designed to be used in conjunction with negative pressure wound therapy. The meshed bilayer provides a flexible wound covering and allows drainage of wound exudate. FDA product code: MDD.

TransCyte™ (Advanced Tissue Sciences) consists of human dermal fibroblasts grown on nylon mesh, combined with a synthetic epidermal layer, and was approved by FDA in 1997. TransCyte is intended as a temporary covering over burns until autografting is possible. It can also be used as a temporary covering for some burn wounds that heal without autografting.

Synthetic Products

Suprathel® (PolyMedics Innovations) is a synthetic copolymer membrane fabricated from a tripolymer of polylactide, trimethylene carbonate, and s-caprolactone. It is used to provide temporary coverage of superficial dermal burns and wounds. Suprathel® is covered with gauze and a dressing that is left in place until the wound has healed.

IV. RATIONALE

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Summary of Evidence

Breast Reconstruction

For individuals who are undergoing breast reconstruction who receive allogeneic ADM products, the evidence incudes RCTs and systematic reviews. Relevant outcomes are symptoms, morbid events, functional outcomes, quality of life, and treatment-related morbidity. A systematic review found no difference in overall complication rates with ADM allograft compared with standard procedures for breast reconstruction. Reconstructions with ADM have been reported to have higher seroma, infection, and necrosis rates than reconstructions without ADM. However, capsular contracture and malposition of implants may be reduced. Thus, in cases where there is limited tissue coverage, the available evidence may inform patient decision making about reconstruction options. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

Tendon Repair

For individuals who are undergoing tendon repair who receive Graftjacket, the evidence incudes RCT. Relevant outcomes are symptoms, morbid events, functional outcomes, quality of life, and treatment-related morbidity. The RCT identified found improved outcomes with the Graftjacket ADM allograft for rotator cuff repair. Although these results were positive, additional study with a larger number of patients is needed to evaluate the consistency of the effect. The evidence is insufficient to determine the effects of the technology on health outcomes.

Surgical Repair of Hernias or Parastomal Reinforcement

For individuals who are undergoing surgical repair of hernias or parastomal reinforcement who receive acellular collagen-based scaffolds, the evidence incudes RCTs. Relevant outcomes are symptoms, morbid events, functional outcomes, quality of life, and treatment-related morbidity. Several comparative studies including RCTs have shown no difference in outcomes between tissue-engineered skin substitutes and either standard synthetic mesh or no reinforcement. The evidence is sufficient to determine that the technology is unlikely to improve the net health outcome.

Diabetic Lower-Extremity Ulcers

For individuals who have diabetic lower-extremity ulcers who receive AlloPatch, Apligraf, Dermagraft, or Integra, the evidence includes RCTs. Relevant outcomes are symptoms, change in disease status, morbid events, and quality of life. RCTs have demonstrated the efficacy of AlloPatch (reticular ADM), Apligraf and Dermagraft (living cell therapy), and Integra (biosynthetic) over the standard of care. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals who have diabetic lower-extremity ulcers who receive ADM products other than AlloPatch, Apligraf, Dermagraft, or Integra, the evidence includes RCTs. Relevant outcomes are symptoms, change in disease status, morbid events, and quality of life. Results from a multicenter RCT showed some benefit of DermACELL that was primarily for the subgroup of patients who only required a single application of the ADM. Studies are needed to further define the population who might benefit from this treatment. Additional study with a larger number of subjects is needed to evaluate the effect of Graftjacket, TheraSkin, DermACELL, Cytal, PriMatrix, and Oasis Wound Matrix, compared with current SOC or other advanced wound therapies. The evidence is insufficient to determine the effects of the technology on health outcomes.

Lower-Extremity Ulcers due to Venous Insufficiency

For individuals who have lower-extremity ulcers due to venous insufficiency who receive Apligraf or Oasis Wound Matrix, the evidence includes RCTs. Relevant outcomes are disease-specific survival, symptoms, change in disease status, morbid events, and quality of life. RCTs have demonstrated the efficacy of Apligraf living cell therapy and xenogenic Oasis Wound Matrix over the standard of care. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals who have lower-extremity ulcers due to venous insufficiency who receive bioengineered skin substitutes other than Apligraf or Oasis Wound Matrix, the evidence includes RCTs. Relevant outcomes are disease-specific survival, symptoms, change in disease status, morbid events, and quality of life. In a moderately large RCT, Dermagraft was not shown to be more effective than controls for the primary or secondary end points in the entire population and was only slightly more effective than controls (an 8%-15% increase in healing) in subgroups of patients with ulcer durations of 12 months or less or size of 10 cm or less. Additional study with a larger number of subjects is needed to evaluate the effect of the xenogenic PriMatrix skin substitute vs the current standard of care. The evidence is insufficient to determine the effects of the technology on health outcomes.

