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MEDICAL POLICY – 7.01.582

Bioengineered Skin and Soft Tissue Substitutes

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Effective Date:	**Jul. 3, 2025***
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Replaces:	7.01.113

*This policy is effective July 3, 2025. Click here to view the current policy.

RELATED MEDICAL POLICIES:

2.01.543	Recombinant and Autologous Platelet-Derived Growth Factors for Wound Healing and Other Non-Orthopedic Conditions
7.01.583	Amniotic Membrane and Amniotic Fluid Injections

Select a hyperlink below to be directed to that section.

POLICY CRITERIA | DOCUMENTATION REQUIREMENTS | CODING
RELATED INFORMATION | EVIDENCE REVIEW | REFERENCES | HISTORY

∞ Clicking this icon returns you to the hyperlinks menu above.

Introduction

Bioengineered skin and soft tissue substitutes are artificial alternatives to live skin grafts for wound care and tissue reconstruction. The products are made from various sources including human tissue (from the individual or others), nonhuman tissue (cows, pigs, horses), synthetic materials (man-made), or a combination of these materials. Some skin substitutes are labeled for specific uses such as for healing severe diabetic foot sores or during surgery for severe burns or breast reconstruction; other uses are being researched. This policy outlines when specific bioengineered skin and soft tissue substitutes might be medically necessary.

Note: The Introduction section is for your general knowledge and is not to be taken as policy coverage criteria. The rest of the policy uses specific words and concepts familiar to medical professionals. It is intended for providers. A provider can be a person, such as a doctor, nurse, psychologist, or dentist. A provider also can be a place where medical care is given, like a hospital, clinic, or lab. This policy informs them about when a service may be covered.

Policy Coverage Criteria

Products	Medical Necessity
Allogeneic Acellular Dermal Matrix Products, including but not limited to: • **AlloDerm[a]** • **AlloMend[a]** • **Cortiva [AlloMax][a]** • **DermACELL[a]** • **DermaMatrix[a]** • **FlexHD[a]** • **FlexHD Pliable[a]** • **GraftJacket[a]**	**Breast reconstructive surgery using allogeneic acellular dermal matrix products listed in the left column may be considered medically necessary when:** • There is insufficient tissue expander or implant coverage by the pectoralis major muscle and additional coverage is required **OR** • 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
• **AlloPatch[a]** • **Apligraf[b]** • **Dermagraft[b]** • **Integra Omnigraft Dermal Regeneration Matrix (also known as Omnigraft)** • **IntegraFlowable Wound Matrix** • **mVasc** • **TheraSkin**	**Treatment of chronic, non-infected, full-thickness diabetic lower-extremity ulcers using the tissue-engineered skin substitute products listed in the left column may be considered medically necessary.** **Note**: Criteria for using human amniotic membrane products are addressed in a separate medical policy (see **Related Policies**).
• **Apligraf[b]** • **Oasis Wound Matrix[c]**	**Treatment of chronic, non-infected, partial or full-thickness lower-extremity skin ulcers due to venous insufficiency using the tissue-engineered skin substitute products listed in the left column may be considered medically necessary when:** • A one-month period of conventional ulcer therapy has failed to promote healing
• **OrCel[d]**	**Treatment of dystrophic epidermolysis bullosa using the tissue-engineered skin substitute product listed in the left column may be considered medically necessary when:** • Standard wound therapy has failed for the treatment of mitten-hand deformity **AND** • It is provided in accordance with the humanitarian device exemption (HDE) specifications of the US Food and Drug Administration (FDA)

Products	Medical Necessity
• **Epicel[d]** • **Integra Dermal Regeneration Template[b]**	**Treatment of second- and third-degree burns using the tissue-engineered skin substitute products listed in the left column may be considered medically necessary when:** • **Epicel only:** It is used for the treatment of deep dermal or full-thickness burns covering a total body surface area ≥30% when provided in accordance with the HDE specifications of the FDA[d] • **Integra Dermal Regeneration Template[b]:** No additional criteria required
All other uses of the bioengineered skin and soft tissue substitutes listed above are considered investigational.	

Note: [a]Banked human tissue; [b]FDA premarket approval; [c]FDA 510(k) cleared; [d]FDA-approved under an HDE

Note: Amniotic membrane and amniotic fluid products are reviewed in a **Related Policy**.

Investigational		
All other bioengineered skin and soft tissue substitute products not listed above are considered investigational, including, but not limited to:		
• **AC5** • **ACell UBM Hydrated Wound Dressing** • **ACell UBM Lyophilized Wound Dressing** • **AlloSkin** • **AlloSkin RT** • **Aongen Collagen Matrix** • **Apis** • **Architect ECM, PX, FX** • **ArthroFlex (Flex Graft)** • **AxoGuard Nerve Protector (AxoGen)** • **BEAR (Bridge-Enhanced ACL Repair) Implant** • **BellaCell HD** • **Biobrane/Biobrane-L** • **Bio-ConneKt Wound Matrix** • **CollaCare** • **CollaCare Dental**	• **Endoform Dermal Template** • **ENDURAGen** • **Excellagen** • **ExpressGraft** • **E-Z Derm** • **FlowerDerm** • **GammaGraft** • **Geistlich Derma-Gide** • **GraftJacket Xpress, injectable** • **Helicoll** • **hMatrix** • **Hyalomatrix** • **Hyalomatrix PA** • **InnovaMatrix** • **Integra Bilayer Wound Matrix** • **Integra Matrix Wound Dressing (previously Avagen)** • **IntéguPly**	• **Omeza Collagen Matrix** • **Permacol** • **PermeaDerm B** • **PermeaDerm C** • **PermeaDerm Glove** • **Phoenix Wound Matrix** • **PriMatrix** • **PriMatrix Dermal Repair Scaffold** • **Progenamatrix** • **Puracol/Puracol Plus Collagen Wound Dressings** • **PuraPly Wound Matrix (previously FortaDerm)** • **PuraPly AM (Antimicrobial Wound Matrix)** • **Puros Dermis** • **RegenePro** • **Repliform** • **ReCell** • **Repriza**

