



FEP Medical Policy Manual

FEP 7.01.113 Bioengineered Skin and Soft Tissue Substitutes

Effective Policy Date: April 1, 2021 **Related Policies:**

Original Policy Date: September 2011 2.01.16 - Recombinant and Autologous Platelet-Derived Growth Factors for Wound Healing and Other Non-Orthopedic Conditions
7.01.149 - Amniotic Membrane and Amniotic Fluid

Bioengineered Skin and Soft Tissue Substitutes

Description

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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 and healing lower-extremity ulcers and severe burns. Acellular dermal matrix (ADM) products are also being evaluated for soft tissue repair.

OBJECTIVE

The objective of this review is to determine whether the use of artificial skin and soft-tissue substitutes for reinforcement for surgical procedures and healing of chronic wounds and burns improves the net health outcome.

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POLICY STATEMENT

Breast reconstructive surgery using allogeneic acellular dermal matrix products^a (including each of the following: AlloDerm, AlloMend, Cortiva [AlloMax™], DermACELL™, DermaMatrix™, FlexHD, FlexHD Pliable™, GraftJacket; 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^a
- Apligraf^b
- Dermagraft^b
- Integra Omnigraft™ Dermal Regeneration Matrix (also known as Omnigraft™) and Integra Flowable Wound Matrix.

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^b
- Oasis™ Wound Matrix^c.

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])^d.

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 $\geq 30\%$ when provided in accordance with the HDE specifications of the FDA)^d
- Integra Dermal Regeneration Template^b.

^a Banked human tissue. ^b FDA premarket approval. ^c FDA 510(k) clearance. ^d FDA-approved under an HDE.

All other uses of the bioengineered skin and soft tissue substitutes listed above are considered **investigational**.

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

- ACell UBM Hydrated/Lyophilized Wound Dressing
- AlloSkin™
- AlloSkin™ RT
- Aongen™ Collagen Matrix
- Architect ECM, PX, FX
- ArthroFlex™ (Flex Graft)
- AxoGuardNerve Protector (AxoGen)
- Biobrane/Biobrane-L
- Bio-ConneKt Wound Matrix
- CollaCare
- CollaCare Dental
- Collagen Wound Dressing (Oasis Research)
- CollaGUARD
- CollaMend™
- CollaWound™
- Coll-e-derm
- Collexa
- Collieva
- Conexa™
- Coreleader Colla-Pad
- CorMatrix
- Cymetra™ (Micronized AlloDerm)™
- Cytal™ (previously MatriStem)
- Dermadapt™ Wound Dressing
- Derma-gide
- DermaPure™
- DermaSpan™

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- DressSkin
- Durepair Regeneration Matrix
- Endoform Dermal Template™
- *ENDURAGen*™
- Excellagen
- ExpressGraft™
- E-Z Derm™
- FlowerDerm™
- GammaGraft
- Geistlich Derma-Gide™
- GraftJacket Xpress, injectable
- Helicoll™
- hMatrix
- Hyalomatrix
- Hyalomatrix PA
- Integra™ Bilayer Wound Matrix
- Integra Matrix Wound Dressing (previously Avagen)
- InteguPly
- Keramatrix
- Kerecis™ Omega3
- Keroxx™
- MatriDerm
- MatriStem
- Matrix HD™
- MicroMatrix
- Miroderm
- Mediskin
- MemoDerm™
- Microderm biologic wound matrix
- MyOwn skin
- Oasis Burn Matrix

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- Oasis Ultra
- Ologen™ Collagen Matrix
- Omega3 Wound (originally Merigen wound dressing)
- Permacol™
- PriMatrix™
- PriMatrix™ Dermal Repair Scaffold
- Progenamatrix
- Puracol and Puracol Plus Collagen Wound Dressings
- PuraPly™ Wound Matrix (previously FortaDerm™)
- PuraPly™ AM (Antimicrobial Wound Matrix)
- Puros Dermis
- RegenePro™
- Repliform
- Repriza™
- SkinTE™
- StrataGraft
- Stratlice™
- Suprathel
- SurgiMend
- Talymed
- TenoGlide™
- TenSIX™ Acellular Dermal Matrix
- TissueMend
- TheraForm™ Standard/Sheet
- TheraSkin
- TransCyte™
- TruSkin™
- Veritas Collagen Matrix
- XCM Biologic Tissue Matrix
- XenMatrix™ AB

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POLICY GUIDELINES

Note that amniotic and placental products are reviewed in evidence review 7.01.149.

Clinical input has indicated that the various acellular dermal matrix products used in breast reconstruction have similar efficacy. The products listed are those that have been identified for use in breast reconstruction. Additional acellular dermal matrix products may become available for this indication.

See the Agency for Healthcare Research and Quality Technology Review by Snyder et al (2020) for detailed description of skin substitute products for treatment of chronic wounds.

BENEFIT APPLICATION

Experimental or investigational procedures, treatments, drugs, or devices are not covered (See General Exclusion Section of brochure).

FDA 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

Acellular Dermal Matrix 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 (ie, 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 clarification of what is considered minimal manipulation and homologous use for human cells, tissues, and cellular and tissue-based products (HCT/Ps)²

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

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4. Either:

1. 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
2. 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."

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.³

- 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 acellular hydrated 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.

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 (eg, abrasions, lacerations, second-degree burns, 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

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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 3 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 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 1 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 the 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 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 embedded 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.

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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 postexcisional 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 the 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.