Dystrophic Epidermolysis Bullosa

For individuals who have dystrophic epidermolysis bullosa who receive OrCel, the evidence includes case series. Relevant outcomes are symptoms, change in disease status, morbid events, and quality of life. OrCel was approved under a humanitarian drug exemption for use in patients with dystrophic epidermolysis bullosa undergoing hand reconstruction surgery, to close and heal wounds created by the surgery, including those at donor sites. Outcomes have been reported in small series (e.g., five patients). The evidence is insufficient to determine the effects of the technology on health outcomes.

Deep Dermal Burns
For individuals who have deep dermal burns who receive bioengineered skin substitutes (i.e., Epicel, Integra Dermal Regeneration Template), the evidence includes RCTs. Relevant outcomes are disease-specific survival, symptoms, change in disease status, morbid events, functional outcomes, quality of life, and treatment-related morbidity. Overall, few skin substitutes have been approved, and the evidence is limited for each product. Epicel (living cell therapy) has received FDA approval under a humanitarian device exemption for the treatment of deep dermal or full-thickness burns comprising a total body surface area of 30% or more. Comparative studies have demonstrated improved outcomes for biosynthetic skin substitute Integra Dermal Regeneration Template for the treatment of burns. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

V. DEFINITIONS

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ANKLE-BRACHIAL INDEX (ABI) – is a noninvasive test used to detect evidence of significant arterial insufficiency and to assess client's need for further testing. An accurate diagnosis is essential to determine appropriate interventions to treat the ulcer. The main determination that must be done is whether the arterial blood supply is adequate to attempt to heal the wound. If the arterial blood supply is inadequate, the clinician will employ interventions aimed at reducing risk of infection and spread of the ulcer (palliation/maintenance) as opposed to healing. ABI is determined by dividing the systolic blood pressure measured at the ankle by that obtained in the brachial artery. ABI reading results indicate the following:

- An ABI >1.3 implies calcified arteries and requiring further testing
- An ABI ≥ 0.9 to 1.3 Normal Arterial Circulation
- An ABI ≥ 0.4 to 0.9 suggests a degree of arterial obstruction often associated with claudication
- An ABI < 0.4 represents multilevel disease (any combination of iliac, femoral, or tibial vessel disease) and may be associated with non-healing ulcerations, ischemic rest pain, or pedal gangrene

In general, a palpable pulse of the dorsalis pedis and posterior tibial artery implies an ABI of at least 0.8.

AMNION is a membrane, continuous with and covering the fetal side of the placenta, that forms the outer surface of the umbilical cord and becomes the outermost layer of the skin of the developing fetus.

BIO-ENGINEERING refers to the application of engineering concepts, equipment, skills, and techniques, to solve medical problems.

DECUBITUS ULCER is a type of wound that forms as a result of prolonged pressure against areas of the skin.

DERMIS is the layer of skin lying immediately under the epidermis: the true skin.

DIABETIC NEUROPATHIC ULCERS — Chronic ulceration in patients with diabetes is multifactorial, due to a combination of diabetic neuropathy, autonomic dysfunction, and vascular insufficiency. Non-ischemic neuropathic foot ulcers in the diabetic patient are due to a

combination of foot deformities and neuropathy preventing the sensation of pain in areas of the foot that are traumatized. Characteristics of neuropathic diabetic ulcers include the following; Location at areas of repeated trauma such as the plantar metatarsal heads or dorsal interphalangeal joints, overgrowth of hyperkeratotic tissue (corns or callouses) on other regions of the foot, hyperkeratotic callous formation may imply adequate vascularity, undermined borders, lack of sensation and signs of neuropathy present on physical examination.

EPIDERMIS is the outermost layer of skin.

FIBROBLAST is any cell from which connective tissue is developed.

FIRST DEGREE BURN is a superficial burn in which damage is limited to the outer layer of epidermis and is marked by redness, tenderness, and mild pain. Blisters do not form, and the burn heals without scar formation. A common example is sunburn.

KERATINOCYTE refers to any one of the cells in the skin that makes keratin.

NECRECTOMY refers to the surgical removal of necrotic tissue.

NEUROPATHIC ULCERS are related to the loss of protective sensation (LOPS) in the feet and legs as a result of a primary neurological condition, metabolic disease process (e.g., diabetes and/or renal failure), trauma, or surgery. They are usually painless unless an arterial component or infection is present. They have even, well-defined wound margins with or without undermining.