Investigational

- **Collagen Wound Dressing (Oasis Research)**
- **CollaGUARD**
- **CollaMend**
- **CollaWound**
- **Coll-e-derm**
- **Collexa**
- **Collieva**
- **Conexa**
- **Coreleader Colla-Pad**
- **CorMatrix**
- **Cymetra (Micronized AlloDerm)**
- **Cytal (previously MatriStem)**
- **DeNovoSkin**
- **Derm-Maxx**
- **Dermadapt Wound Dressing**
- **Derma-gide**
- **DermaPure**
- **DermaSpan**
- **DressSkin**
- **Durepair Regeneration Matrix**
- **Keramatrix**
- **Kerecis Omega3**
- **Keroxx**
- **MatriDerm**
- **MatriStem**
- **Matrix HD**
- **MicroMatrix**
- **Miroderm**
- **Mediskin**
- **MemoDerm**
- **Microderm biologic wound matrix**
- **Microlyte matrix**
- **MyOwn skin**
- **Novosorb Biodegradable Temporizing Matrix (BMT)**
- **Oasis Burn Matrix**
- **Oasis Ultra**
- **OlogenCollagen Matrix**
- **Omega3 Wound (previously Merigen wound dressing)**
- **Restrata**
- **SkinTE**
- **StrataGraft**
- **Strattice**
- **Supra SDRM**
- **Suprathel**
- **SureDerm per sq cm**
- **SurgiMend**
- **Symphony**
- **Talymed**
- **TenoGlide**
- **TenSIX Acellular Dermal Matrix**
- **TissueMend**
- **TheraForm Standard/Sheet**
- **TheraGenesis**
- **TransCyte**
- **TruSkin**
- **Tutomesh Fenestrated Bovine Pericardium**
- **Veritas Collagen Matrix**
- **XCelliStem**
- **XCM Biologic Tissue Matrix**
- **XenMatrix AB**

Documentation Requirements

For wound care, detailed history and physical, with the record to include the following:

- Associated medical comorbidities
- Description of wound (e.g., full thickness [affecting all layers of the skin], deep dermal [deeper than a superficial wound but not a full thickness wound])
- Standard wound therapy treatment provided, including duration and effectiveness or failure of treatment

Coding

Note: The list of products named in this policy is not a complete list of all commercially available products.

Code	Description
CPT	
15011	Harvest of skin for skin cell suspension autograft; first 25 sq cm or less (new code effective 01/01/25)
15012	Harvest of skin for skin cell suspension autograft; each additional 25 sq cm or part thereof (List separately in addition to code for primary procedure) (new code effective 01/01/25)
15013	Preparation of skin cell suspension autograft, requiring enzymatic processing, manual mechanical disaggregation of skin cells, and filtration; first 25 sq cm or less of harvested skin (new code effective 01/01/25)
15014	Preparation of skin cell suspension autograft, requiring enzymatic processing, manual mechanical disaggregation of skin cells, and filtration; each additional 25 sq cm of harvested skin or part thereof (List separately in addition to code for primary procedure) (new code effective 01/01/25)
15015	Application of skin cell suspension autograft to wound and donor sites, including application of primary dressing, trunk, arms, legs; first 480 sq cm or less (new code effective 01/01/25)
15016	Application of skin cell suspension autograft to wound and donor sites, including application of primary dressing, trunk, arms, legs; each additional 480 sq cm or part thereof (List separately in addition to code for primary procedure) (new code effective 01/01/25)
15017	Application of skin cell suspension autograft to wound and donor sites, including application of primary dressing, face, scalp, eyelids, mouth, neck, ears, orbits, genitalia, hands, feet, and/or multiple digits; first 480 sq cm or less (new code effective 01/01/25)
15018	Application of skin cell suspension autograft to wound and donor sites, including application of primary dressing, face, scalp, eyelids, mouth, neck, ears, orbits, genitalia, hands, feet, and/or multiple digits; each additional 480 sq cm or part thereof (List separately in addition to code for primary procedure) (new code effective 01/01/25)
HCPCS	
Reviewed for Medical Necessity	
A4100	Skin substitute, FDA cleared as a device, not otherwise specified
Q4100	Skin substitute, not otherwise specified
Investigational (Not Eligible for Coverage)	
A2001	InnovaMatrix AC, per sq cm
A2002	Mirragen Advanced Wound Matrix, per sq cm
A2004	XCelliStem, per sq cm

