Corporate Medical Policy

Skin and Soft Tissue Substitutes

File Name: skin_and_soft_tissue_substitutes
Origination: 1/1994
Last Review: 8/2023

Description of Procedure or Service

For use of amniotic membrane products, this policy only addresses usage in wounds and burns. This policy does not address the use of amniotic products for ophthalmic indications. Please see related policy for ophthalmic indications.

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 products can differ in a number of ways, including as species source (human, bovine, porcine), tissue source (e.g. dermis, pericardium, intestinal mucosa), additives (e.g. antibiotics, surfactants), hydration (wet, freeze dried), and required preparation (multiple rinses, rehydration).

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

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.

The preferred outcomes for the healing of lower-extremity ulcers and burn wounds are the percentage of patients with complete wound healing and the time to complete wound healing. The percentage of patients with 50% wound healing and time to 50% wound healing have also been considered appropriate outcomes for these conditions. The percent change in wound area at 4 weeks is predictive of complete healing at 12 weeks in patients with diabetic foot ulcers. Thus, minimal improvement at 30 days can be considered as an indicator that a wound is unlikely to heal in patients with comorbidities known to affect wound healing.

Peripheral nerve injuries may occur as a result of trauma or acute compression. The nerve injury may result in demyelination and/or axonal degeneration, which can disrupt sensory function, motor function or both in the injured nerve. Several methods of nerve grafting have been investigated when a large gap exists between the proximal and distal ends of the injured nerve. The use of autologous nerve grafts for bridging gaps in nerve continuity is the gold standard for nerve repair, however it requires the sacrifice of healthy nerves. Nerve allograft transplantation from cadavers offers an alternative without the morbidities associated with nerve autografts, but these grafts require appropriate immunosuppression. The limitations of nerve autografting and allografting have led to the engineering of processed, acellular nerve allografts and nerve

guidance conduits. Acellular nerve grafts are processed to remove antigenic factors such as Schwann cells and myelin to reduce immunogenicity, while retaining the natural basement membrane and three-dimensional extra-cellular matrix to guide axonal regeneration. Nerve conduits, also known as nerve tubulization, involves the use of nonabsorbable or absorbable single-lumen tubes, designed to bridge the gap of a sectioned nerve. The tube serves to protect the nerve during nerve regeneration and guide the regenerating axons to the distal nerve stump. A closed tube system may also allow for accumulation of neurotropic factors.

Other situations in which bioengineered skin products might substitute for living skin grafts include certain postsurgical states (e.g., breast reconstruction) in which skin coverage is inadequate for the procedure performed, or for surgical wounds in patients with compromised ability to heal. Second- and third-degree burns are another indication in which artificial skin products may substitute for auto- or allografts. Certain primary dermatologic conditions that involve large areas of skin breakdown (e.g., bullous diseases) may also be conditions in which artificial skin products can be considered as substitutes for skin grafts. Acellular dermal matrix 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.

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

Fresh amniotic membrane contains collagen, fibronectin, and hyaluronic acid, along with a combination of growth factors, cytokines, and anti-inflammatory proteins such as interleukin-1 receptor antagonist. There is evidence that the tissue has anti-inflammatory, antifibroblastic, and antimicrobial properties. HAM is considered nonimmunogenic and has not been observed to cause substantial immune response. It is believed that these properties are retained in cryopreserved HAM and dehydrated HAM products, resulting in a readily available tissue with regenerative potential. In support, one d-HAM product has been shown to elute growth factors into saline and stimulate the migration of mesenchymal stem cells both in vitro and in vivo.

HAM is an established treatment for corneal reconstruction and is being evaluated for the treatment of various conditions, including skin wounds, burns, leg ulcers, and prevention of tissue adhesion in surgical procedures. Additional indications studied in preclinical models include tendonitis, tendon repair, and nerve repair. The availability of HAM opens the possibility of regenerative medicine for a wide variety of conditions.

Related policies:
Amniotic Membrane and Amniotic Fluid Injections for Ophthalmic Indications
Growth Factors in Wound Healing
Meniscal Allograft and Collagen Meniscus Implants
Orthopedic Applications of Stem Cell Therapy
Plugs for Fistula Repair
Breast Surgeries
Facility Billing Requirements

******Note: This Medical Policy is complex and technical. For questions concerning the technical language and/or specific clinical indications for its use, please consult your physician.***

Policy

BCBSNC will provide coverage for skin and soft tissue substitutes when it is determined to be medically necessary because the medical criteria and guidelines shown below have been met.

Benefits Application

This medical policy relates only to the services or supplies described herein. Please refer to the Member's Benefit Booklet for availability of benefits. Member's benefits may vary according to benefit design; therefore member benefit language should be reviewed before applying the terms of this medical policy.