SECOND DEGREE BURN is a burn that damages epidermal and some dermal tissues but does not damage the lower-lying hair follicle, sweat, or sebaceous glands. The burn is painful and red; blisters form, and wounds may heal with a scar.

STANDARD (CONVENTIONAL) WOUND CARE: Includes documentation by a physician prior to referral or at the wound clinic of assessment of a patient's vascular status and correction of any vascular problems in the affected limb if possible, optimization of nutrition status, debridement by any means to remove devitalized tissue, maintenance of a clean, moist bed of granulation tissue with appropriate moist dressings, appropriate off-loading, and necessary treatment to resolve any infection that might be present.

THIRD DEGREE BURN is a burn that extends through the full thickness of the skin layer and often into underlying tissues. The skin has a pale, brown, gray, or blackened appearance. The burn is painless because it destroys nerves in the skin. Scar formation is likely.

VI. BENEFIT VARIATIONS

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The existence of this medical policy does not mean that this service is a covered benefit under the member's health benefit plan. Benefit determinations should be based in all cases on the applicable health benefit plan language. Medical policies do not constitute a description of benefits. A member's health benefit plan governs which services are covered, which are excluded, which are subject to benefit limits, and which require preauthorization. There are

different benefit plan designs in each product administered by Capital Blue Cross. Members and providers should consult the member's health benefit plan for information or contact Capital Blue Cross for benefit information.

VII. DISCLAIMER

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Capital Blue Cross's medical policies are developed to assist in administering a member's benefits, do not constitute medical advice, and are subject to change. Treating providers are solely responsible for medical advice and treatment of members. Members should discuss any medical policy related to their coverage or condition with their provider and consult their benefit information to determine if the service is covered. If there is a discrepancy between this medical policy and a member's benefit information, the benefit information will govern. If a provider or a member has a question concerning the application of this medical policy to a specific member's plan of benefits, please contact Capital Blue Cross' Provider Services or Member Services. Capital Blue Cross considers the information contained in this medical policy to be proprietary and it may only be disseminated as permitted by law.

VIII. CODING INFORMATION

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Note: This list of codes may not be all-inclusive, and codes are subject to change at any time. The identification of a code in this section does not denote coverage as coverage is determined by the terms of member benefit information. In addition, not all covered services are eligible for separate reimbursement.

Investigational; therefore, not covered skin substitutes:
See investigational section of policy above

Covered when medically necessary:

Procedure Codes							
Q4279	Q4288	Q4289	Q4290	Q4291	Q4292	Q4293	Q4294
Q4295	Q4296	Q4297	Q4298	Q4299	Q4300	Q4301	Q4302
Q4303	Q4304						

Covered when medically necessary:

Procedure Codes							
15271	15272	15273	15274	15275	15276	15277	15278
	C5271	C5272	C5273	C5274	C5275	C5276	C5277
C5278	A4100						

Allogeneic acellular dermal matrix products are covered, when medically necessary, for breast reconstructive surgery:

HCPCS Codes

POLICY TITLE	BIO-ENGINEERED SKIN AND SOFT TISSUE SUBSTITUTES
POLICY NUMBER	MP- 1.017

Q4100	Q4107	Q4116	Q4122	Q4128

ICD-10 Diagnosis Codes	Description
C50.011	Malignant neoplasm of nipple and areola, right female breast
C50.012	Malignant neoplasm of nipple and areola, left female breast
C50.021	Malignant neoplasm of nipple and areola, right male breast
C50.022	Malignant neoplasm of nipple and areola, left male breast
C50.111	Malignant neoplasm of central portion of right female breast
C50.112	Malignant neoplasm of central portion of left female breast
C50.121	Malignant neoplasm of central portion of right male breast
C50.122	Malignant neoplasm of central portion of left male breast
C50.211	Malignant neoplasm of upper-inner quadrant of right female breast
C50.212	Malignant neoplasm of upper-inner quadrant of left female breast
C50.221	Malignant neoplasm of upper-inner quadrant of right male breast
C50.222	Malignant neoplasm of upper-inner quadrant of left male breast
C50.311	Malignant neoplasm of lower-inner quadrant of right female breast
C50.312	Malignant neoplasm of lower-inner quadrant of left female breast
C50.321	Malignant neoplasm of lower-inner quadrant of right male breast
C50.322	Malignant neoplasm of lower-inner quadrant of left male breast
C50.411	Malignant neoplasm of upper-outer quadrant of right female breast
C50.412	Malignant neoplasm of upper-outer quadrant of left female breast
C50.421	Malignant neoplasm of upper-outer quadrant of right male breast
C50.422	Malignant neoplasm of upper-outer quadrant of left male breast
C50.511	Malignant neoplasm of lower-outer quadrant of right female breast
C50.512	Malignant neoplasm of lower-outer quadrant of left female breast
C50.521	Malignant neoplasm of lower-outer quadrant of right male breast
C50.522	Malignant neoplasm of lower-outer quadrant of left male breast
C50.611	Malignant neoplasm of axillary tail of right female breast
C50.612	Malignant neoplasm of axillary tail of left female breast
C50.621	Malignant neoplasm of axillary tail of right male breast
C50.622	Malignant neoplasm of axillary tail of left male breast
C50.811	Malignant neoplasm of overlapping sites of right female breast
C50.812	Malignant neoplasm of overlapping sites of left female breast
C50.821	Malignant neoplasm of overlapping sites of right male breast
C50.822	Malignant neoplasm of overlapping sites of left male breast
C50.911	Malignant neoplasm of unspecified site of right female breast
C50.912	Malignant neoplasm of unspecified site of left female breast
C50.921	Malignant neoplasm of unspecified site of right male breast

C50.922	Malignant neoplasm of unspecified site of left male breast
C79.81	Secondary malignant neoplasm of breast
Z42.1	Encounter for breast reconstruction following mastectomy
Z85.3	Personal history of malignant neoplasm of breast
Z90.11	Acquired absence of right breast and nipple
Z90.12	Acquired absence of left breast and nipple
Z90.13	Acquired absence of bilateral breasts and nipples

Covered, when medically necessary, for use in the treatment of chronic, non-infected, full thickness, neuropathic, diabetic lower extremity ulcers:

HCPCS Codes					
Q4101	Q4105	Q4106	Q4114	Q4128	Q4259
Q4260					

ICD-10 Diagnosis Codes	Description
E10.621	Type 1 diabetes mellitus with foot ulcer
E10.622	Type 1 diabetes mellitus with other skin ulcer
E11.621	Type 2 diabetes mellitus with foot ulcer
E11.622	Type 2 diabetes mellitus with other skin ulcer
L97.111	Non-pressure chronic ulcer of right thigh limited to breakdown of skin
L97.112	Non-pressure chronic ulcer of right thigh with fat layer exposed
L97.115	Non-pressure chronic ulcer of right thigh with muscle involvement without evidence of necrosis
L97.116	Non-pressure chronic ulcer of right thigh with bone involvement without evidence of necrosis
L97.118	Non-pressure chronic ulcer of right thigh with other specified severity
L97.121	Non-pressure chronic ulcer of left thigh limited to breakdown of skin
L97.122	Non-pressure chronic ulcer of left thigh with fat layer exposed
L97.125	Non-pressure chronic ulcer of left thigh with muscle involvement without evidence of necrosis
L97.126	Non-pressure chronic ulcer of left thigh with bone involvement without evidence of necrosis
L97.128	Non-pressure chronic ulcer of left thigh with other specified severity
L97.208	Non-pressure chronic ulcer of unspecified calf with other specified severity
L97.211	Non-pressure chronic ulcer of right calf limited to breakdown of skin
L97.212	Non-pressure chronic ulcer of right calf with fat layer exposed
L97.215	Non-pressure chronic ulcer of right calf with muscle involvement without evidence of necrosis
L97.216	Non-pressure chronic ulcer of right calf with bone involvement without evidence of necrosis