Code	Description
A2005	Microlyte Matrix, per sq cm
A2006	NovoSorb SynPath dermal matrix, per sq cm
A2007	Restrata, per sq cm
A2008	TheraGenesis, per sq cm
A2009	Symphony, per sq cm
A2010	Apis, per sq cm
A2011	Supra SDRM, per square centimeter
A2012	Suprathel, per square centimeter
A2013	InnovaMatrix FS, per square centimeter
A2014	Omeza Collagen Matrix, per 100 mg
A2015	Phoenix Wound Matrix, per sq cm
A2016	PermeaDerm B, per sq cm
A2017	PermeaDerm Glove, each
A2018	PermeaDerm C, per sq cm
A2019	Kerecis omega3 marigen shield, per square centimeter
A2020	Ac5 advanced wound system (ac5)
A2021	Neomatrix, per square centimeter
A2022	Innovaburn or innovamatrix xl, per square centimeter
A2023	Innovamatrix pd, 1 mg
A2024	Resolve matrix, per square centimeter
A2025	Miro3d, per cubic centimeter
A2026	Restrata minimatrix, 5 mg
A2027	Matriderm, per square centimeter (new code effective 10/01/24)
A2028	Micromatrix flex, per mg (new code effective 10/01/24)
A2029	Mirotract wound matrix sheet, per cubic centimeter (new code effective 10/01/24)
A2030	Miro3d fibers, per milligram (new code effective 01/01/25)

Code	Description
A2031	Mirodry wound matrix, per square centimeter (new code effective 01/01/25)
A2032	Myriad matrix, per square centimeter (new code effective 01/01/25)
A2033	Myriad morcells, 4 milligrams (new code effective 01/01/25)
A2034	Foundation drs solo, per square centimeter (new code effective 01/01/25)
A6460	Synthetic resorbable wound dressing, sterile, pad size 16 sq. in. or less, without adhesive border, each dressing
A6461	Synthetic resorbable wound dressing, sterile, pad size more than 16 sq. in. but less than or equal to 48 sq. in., without adhesive border, each dressing
C1763	Connective tissue, nonhuman (includes synthetic) (use to report: BEAR [Bridge-Enhanced ACL Repair] implant)
C1832	Autograft suspension, including cell processing and application, and all system components
C9353	Microporous collagen implantable slit tube (NeuraWrap Nerve Protector), per cm length (used to report: AxoGuard)
C9354	Acellular pericardial tissue matrix of nonhuman origin (Veritas), per sq cm
C9356	Tendon, porous matrix of cross-linked collagen and glycosaminoglycan matrix (TenoGlide Tendon Protector Sheet), per sq cm
C9358	Dermal substitute, native, nondenatured collagen, fetal bovine origin (SurgiMend Collagen Matrix), per 0.5 sq cm
C9360	Dermal substitute, native, nondenatured collagen, neonatal bovine origin (SurgiMend Collagen Matrix), per 0.5 sq cm
C9363	Skin substitute (Integra Meshed Bilayer Wound Matrix), per sq cm
C9364	Porcine implant, Permacol, per sq cm
Q4103	Oasis Burn Matrix, per square centimeter
Q4104	Integra bilayer matrix wound dressing (BMWD), per sq cm
Q4108	Integra Matrix, per square centimeter
Q4110	PriMatrix, per square centimeter
Q4111	GammaGraft, per square centimeter
Q4112	Cymetra, injectable, 1 cc
Q4113	Graftjacket Xpress, injectable, 1 cc
Q4115	AlloSkin, per square centimeter

Code	Description
Q4117	Hyalomatrix, per square centimeter
Q4118	MatriStem micromatrix, 1 mg
Q4121	TheraSkin, per square centimeter
Q4123	AlloSkin RT, per square centimeter
Q4124	Oasis Ultra Tri-Layer Wound Matrix, per square centimeter
Q4125	ArthroFlex, per square centimeter
Q4126	Memoderm, Dermaspan, TranZgraft or Integuply, per square centimeter
Q4127	Talymed, per square centimeter
Q4130	Strattice TM, per square centimeter
Q4134	hMatrix, per square centimeter
Q4135	Mediskin, per square centimeter
Q4136	E-Z derm, per square centimeter
Q4141	AlloSkin AC, per square centimeter
Q4142	XCM biologic tissue matrix, per square centimeter
Q4143	Repriza, per square centimeter
Q4146	TenSIX, per square centimeter
Q4147	Architect, Architect PX, or Architect FX, extracellular matrix, per square centimeter
Q4149	Excellagen, 0.1 cc
Q4152	DermaPure per square centimeter
Q4158	Kerecis Omega3, per sq cm
Q4161	bio-ConneKt Wound Matrix, per square centimeter
Q4164	Helicoll, per square centimeter
Q4165	Keramatrix or Kerasorb, per square centimeter
Q4166	Cytal, per square centimeter
Q4167	Truskin, per square centimeter
Q4175	Miroderm, per square centimeter

Code	Description
Q4179	FlowerDerm, per square centimeter
Q4182	Transcyte, per square centimeter
Q4193	Coll-e-derm, per square centimeter
Q4195	PuraPly, per square centimeter
Q4196	PuraPly am, per square centimeter
Q4197	PuraPly xt, per square centimeter
Q4200	SkinTE, per square centimeter
Q4203	Derma-Gide, per square centimeter
Q4220	BellaCell HD or Surederm, per sq cm
Q4222	ProgenaMatrix, per sq cm
Q4226	MyOwn Skin, includes harvesting and preparation procedures, per sq cm
Q4238	Derm-Maxx, per sq cm
Modifiers	
JC	Skin substitute used as a graft
JD	Skin substitute not used as a graft

Related Information

There is no standard definition of "skin substitute". Products in this policy cover products that do not require US Food and Drug Administration (FDA) approval or clearance as well as a number of products cleared through the 510(k) pathway with a variety of FDA product codes. The FDA product codes that include these products are not limited to skin substitute products and may include other indications not related to wounds. The list of products named in this review is not a complete list of all commercially available products.