RATIONALE

Summary of Evidence

Breast Reconstruction

For individuals who are undergoing breast reconstruction who receive allogeneic acellular dermal matrix (ADM) products, the evidence includes randomized controlled trials (RCTs) and systematic reviews. Relevant outcomes are symptoms, morbid events, functional outcomes, quality of life (QOL), 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 an improvement in the net health outcome.

Tendon Repair

For individuals who are undergoing tendon repair who receive GraftJacket, the evidence includes an RCT. Relevant outcomes are symptoms, morbid events, functional outcomes, QOL, 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 that the technology results in an improvement in the net health outcome.

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 includes RCTs. Relevant outcomes are symptoms, morbid events, functional outcomes, QOL, and treatment-related morbidity. Several comparative studies including RCTs have shown no difference in outcomes between tissue-engineered skin

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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 QOL. RCTs have demonstrated the efficacy of AlloPatch (reticular ADM), Apligraf and Dermagraft (living cell therapy), and Integra (biosynthetic) over the standard of care (SOC). The evidence is sufficient to determine that the technology results in an 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 QOL. 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 that the technology results in an improvement in the net health outcome.

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 symptoms, change in disease status, morbid events, and QOL. RCTs have demonstrated the efficacy of Apligraf living cell therapy and xenogenic Oasis Wound Matrix over the SOC. The evidence is sufficient to determine that the technology results in an 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 QOL. In a moderately large RCT, Dermagraft was not shown to be more effective than controls for the primary or secondary endpoints 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 versus the current SOC. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

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 QOL. 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 (eg, 5 patients). The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

Deep Dermal Burns

For individuals who have deep dermal burns who receive bioengineered skin substitutes (ie, Epicel, Integra Dermal Regeneration Template), the evidence includes RCTs. Relevant outcomes are symptoms, change in disease status, morbid events, functional outcomes, QOL, 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 U.S. Food and Drug administration 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 an improvement in the net health outcome.

SUPPLEMENTAL INFORMATION

Practice Guidelines and Position Statements

National Institute for Health and Care Excellence

In 2019, the National Institute for Health and Care Excellence updated its guidance on the prevention and management of diabetic foot problems.⁷¹ The Institute recommended that clinicians "consider dermal or skin substitutes as an adjunct to standard care when treating diabetic foot ulcers, only when healing has not progressed and on the advice of the multidisciplinary foot care service."

U.S. Preventive Services Task Force Recommendations

Not applicable.

Medicare National Coverage

The Centers for Medicare & Medicaid Services (CMS) issued the following national coverage determination: porcine (pig) skin dressings are covered, if reasonable and necessary for the individual patient as an occlusive dressing for burns, donor sites of a homograft, and decubiti and other ulcers.⁷²

In 2019, CMS reported that it is finalizing the proposal to continue the policy established in CY 2018 to assign skin substitutes to the low cost or high-cost group.⁷³ In addition, CMS presented several payment ideas to change how skin substitute products are paid and solicited comments on these ideas to be used for future rulemaking.

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POLICY HISTORY - THIS POLICY WAS APPROVED BY THE FEP® PHARMACY AND MEDICAL POLICY COMMITTEE ACCORDING TO THE HISTORY BELOW:

Date	Action	Description
September 2011	New policy	
March 2013	Replace policy	Policy updated and scope expanded; policy statements added for other indications; title changed to "Bio- Engineered Skin and Soft Tissue Substitutes"

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Date	Action	Description
March 2014	Replace policy	Policy updated with literature search adding references 1, 13-15, 24, 36, 40, 48, 59, 66, and 68. First policy statement expanded to include other acellular dermal matrix products
March 2015	Replace policy	Policy updated with literature review through December 3, 2014; references 2, 17, 27, 37, 41, 42, and 44 added; EpiFix considered medically necessary for treatment of diabetic foot ulcers was added to the policy statement
December 2016	Replace policy	Policy updated with literature review through October 30, 2015; references added and renumbered. Clinical input reviewed. Integra Dermal Regeneration Template, Biovance and Grafix were added as medically necessary for the treatment of diabetic foot ulcers. TransCyte removed from the medically necessary statement; it is no longer commercially available. Acellular dermal matrix products used in breast reconstruction clarified; investigational list updated with new products and name changes; wound dressing products removed from list.
March 2017	Replace policy	Policy updated with literature review through November 7, 2016; references 6, 19, 26, and 28-29 added. Review of amniotic membrane products moved to evidence review 7.01.149; section on laryngoplasty removed. Products with new HCPCS codes (Microderm, TruSkin) added to investigational statement; Unite Biomatrix no longer available; MatriStem renamed Cytal; FortaDerm renamed PuraPly. Rationale revised to focus on randomized controlled trials and some references removed. AlloMend added to medically necessary statement for breast reconstructive surgery. AlloPatch added to medically necessary statement for diabetic lower-extremity ulcers.
June 2018	Replace policy	Policy updated with literature review through November 6, 2017; references 4-5, 7, 9, 15, 20, 29, 35, and 54 added; references 59 and 61 updated. 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.

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Date	Action	Description
March 2019	Replace policy	Policy updated with literature review through December 4, 2018; references 28 and 43 added. Policy statements unchanged except Flexigraft not categorized as bioengineered skin or soft tissue substitutes by FEP therefore removed from policy
March 2020	Replace policy	Policy updated with literature review through November 12, 2019; references added. Policy statements unchanged except TransCyte re-added to medically necessary burn statement.
March 2021	Replace policy	Policy updated with literature review through December 6, 2020; references added. Products added to investigational list and cross checked with HCPS codes. Policy statements unchanged except TransCyte removed as not commercially available.

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