POLICY TITLE	BIO-ENGINEERED SKIN AND SOFT TISSUE SUBSTITUTES
POLICY NUMBER	MP- 1.017

ICD-10 Diagnosis Codes	Description
L97.218	Non-pressure chronic ulcer of right calf with other specified severity
L97.221	Non-pressure chronic ulcer of left thigh limited to breakdown of skin
L97.222	Non-pressure chronic ulcer of left thigh with fat layer exposed
L97.225	Non-pressure chronic ulcer of left calf with muscle involvement without evidence of necrosis
L97.226	Non-pressure chronic ulcer of left calf with bone involvement without evidence of necrosis
L97.228	Non-pressure chronic ulcer of left calf with other specified severity
L97.311	Non-pressure chronic ulcer of right ankle limited to breakdown of skin
L97.312	Non-pressure chronic ulcer of right ankle with fat layer exposed
L97.315	Non-pressure chronic ulcer of right ankle with muscle involvement without evidence
L97.316	Non-pressure chronic ulcer of right ankle with bone involvement without evidence of necrosis
L97.318	Non-pressure chronic ulcer of right ankle with other specified severity
L97.321	Non-pressure chronic ulcer of left ankle limited to breakdown of skin
L97.322	Non-pressure chronic ulcer of left ankle with fat layer exposed
L97.325	Non-pressure chronic ulcer of left ankle with muscle involvement without evidence of necrosis
L97.326	Non-pressure chronic ulcer of left ankle with bone involvement without evidence of necrosis
L97.328	Non-pressure chronic ulcer of left ankle with other specified severity
L97.411	Non-pressure chronic ulcer of right heel and midfoot limited to breakdown of skin
L97.412	Non-pressure chronic ulcer of right heel and midfoot with fat layer exposed
L97.415	Non-pressure chronic ulcer of right heel and midfoot with muscle involvement without evidence of necrosis
L97.416	Non-pressure chronic ulcer of right heel and midfoot with bone involvement without evidence of necrosis
L97.418	Non-pressure chronic ulcer of right heel and midfoot with other specified severity
L97.421	Non-pressure chronic ulcer of left heel and midfoot limited to breakdown of skin
L97.422	Non-pressure chronic ulcer of left heel and midfoot with fat layer exposed
L97.425	Non-pressure chronic ulcer of left heel and midfoot with muscle involvement without evidence of necrosis
L97.426	Non-pressure chronic ulcer of left heel and midfoot with bone involvement without evidence of necrosis
L97.428	Non-pressure chronic ulcer of left heel and midfoot with other specified severity
L97.511	Non-pressure chronic ulcer of other part of right foot limited to breakdown of skin
L97.512	Non-pressure chronic ulcer of other part of right foot with fat layer exposed

POLICY TITLE	BIO-ENGINEERED SKIN AND SOFT TISSUE SUBSTITUTES
POLICY NUMBER	MP- 1.017

ICD-10 Diagnosis Codes	Description
L97.515	Non-pressure chronic ulcer of other part of right foot with muscle involvement without evidence of necrosis
L97.516	Non-pressure chronic ulcer of other part of right foot with bone involvement without evidence of necrosis
L97.518	Non-pressure chronic ulcer of other part of right foot with other specified severity
L97.521	Non-pressure chronic ulcer of other part of left foot limited to breakdown of skin
L97.522	Non-pressure chronic ulcer of other part of left foot with fat layer exposed
L97.525	Non-pressure chronic ulcer of other part of left foot with muscle involvement without evidence of necrosis
L97.526	Non-pressure chronic ulcer of other part of left foot with bone involvement without evidence of necrosis
L97.528	Non-pressure chronic ulcer of other part of left foot with other specified severity
L97.811	Non-pressure chronic ulcer of other part of right lower leg limited to breakdown of skin
L97.812	Non-pressure chronic ulcer of other part of right lower leg with fat layer exposed
L97.815	Non-pressure chronic ulcer of other part of right lower leg with muscle involvement without evidence of necrosis
L97.816	Non-pressure chronic ulcer of other part of right lower leg with bone involvement without evidence of necrosis
L97.818	Non-pressure chronic ulcer of other part of right lower leg with other specified severity
L97.821	Non-pressure chronic ulcer of other part of left lower leg limited to breakdown of skin
L97.822	Non-pressure chronic ulcer of other part of left lower leg with fat layer exposed
L97.825	Non-pressure chronic ulcer of other part of left lower leg with muscle involvement without evidence of necrosis
L97.826	Non-pressure chronic ulcer of other part of left lower leg with bone involvement without evidence of necrosis
L97.828	Non-pressure chronic ulcer of other part of left lower leg with other specified severity
L97.915	Non-pressure chronic ulcer of unspecified part of right lower leg with muscle involvement without evidence of necrosis
L97.916	Non-pressure chronic ulcer of unspecified part of right lower leg with bone involvement without evidence of necrosis
L97.918	Non-pressure chronic ulcer of unspecified part of right lower leg with other specified severity
L97.925	Non-pressure chronic ulcer of unspecified part of left lower leg with muscle involvement without evidence of necrosis
L97.926	Non-pressure chronic ulcer of unspecified part of left lower leg with bone involvement without evidence of necrosis