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.

The Women's Health and Cancer Rights Act (WHCRA) helps protect many women with breast cancer who choose to have their breasts rebuilt (reconstructed) after a mastectomy. Mastectomy

is surgery to remove all or part of the breast. This federal law requires most group insurance plans that cover mastectomies to also cover breast reconstruction. It was signed into law on October 21, 1998. The United States Departments of Labor and Health and Human Services oversee this law.

Benefit Application

Many states have mandates related to breast reconstruction that may impact the application of this policy.

Evidence Review

Description

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.

Background

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 by 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 individuals with compromised ability to heal. Second and third-degree burns are another indication in which artificial skin products may substitute for autografts 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.

BEAR (Bridge-Enhanced Anterior Cruciate Ligament Repair) Implant

The BEAR (bridge-enhanced anterior cruciate ligament repair) implant is a bovine decellularized extracellular matrix collagen-based scaffolding used in the treatment of anterior cruciate ligament repairs. It is considered an alternative to ACL reconstruction. It is indicated for those who are skeletally mature and 14 years of age or older with a complete rupture of the ACL, confirmed by MRI. Individuals must have an ACL stump attached to the tibia to construct the repair as sutures are arthroscopically placed on both sides of the ACL tear. The implant is 44mm x 22 mm in size. It is saturated with 10 ml of autologous blood and implanted through a mini-arthrotomy surgical procedure into the intercondylar notch to help form a fibrin clot, which inhibits synovial plasmin (enzyme) break down, and bridges the gap between the torn ends of

the ACL with the release of growth factors that will help stimulate ligament repair. The implant will be reabsorbed within eight weeks of implantation and replaced with native tissue which will remodel and strengthen over time to bring about healing of the torn ligaments. Proposed benefits are no donor site is required and there may be a potential for decreased post-traumatic osteoarthritis.

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, 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 individual 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, quality of life, and treatment-related morbidity. The RCT identified improved outcomes with the GraftJacket ADM allograft for rotator cuff repair. Although these results were positive, additional studies with a larger number of individuals are needed to evaluate 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 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 results in an improvement in the net health outcome.

Diabetic Lower-Extremity Ulcers

For individuals who have diabetic lower-extremity ulcers who receive AlloPatch, Apligraf, Dermagraft, Integra, mVASC, or TheraSkin, the evidence includes RCTs. Relevant outcomes are symptoms, change in disease status, morbid events, and quality of life. RCTs reporting complete wound healing outcomes with at least 12 weeks of follow-up have demonstrated the efficacy of AlloPatch (reticular ADM), Apligraf and Dermagraft (living cell therapy), Integra (biosynthetic), mVASC, and TheraSkin over the standard of care (SOC). 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, Integra, , mVASC, or TheraSkin, 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 individuals 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, DermACELL, Cytal, PriMatrix, and Oasis Wound Matrix, compared with current SOC or other advanced wound therapies. An RCT of Omega3 Wound (Kerecis) has been published and 2 larger RCTs are registered and reported as completed but have not been published. 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 quality of life. 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 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% to15% increase in healing) in subgroups of individuals with ulcer durations of 12 months or less or size of 10 cm or less. Additional studies with a larger number of subjects are 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 a 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 individuals 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 a small series (e.g., five individuals). 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 (i.e., Epicel, Integra Dermal Regeneration Template), the evidence includes RCTs. Relevant outcomes are 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 US 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.

BEAR (Bridge-Enhanced Anterior Cruciate Ligament Repair) Implant

For individuals who have a torn ACL who receive the BEAR implant, the evidence includes RCTs and systematic review of RCTs. Barnett (2021) and Murray (2020) both reported on the results of the BEAR II clinical trial which consisted of n=100 participants with complete ACL tear aged 13 to 35 years of age randomized 2:1 to either the BEAR implant (n=65) or autograft ACL reconstruction (n=35) with either a bone-patellar tendon-bone (BPTB) or hamstring autograft. Participants were blinded to treatment until after the 2 year follow-up visit. An independent examiner was blinded to the surgical side and group assignment when doing the arthrometer testing and physical examination until the end of each visit when effusion was assessed. Results demonstrated that the BEAR group had significantly higher International Knee Documentation Committee Subjective (IKDC) scores than the ACLR group, (P=.001) at 6 months postoperatively but at 1 and 2 years the differences between the groups was not statistically significant. The BEAR group had significantly better Knee injury and Osteoarthritis Outcome Score (KOOS) Symptoms scores than the ACLR group at one year (P=.009), however at 2 years eventhough the BEAR goup scores remained higher they were not statistically significant. The BEAR group had superior hamstring strength (P< .001) across postsurgical assessments (93% of the contralateral knee as compared with 59% in the ACLR group), which weak hamstrings have correlated.with future reinjury. Of note, in this study 33 of the 35 participants in the ACLR group used autograft hamstring tendons. These differences did not reduce the time to medical clearance for return to sports. Limitations of the study: Because the majority of the ACLR group autografts were from hamstring tendons BEAR outcomes with bone-patellar tendon-bone autografts cannot be made from this study. The participants were young in this study and so the results may not be extrapolated to an older population. Longer term follow-up beyond two years is needed to determine the durability of the implant. Murray reported that noninferiority criteria were met for both the IKDC Subjective Score (BEAR, 88.9 points vs. 84.8 points for ACLR and the side-to-side difference in anteroposterior (AP) knee laxity (BEAR, 1.61 mm; ACLR, 1.77 mm) at 2 year follow-up. A second ipsilateral ACL surgical procedure (P=.32) was required due to reinjury in 14% of the BEAR group compared to 6% of the ACLR group. The authors note that revision rates for similar populations have ranged from 10 to 28%. Limitations of the study included that only one surgeon in the study had performed the BEAR implant previous to the study and so if a learning curve was present, it may have been reflected in this early study. Saad Berreta, et al (2024) concluded in their systematic review that BEAR implants were similar in individual-reported