POLICY TITLE	BIO-ENGINEERED SKIN AND SOFT TISSUE SUBSTITUTES
POLICY NUMBER	MP- 1.017

ICD-10 Diagnosis Codes	Description
L97.928	Non-pressure chronic ulcer of unspecified part of left lower leg with other specified severity
L98.415	Non-pressure chronic ulcer of buttock with muscle involvement without evidence of necrosis
L98.416	Non-pressure chronic ulcer of buttock with bone involvement without evidence of necrosis
L98.418	Non-pressure chronic ulcer of buttock with other specified severity
L98.425	Non-pressure chronic ulcer of back with muscle involvement without evidence of necrosis
L98.426	Non-pressure chronic ulcer of back with bone involvement without evidence of necrosis
L98.428	Non-pressure chronic ulcer of back with other specified severity

Covered, when medically necessary, for use in the treatment of venous insufficiency ulcers:

HCPCS Codes					
Q4101	Q4102	Q4260			

ICD-10 Diagnosis Codes	Description
I87.2	Venous insufficiency (chronic) (peripheral)
I87.311	Chronic venous hypertension (idiopathic) with ulcer of right lower extremity
I87.312	Chronic venous hypertension (idiopathic) with ulcer of left lower extremity
I87.313	Chronic venous hypertension (idiopathic) with ulcer of bilateral lower extremity
I87.331	Chronic venous hypertension (idiopathic) with ulcer and inflammation of right lower extremity
I87.332	Chronic venous hypertension (idiopathic) with ulcer and inflammation of left lower extremity
I87.333	Chronic venous hypertension (idiopathic) with ulcer and inflammation of bilateral lower extremity

Covered, when medically necessary, for the treatment of dystrophic epidermolysis bullosa:

HCPCS Code	Description
Q4100	Skin substitute, not otherwise specified ***(Use Q4100 for OrCel™)***

ICD-10 Diagnosis Codes	Description
Q81.2	Epidermolysis bullosa dystrophica

Covered, when medically necessary, for use in the treatment of second and third-degree burns:

HCPCS Codes					
Q4100	Q4105				

Covered for Diagnosis when 2nd or 3rd degree burns cover more than 30% of the body surface area

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X. POLICY HISTORY

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MP 1.017	**CAC 4/27/04**
	CAC 9/28/04
	CAC 10/26/04
	CAC 7/26/05
	CAC 2/28/06
	CAC 11/27/07
	CAC 11/25/08

POLICY TITLE	BIO-ENGINEERED SKIN AND SOFT TISSUE SUBSTITUTES
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	CAC 11/24/09 Consensus review
	CAC 7/27/10 Consensus review. Updated Medicare variation. Added information regarding Endoform Dermal Template.
	CAC 4/26/11 Consensus review.
	CAC 10/30/12 Minor **review**. Partially Adopting BCBSA for the following changes: • Title changed to match BCBSA. (Formerly Biologic and Burn Wound Dressings) • Added criteria for use of Alloderm® for breast reconstruction. • The following was changed regarding treatment of venous insufficiency ulcers using Apligraf®: o Deleted criteria – ulcer of at least 12 weeks duration. o Changed trial of conventional wound care from 8 weeks to one month. o Added requirement to use Apligraf® with standard therapeutic compression. o Added requirement - The patient has adequate arterial blood supply to support tissue growth as documented by an Ankle-Brachial Index no less than 0.65 o Added requirement to be used in conjunction with conventional wound care regimens. • The following was changed regarding treatment of diabetic ulcers using Apligraf®: o Changed duration of conventional therapy trial from 4 weeks to 3 weeks. o Deleted contraindication for heel wounds o Deleted requirement for absence of active Charcot's arthropathy. o Added requirement to be used in conjunction with conventional wound care regimens. o Added requirement - The patient has adequate arterial blood supply to support tissue growth as documented by an Ankle-Brachial Index no less than 0.65 • Deleted general statements regarding documentation requirements and frequency of Apligraf® device application. • The following was changed regarding treatment of diabetic ulcers using Dermagraft®. o Deleted time period of minimum of 6 weeks for medical management of patient with documented Type 1 or 2 diabetes. Now no time period for medical management specified. o Changed duration of conventional wound care therapy trial from 4 weeks to 3 weeks o Added statement - Dermagraft® must be used in conjunction with conventional wound care regimens.