outcome measures compared to ACLR, but they may be associated with greater rates of failure, given re-rupture rates of up to 14 %.

Ongoing and Unpublished Clinical Trials

Some currently ongoing and unpublished trials that might influence this review are listed in **Table 1**.

Table 1. Summary of Key Trials

NCT No.	Trial Name	Planned Enrollment	Completion Date
Ongoing			
NCT05398341	A Prospective Cohort Post Market Registry Evaluating Outcomes of Bridge-Enhanced ACL Restoration (BEAR®)	750	Jan 2027
NCT03776162	BEAR - MOON: A Two Arm Non-Inferiority Randomized Clinical Trial Comparing ACL Repair With BEAR Device vs. Autograft Patellar Tendon ACL Reconstruction	200	May 2027
NCT05291169	A Randomized, Multicenter, Open Label Study Comparing Omeza Combination Therapy with Standard of Care to Standard of Care alone for Chronic Venous Leg Ulcers over the course of 4 weeks	110	Oct 2023
NCT05084183	An Adaptive, Randomized, Controlled Trial Evaluating the Effectiveness of PermeaDerm® (PD) as Compared to Mepilex Ag® Used as Standard of Care in the Treatment of Adult and Pediatric Partial Thickness Burns	68	Nov 2023
NCT05439746	Clinical Trial to Assess the Efficacy of Microlyte Matrix on the Healing of Surgically Created Partial Thickness Donor Site Wounds on Patients Requiring Split-thickness Skin Grafting	53	Jan 2024
NCT05506215	A Prospective, Multicenter, Open Label, Randomized, Controlled Clinical Study Evaluating the Effect of NovoSorb ® SynPath™ Dermal Matrix Compared to Standard of Care (SOC) In the Treatment of Nonresponsive, Chronic Diabetic Foot Ulcers.	138	Mar 2024
NCT05372809	Closure Obtained With Vascularized Epithelial Regeneration for DFUs With SkinTE®	100	Jun 2024

NCT No.	Trial Name	Planned Enrollment	Completion Date
NCT02587403[a]	A Randomized, Prospective Study Comparing Fortiva Porcine Dermis vs. Strattice Reconstructive Tissue Matrix in Patients Undergoing Complex Open Primary Ventral Hernia Repair	120	Feb 2024
NCT04927702	Assessment of Wound Closure Comparing Synthetic Hybrid-Scale Fiber Matrix (Restrata®) With Standard of Care in Treating Diabetic Foot Ulcers (DFU) and With Living Cellular Skin Substitute (Apligraf®) in Treating Venous Leg Ulcers (VLU)	170	Jul 2024
NCT06035536	A Multi-Center, Randomized Controlled Clinical Investigation Evaluating Wound Closure With Symphony™ Versus Standard of Care in the Treatment of Non-Healing Diabetic Foot Ulcers	120	Dec 2024
NCT05517902	A Phase 3 Multicenter, Single-Arm, Open-Label Study Evaluating the Safety, Tolerability and Efficacy of StrataGraft® Construct in Pediatric Subjects With Deep Partial Thickness (DPT) Thermal Burns	50	Jun 2025
NCT04090424	A Pivotal Study to Assess the Safety and Effectiveness of NovoSorb® Biodegradable Temporizing Matrix (BTM) in the Treatment of Severe Burn Skin Injuries	150	Dec 2025
NCT03394612	A Phase II, Prospective, Intra-patient Randomised Controlled, Multicentre Study to Evaluate the Safety and Efficacy of an Autologous Bio-engineered Dermo-epidermal Skin Substitute (EHSG-KF; denovoSkin) for the Treatment of Full-Thickness Defects in Adults and Children in Comparison to Autologous Split-thickness Skin Grafts (STSG)	20	Dec 2026
Unpublished			
NCT02322554	The Registry of Cellular and Tissue Based Therapies for Chronic Wounds and Ulcers	50,000	Jan 2020
NCT03935386[a]	A Prospective Randomized Clinical Trial Comparing Multi-layer Bandage Compression Therapy With and Without a Biologically Active Human Skin Allograft (Theraskin) for the Treatment of Chronic Venous Leg Ulcers	100	Dec 2020
NCT03589586[a]	An Open-Label Trial to Assess the Clinical Effectiveness of DermACELL AWM in Subjects With Chronic Venous Leg Ulcers	100	Jan 2021

NCT No.	Trial Name	Planned Enrollment	Completion Date
NCT03881254	A Multi-center, Randomized Controlled Clinical Trial Evaluating the Effects of SkinTE™ in the Treatment of Wagner One Diabetic Foot Ulcers	100	Jul 2021
NCT04198441	A Randomized, Multicenter, Open Label Study Comparing the Omeza® Products Bundle to Standard of Care for Chronic Venous Leg Ulcers and Chronic Diabetic Foot Ulcers	78	Dec 2021
NCT04257370[a]	An Open Label, Randomized Controlled Study to Compare Healing of Severe Diabetic Foot Ulcers and Forefoot Amputations in Diabetics With and Without Moderate Peripheral Arterial Disease Treated With Kerecis Omega3 Wound and SOC vs. SOC Alone	330	Oct 2022
NCT04537520[a]	Interventional Multi-Center Post Market Randomized Controlled Open-Label Clinical Trial Comparing Kerecis Omega3 Wound Versus SOC in Hard to Heal Diabetic Foot Wounds	180	Dec 2022
NCT04918784	Assessment of Wound Closure Comparing Synthetic Hybrid-Scale Fiber Matrix (Restrata®, Acera Surgical, Inc.) With Standard of Care in Treating Diabetic Foot Ulcer	46	Dec 2022
NCT05883098	Effectiveness of Supra SDRM® vs. Fibracol Plus Collagen in the Treatment of Diabetic Foot Ulcers: a Pilot Randomized Controlled Trial	30	Jun 2023

NCT: national clinical trial.

[a] Denotes industry-sponsored or cosponsored trial.

Practice Guidelines and Position Statements

The purpose of the following information is to provide reference material. Inclusion does not imply endorsement or alignment with the policy conclusions.

Guidelines or position statements will be considered for inclusion if they were issued by, or jointly by, a US professional society, an international society with US representation, or National Institute for Health and Care Excellence (NICE). Priority will be given to guidelines that are informed by a systematic review, include strength of evidence ratings, and include a description of management of conflict of interest.

National Institute for Health and Care Excellence

In 2023, the National Institute for Health and Care Excellence (NICE) 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."

In 2019, NICE published guidance on the ReCell system for treating skin loss, scarring, and depigmentation after burn injury.[72] The guidance recommended that additional research was needed to address the uncertainties regarding the potential benefits of ReCell.

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.[73]

In 2019, CMS reported that it is finalizing the proposal to continue the policy established in calendar year (CY) 2018 to assign skin substitutes to the low cost or high-cost group.[74] 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.

In 2022, CMS proposed changing the terminology of skin substitutes to "wound care management products", and to treat and pay for these products as incident to supplies under the Physician Fee Schedule (PFS) beginning on January 1, 2024. However, in November 2022, CMS posted this update on the process: "After reviewing comments on the proposals, we understand that it would be beneficial to provide interested parties more opportunity to comment on the specific details of changes in coding and payment mechanisms prior to finalizing a specific date when the transition to more appropriate and consistent payment and coding for these products will be completed. We plan to conduct a Town Hall in early CY 2023 with interested parties to address commenters' concerns as well as discuss potential approaches to the methodology for payment of skin substitute products under the PFS. We will take into account the comments we received in response to CY 2023 rulemaking and feedback received in association with the Town Hall in order to strengthen proposed policies for skin substitutes in future rulemaking."[75]

Regulatory Status

The U.S. Food and Drug Administration (FDA) does not refer to any single product or class of products as "skin substitutes". Products in this policy cover products that do not require FDA approval or clearance as well as a number of products cleared through the 510(k) pathway with a variety of FDA product codes. A large number of artificial skin and soft-tissue products are commercially available or in development. Commercial availability is not a reflection of a product's regulatory status. The following section summarizes a subset of commercially available skin and soft-tissue substitutes. This is not a complete list of all commercially available products. 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 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 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 Public Health Service (PHS) Act and 21 Code of Federal Regulations (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:

   i. 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

   ii. 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.

- 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.

- Cortiva (previously marketed as AlloMax Surgical Graft, and before that as NeoForm) is an acellular non-cross-linked human dermis allograft.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 singlelayer 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 US tissue banks. The allograft is minimally processed to remove the epidermal and dermal cells, while preserving dermal structure. Graftjacket Xpress is an injectable product.

- mVASC (MicroVascular Tissues, Inc.) is a microvascular tissue structural allograft made of small blood vessels and extracellular matrix, inherent non-viable cells, and associated biological signaling factors harvested from subcutaneous tissue of cadaveric human donors.
- TheraSkin (LifeNet Health) 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 the FDA.