	o Added requirement - The patient has adequate arterial blood supply to support tissue growth as documented by an Ankle-Brachial Index no less than 0.65 o Added criteria – the ulcer is without infection, tunnels, and tracts. o Deleted requirement for absence of active Charcot's arthropathy • Endoform Dermal Template™ changed from medically necessary to investigational for all indications. • Added MN indications for use of Epicel and Orcel. Previously silent. • Separate sections created for TransCyte® and Integra Dermal Regeneration Template® • The following was changed regarding treatment of diabetic ulcers using Integra® Dermal Regeneration Template. o Changed MN statement. Previous statement indicated MN for severe full thickness or deep partial-thickness thermal injury and for thermal injuries, superficial scald burns or flame injury of the hand with specific criteria. o Now MN for treatment of second- and third-degree burns. o Added requirement to be used in conjunction with conventional wound care regimens • Oasis® Wound Matrix is now medically necessary for chronic, non-infected, partial or full-thickness lower extremity skin ulcers due to venous insufficiency with the following criteria o inadequate response following a 1-month period of conventional ulcer therapy. (Previously there was no requirement for a trial of conservative therapy). o The patient has adequate arterial blood supply to support tissue growth as documented by an Ankle-Brachial Index no less than 0.65. o Oasis ® Wound Matrix will be used in conjunction with conventional wound care regimens o Use of Oasis® Wound Matrix is now considered **investigational** for other wounds not meeting criteria. • The following was changed regarding treatment of diabetic ulcers using TransCyte® o TransCyte® was considered MN for severe full-thickness burns or deep partial-thickness thermal injury and for the treatment of thermal injuries, superficial scald burns or flame injury of the hand with specific wound criteria. o Now MN for treatment of second- and third-degree burns. • Silent on general category of "biological dressings" • Adopted BCBSA's Background/Description • Added definition of conventional wound therapy • Added a Medicare variation referencing CMS) National Coverage Determination (NCD) 270.5 Porcine Skin and Gradient Pressure Dressings.

- Added list of investigational products.

Codes reviewed 9/19/12

12/19/2013 Administrative update. New 2014 Code updates made.

CAC 3/25/14 Minor review. Changed Alloderm to include other acellular dermal matrix products (i.e., AlloDerm®, AlloMax™, DermaMatrix™, FlexHD®, GraftJacket®). AlloMax™, FlexHD® and, GraftJacket® deleted from the investigational list. Updated Rationale and Reference Sections. Added the following to the list of investigational products.

ACell® UBM Hydrated Wound Dressing	ACell® UBM Lyophilized Wound Dressing	Aongen™ Collagen Matrix	Atlas Wound Matrix
Avagen Wound Dressing	Collagen Sponge (Innocoll)	Collagen Wound Dressing (Oasis Research)	Collaguard®
CollaSorb™	CollaWound™	Collexa®	Collieva®
Coreleader Colla-Pad	Dermadapt™ Wound Dressing	DressSkin	Excellagen
FortaDerm™ Wound Dressing	HA Absorbent Wound Dressing	Helicoll	Hyalomatrix® (Laserskin®)
Jaloskin®	Matrix Collagen Wound Dressing	Primatrix™ Dermal Repair Scaffold	Puros® Dermis
Repliform®	Stimulen™ Collagen	Suprathel®	TheraForm™ Standard/Sheet
Unite® Biomatrix			

03/17/2014 All CPT and HCPCS codes reviewed.

8/25/14 Administrative update. Deleted GraftJacket® Regenerative Tissue Matrix from investigational list.

CAC 3/24/15 Minor revision. EpiFix added considered medically necessary for treatment of diabetic foot ulcers. Additional skin substitutes added as investigational to include the following: Affinity™;A llowrap™; Alphaplex™ with MariGen Omega3™; AmnioBand™; Biovance®[Clarix® Flo; Clarix® Flo; Dermavest™; GUARDIAN; Neox® Flo; Neox 1K; NuShield™; and

Revitalon™ References and rationale updated. Medicare variation revised. Medicare LCD title changed to “Application of Bioengineered Skin Substitutes to Lower Extremity Chronic Non-Healing Wounds.”
11/2/15 Administrative update. LCD number changed from L27549 to L35041 due to Novitas update to ICD-10
5/23/16 Administrative update. Revised name of FortaDerm™ Wound Dressing to “PuraPly™ Antimicrobial Wound Matrix” as the product name changed**.**
1/1/17Administrative update. Product variation section updated.
1/1/18 Administrative update. Medicare variations removed from Commercial Policies. Added new ICD-10 codes; effective 10/1/17. New HCPCS codes Q4179 and Q4182 added; effective 1/1/18. Revised code descriptions updated.
CAC 11/28/17 Minor review. BCBSA policy adopted for this review. The following changes have been made: • Integra Dermal Regeneration Template was added as medically necessary for the treatment of diabetic foot ulcers. • TransCyte removed from the policy as it is no longer available. • Acellular dermal matrix products used in breast reconstruction were clarified • Investigational list updated with new products and name changes • Wound dressing products removed from the list • Amniotic membrane products removed and placed in MP-4.042 Amniotic Membrane and Amniotic Fluid Injections • Section on laryngoplasty removed. • Products with new HCPCS codes (Microderm, TruSkin) added to the investigational statement • Matristem renamed Cytal • Fortaderm renamed Puraply • Allomend added to the medically necessary statement for breast reconstructive surgery • Allopatch added to the medically necessary statement for diabetic lower-extremity ulcers Background, rationale, and references revised. Coding Reviewed.
1/1/19 Administrative update. Removed deleted code Q4172. Added new codes Q4193, Q4195-Q4197, Q4200, Q4202, Q4203 effective 1/1/19.