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]

In March 2019, the FDA held an Advisory Committee meeting on breast implants, at which time the panel noted that while there is data about ADM for breast reconstruction, the FDA has not yet determined the safety and effectiveness of ADM use for breast reconstruction. The panel recommended that individuals are informed and also recommended studies to assess the benefit and risk of ADM use in breast reconstruction.[3]

In March 2021, FDA issued a Safety Communication to inform individuals, caregivers, and health care providers that certain ADM products used in implant-based breast reconstruction may have a higher chance for complications or problems. An FDA analysis of patient-level data from real-world use of ADMs for implant-based breast reconstruction suggested that 2 ADMs—FlexHD and Allomax—may have a higher risk profile than others.[4]

In October 2021, an FDA advisory panel on general and plastic surgery voted against recommending FDA approval of the SurgiMend mesh for the specific indication of breast reconstruction. The advisory panel concluded that the benefits of using the device did not outweigh the risks.[4]

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 3 fatty acids and is intended for use in burn wounds, chronic wounds, and other applications.
- Oasis Wound Matrix (Cook Biotech) is a collagen scaffold (extracellular matrix) derived from porcine small intestinal mucosa. In 2000, it was cleared for marketing by the 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.
- 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 the 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.
- 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.
- FDA Product codes: KGN, FTL, FTM.

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 the 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.
- 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.
- Epicel (Genzyme Biosurgery) is an epithelial autograft composed of an individual's own keratinocytes cultured ex vivo and is FDA-approved under a humanitarian device exemption (HDE) 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 individuals for whom split-thickness autografts may not be an option due to the severity and extent of their burns.
- 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 individuals 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 codes: FTM, PFC, OCE, ODS.

Autologous Cell Harvesting Device

- Recell (Avita Medical) was initially approved by the FDA in September 2018 under the PMA process (PMA BP170122). It is an autologous cell harvesting device indicated for the treatment of acute partial-thickness thermal burn wound when used by an appropriately-licensed healthcare professional at the patient's point of care to prepare autologous RES Regenerative Epidermal Suspension. The initial indication was for use in patients 18 years of age and older in combination with meshed autografting. Subsequently, indications were expanded to include direct application to acute partial-thickness thermal burn wounds in patients 18 years of age and older or application in combination with meshed autografting for acute full-thickness thermal burn wounds in pediatric as well as adult patients and for full-thickness skin defects after traumatic avulsion (e.g., degloving) or surgical excision (e.g., necrotizing tissue infection) or resection (e.g., skin cancer) in patients 15 years of age and older.
- FDA product code: QCZ.

Biosynthetic Products

- Biobrane/Biobrane-L (Smith and 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 tri-filament thread, which chemically binds collagen. Blood/sera clot in the nylon matrix, adhering the dressing to the wound until epithelialization occurs.
- 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 the 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 individual 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 the FDA through the 510(k) process for other indications.
- Integra Bilayer Wound Matrix (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.

- 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.
- FDA product codes: FRO, MDD, MGR.

Synthetic Products

- Suprathel (PolyMedics Innovations) is a synthetic copolymer membrane fabricated from a tri-polymer 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.

BEAR (Bridge-Enhanced Anterior Cruciate Ligament Repair) Implant

The BEAR (bridge-enhanced anterior cruciate ligament repair) implant received a De Novo classification in 2020, DEN200035. It is indicated for "skeletally-mature patients at least 14 years of age with a complete rupture of the ACL, as confirmed by MRI. Patients must have an ACL stump attached to the tibia to construct the repair."

FDA product code: QNI.

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History

Date	Comments
09/01/16	New policy, approved August 9, 2016. Add to Surgery section. Some bioengineered skin and soft tissue substitutes may be considered medically necessary when criteria are met. The use of bioengineered skin and soft tissue substitutes is investigational when criteria are not met. The effective date of this policy is December 1, 2016.
01/06/17	Updated effective date. The effective date of this policy has been updated to March 1, 2017.
02/17/17	Coding update. Added new HCPCS codes Q4166-Q4167 and Q4169-Q4175 with effective date 01/01/17. Removed HCPCS codes Q4137, Q4139, Q4151, and Q4163.
04/01/17	Annual Review, approved March 14, 2017. Policy updated with literature review through November 7, 2016; references 6, 19, 26, and 28-29 added; rationale revised and some references removed. Investigational products list updated: Microderm, TruSkin products added; MatriStem renamed Cytal; FortaDerm renamed PuraPly; Unite Biomatrix deleted (no longer available). AlloMend added to medically necessary statement for breast reconstructive surgery. AlloPatch added to medically necessary statement for diabetic lower-extremity ulcers. Criteria for human amniotic membrane