	7/12/18 Minor revision. The following revisions have been made: • CellerateRX® (CRXa™) removed from the investigational policy statement. • Integra Omnigraft deleted from investigational policy statement and added to bullet for Integra® Dermal Regeneration Template. • AlloMax was renamed Cortiva. • DermACELL and FlexHD Pliable added to medically necessary statement on breast reconstructive surgery. • Integra Flowable Wound Matrix added to medically necessary statement on use of Integra Dermal Regeneration Template for diabetic lower-extremity ulcers. • Several products added to investigational list. Description/Background, Rationale, and Reference sections updated. Coding updated. Effective 3/1/19
	4/12/19 Consensus review. No change to policy statements. Background, summary of evidence, and references updated.
	10/1/19 Administrative update. Updated Q4122 and Q4165 descriptions. Added new codes effective 10/1/19.
	04/23/20 Consensus review. No change to policy statements.
	7/1/20 Administrative update. New codes C1849, Q4227, Q4228, Q4231, Q4232, Q4233, Q4234, Q4235, Q4236, Q4237, Q4238, Q4239, Q4240, Q4241, Q4242, Q4244, Q4245, Q4246, Q4247, Q4248 added. Effective 7-1-20.
	10/01/20 Administrative update. New codes Q4250, Q4254, and, Q4249 added.
	2/24/21 Consensus review. Background and references updated. Coding reviewed.
	9/22/21 Administrative update. New codes Q4251 and Q4252 added. Q4228 and Q4236 were deleted. Effective 10-1-21.
	12/1/21 Administrative Update. New codes A2001-A2010 added to policy. Effective 1-2-22.
	2/22/22 Consensus review. Updated investigational products/codes. Removed: (refer instead to MP 4.042): Q4250 (Amnioamp), Q4227 (Amniocore), Q4242 (Amniocyte). Q4239 (Amnio-maxx), Q4249 (Amniply), Q4235 (Amniorepair, Altiply), Q4245 (Amniotext), Q4247 (Amniotext patch), Q4246 Coretext or protext, Q4232 Corplex. Q4231 (corplex p), Q4248 (Dermacyte), Q4254 Novafix, Q4241 Polycyte for topical use, Q4244 Procenta, Q4233 Surfactor or nudyn, Q4251 Vim, Q4252 Vendaje. Added as investigational: Geistlich Derma-GideTM (Q4203); InteguPly® (Q4126); MatriStem Micromatrix (Q4118); Ologen™ Collagen Matrix, Omega3 Wound, Puracol®, and Puracol® Plus Collagen Wound Dressings (Q4100); TranZgraft (Q4126). References updated.

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	3/11/22. Administrative update. New codes added as investigational: A2011, A2012, and A2013; and A4100 (NOS code), coverage to be determined by criteria; effective 4/1/22.
	6/13/2022 Administrative Update. New codes Q4259, Q4260 added as medically necessary. New code Q4261 added as investigational. Updated formatting. Effective 7/1/2022.
	9/14/2022 Administrative update. New codes A2014, A2015, A2016, A2017, A2018 added as investigational. Effective 10/1/2022.
	12/2/2022 Administrative update. New code Q4264 added as investigational. Deleted code C1849 removed from policy. Effective 1/1/2023
	9/7/2023 Admnistrative update. New codes A2022, A2023, A2024, A2025, Q4285. Effective 101/2023.
	10/24/2023 Retirement.
	12/13/2023 Administrative update. Added Q4279, Q4288, Q4289, Q4290, Q4291, Q4292, Q4293, Q4294, Q4295, Q4296, Q4297, Q4298, Q4299, Q4300, Q4301, Q4302, Q4303, Q4304 Effective 1/1/2024.

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