Date	Comments
	products for diabetic foot ulcers moved to policy 7.01.149. Section on laryngoplasty removed. Coding updated, removed HCPCS codes Q4119-Q4120 and Q4129 as they terminated as of 1/1/17. CPT code table removed.
06/20/17	Coding update, removed HCPCS codes Q4148, Q4155, and Q4156 as they are applicable to policy 7.01.149.
08/09/17	Coding update, removed HCPCS codes Q4131-Q4133, Q4145, and Q4154 from policy as they are addressed on a separate medical policy. Moved HCPCS codes Q4104 and Q4108 from investigational to medically necessary.
11/01/17	Interim Review, approved October 10, 2017.CellerateRX (CRXa) and Integra Omnigraft Dermal Regeneration Matrix removed from the investigational policy statement, may be considered medically necessary if criteria are met. The Evidence Review section was reformatted.
12/01/17	Minor update; added DermACELL which was inadvertently left off of policy.
05/01/18	Annual Review, approved April 3, 2018. Policy updated with literature review through November 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.
01/01/19	Coding updated, added new HCPCS codes Q4193, Q4195, Q4196, Q4197, Q4200, Q4201, Q4202, Q4203, and Q4204 new codes effective 1/1/19).
02/01/19	Minor coding updates, Q4102 moved to the "Medically Necessary (Eligible for Coverage)" section. Minor formatting edits.
04/01/19	Annual Review, approved March 19, 2019. Policy updated with literature review through December 2018; references 28 and 43 added. Policy statements unchanged. Added HCPCS codes Q4179 and Q4182 to the "Investigational (Not Eligible for Coverage)" section. Removed HCPCS codes Q4138, Q4140, Q4153, Q4157, Q4159, Q4160, Q4169-Q4171, Q4173, Q4174, Q4201, and Q4202.
01/01/20	Coding update, removed HCPCS code Q4172 as it was terminated 1/1/19.
03/01/20	Coding update, removed HCPCS code Q4150 and Q4204 as they are applicable to a separate policy. Added HCPCS codes A6460 and A6461. Added new HCPCS codes Q4220, Q4222, and Q4226 (new codes effective 10/1/19).
04/01/20	Annual Review, approved March 3, 2020. Policy updated with literature review through November 2019; references added. Policy statements unchanged.
06/25/2020	Coding update. Added HCPCS code Q4238 under investigative section.
07/31/20	Delete policy, approved July 14, 2020. This policy (7.01.113) is replaced with 7.01.582.
08/01/20	New policy, approved July 14, 2020. Policy replaces 7.01.113. Policy statements remain unchanged.

Date	Comments
11/01/20	Coding update, Added HCPCS codes C1849, C9354, C9356, C9358, C9360, C9363 and C9364.
02/01/21	Correction: CPT Q4104 was incorrectly designated as medically necessary and CPT Q4114 was incorrectly designated as investigational. CPT Q4104 is now correctly designated as investigational and CPT Q4114 is now correctly designated as medically necessary.
04/01/21	New policy, approved March 9, 2021. Policy replaces 7.01.582 Bioengineered Skin and Soft Tissue Substitutes. Policy updated with literature review through December 6, 2020; references added. Products added to investigational list. Policy statements unchanged. HCPCS Q4108 changed from medically necessary to investigational.
12/01/21	Coding update, Removed HCPCS codes Q4101, Q4102, Q4105, Q4106, Q4107, Q4114, Q4116, Q4122 and Q4128.
01/01/22	Coding update, Added HCPCS codes A2002, A2003, A2004, A2005, A2006, A2007, A2008, A2009 and A2010.
2/01/22	Coding update. Removed HCPCS code A2003.
04/01/22	Annual Review, approved March 7, 2022. Policy updated with literature review through December 17, 2021; references added. Regulatory status section updated with information on safety of ADM products used in implant-based breast reconstruction. Policy statements unchanged. Added HCPCS A2001 for InnovaMatrix AC as it was incorrectly applied to 7.01.583 (new code effective 1/1/22). Added new HCPC codes A2011, A2012, A2013, & A4100. Added products InnovaMatrix FX, and Supra SDRM.
11/01/22	Coding update. Added HCPCS codes A2014, A2015, A2016, A2017 and A2018. Changed the wording from "patient" to "individual" throughout the policy for standardization.
01/01/23	Coding update. Added term date to HCPC code C1849.
04/01/23	Annual Review, approved March 6, 2023. Policy updated with literature review through December 5, 2022; references added. Added ReCell to list of investigational products. Policy statements otherwise unchanged. Removed Keroxx from investigational section as it is addressed in related policy, 7.01.583. Removed new code date details from HCPC codes A4100 & A2001-A2013. Added new HCPC codes A2019, A2020, and A2021. Added product names Kerecis, AC5, and NeoMatriX.
10/01/23	Coding update. Added new HCPCS codes A2022-A2025.
04/01/24	Coding Update. Added new HCPCS code A2026.
06/01/24	Annual Review, approved May 24, 2024. Policy updated with literature review through November 13, 2023; references added. mVASC and TheraSkin added to medically necessary statement for diabetic lower-extremity ulcers. Several products added to investigational list.
10/1/24	Coding update. Added new HCPCS codes A2027, A2028, A2029.

Date	Comments
01/01/25	Coding update, added new CPT codes 15011-15018. Minor update to related policy. 2.01.16 was replaced with 2.01.543 Recombinant and Autologous Platelet-Derived Growth Factors for Wound Healing and Other Non-Orthopedic Conditions.
04/01/25	Policy 7.01.582 Bioengineered Skin and Soft Tissue Substitutes reinstated, approved March 11, 2025. Policy replaces 7.01.113 Bioengineered Skin and Soft Tissue Substitutes, effective July 3, 2025, following 90-day provider notification. Added new HCPCS codes A2030, A2031, A2032, A2033, A2034. BEAR (bridge-enhanced anterior cruciate ligament repair) implant added to list of investigational bioengineered tissue substitutes used in conjunction with anterior cruciate ligament repair. Added HCPCS C1763.
06/01/25	Coding update. Added HCPCS code C9353.

Scope: Medical policies are systematically developed guidelines that serve as a resource for Company staff when determining coverage for specific medical procedures, drugs or devices. Coverage for medical services is subject to the limits and conditions of the member benefit plan. Members and their providers should consult the member benefit booklet or contact a customer service representative to determine whether there are any benefit limitations applicable to this service or supply. This medical policy does not apply to Medicare Advantage.