When Skin and Soft Tissue Substitutes are covered

Breast reconstructive surgery	
Criteria:	**Skin and Soft Tissue Substitutes:**
Products may be considered medically necessary when used for breast reconstructive surgery.	AlloDerm® AlloMend® Cortiva® [AlloMax™] DermACELL™ DermaMatrix™ FlexHD® FlexHD® Pliable™ Graftjacket®

Diabetic ulcers	
Criteria:	**Skin and Soft Tissue Substitutes:**
Products may be considered medically necessary for treatment of diabetic lower-extremity ulcers if **all** criteria are met: • Chronic • Noninfected • Full thickness • Lower extremity	AlloPatch® AmnioBand® Membrane Apligraf® (limited to no more than 4 weekly applications per wound) Biovance® Dermagraft® (limited to no more than 8 weekly applications per wound) EpiCord® Epifix® (limited to no more than 5 weekly applications per wound) GrafixCore™ or GrafixPrime™ Integra® Omnigraft Dermal Regeneration Matrix [Omnigraft] Integra Flowable Wound Matrix PuraPly®

Venous insufficiency ulcers	
Criteria:	**Skin and Soft Tissue Substitutes:**
Products may be considered medically necessary for treatment of venous insufficiency ulcers if **all** criteria are met: • Chronic • Noninfected • Partial- or full-thickness • Lower-extremity • Not adequately responded to a 1-month period of conventional ulcer therapy.	Oasis™ Wound Matrix Apligraf®

Dystrophic epidermolysis bullosa	
Criteria:	**Skin and Soft Tissue Substitutes:**
Product may be considered medically necessary for treatment of mitten-hand deformity in dystrophic epidermolysis bullosa provided in accordance with the humanitarian device exemption (HDE) specifications of the U.S. Food and Drug Administration (FDA) when standard wound therapy has failed. Humanitarian Device Exemption (HDE)	OrCel™

2nd Degree Burns	
Criteria:	**Skin and Soft Tissue Substitutes:**
Products may be considered medically necessary for treatment of 2nd degree burns if provided in accordance with the specifications of the HDE, premarket approval by the FDA, or American Association of Tissue Banks. American Association of Tissue Banks FDA Tissue & Tissue Products FDA Premarket Approval (PMA)	ActaShield™* Affinity™* AlloDerm® AlloPatch® AmnioBand® AmnioFix®* AmnioMatrix®* Amnioshield®* Aongen™ Collagen Matrix* Architect®* Aquacel®* Atlas Wound Matrix* Avagen Wound Dressing* Biobrane®* Bio-connekt®* Biovance® Clarix™* Collaguard®* CollaSorb™*

	CollaWound™ * Collieva™* Collexa® * Coreleader Colla-Pad * Cytal®* DermaCell® Dermadapt™* DermaMatrix™ DermaPure™* Dermavest™* DressSkin * EndoForm™* Epicel®* EpiFix® Excellagen * EZ Derm®* FlexHD® FortaDerm™* GammaGraft™* GraftJacket™ Grafix®* Helicoll™* Hyalomatrix®* Integra® Bilayer Wound Matrix* Integra Dermal Regeneration Template™ LTM Wound Dressing* Kerecis* (formerly known as MariGen™*) MatriStem® UBM* Matrix Collagen Wound Dressing* Maxxeus™* Medline Collagen Wound Dressing* MicroMatrix* Neox®* NuShield™* Oasis™ Burn Matrix * OrCel™ Primatrix™* PuraPly™* ReadiGraft®* ReCell®* Revitalon™* SIS Wound Dressing* SS Matrix™ * Stimulen™* StrataGraft® Suprathel®* Talymed®* TheraForm™* TheraSkin®* TransCyte™* Unite® Biomatrix* *Products only approved for burn indications

3rd Degree Burns	
Criteria:	**Skin and Soft Tissue Substitutes:**
Products may be considered medically necessary for treatment of 3rd degree burns if provided in accordance with the specifications of the HDE, premarket approval by the FDA, or American Association of Tissue banks. American Association of Tissue Banks FDA Tissue & Tissue Products FDA Premarket Approval (PMA)	Epicel® (for the treatment of deep dermal or full-thickness burns comprising a total body surface area ≥30%)* Integra Dermal Regeneration Template™ (for the treatment of life threatening burn injuries)* ReCell® (in combination with meshed autografting for acute full-thickness thermal burn wounds)* TransCyte™ (for the treatment of full-thickness burn wounds in patients prior to autograft placement)* *Products only approved for burn indications

Dural Reconstruction/Repair	
Criteria:	**Skin and Soft Tissue Substitutes:**
Products may be considered medically necessary for dural reconstruction and/or repair in spinal and/or cranial surgery (i.e., tumor resection, Chiari malformation decompression or trauma) when it is determined that a graft is needed for dural closure.	FDA approved indications

When Skin and Soft Tissue Substitutes are not covered

Skin and soft tissue substitutes are not covered when application site is infected or member has an allergy to the product.

All other skin and soft tissue substitutes are considered investigational for applications not specified in **When Skin and Soft Tissue Substitutes Are Covered.**

The Plan may compare the cost-effectiveness of alternatives when determining which products will be covered.

For ophthalmic indications, please see related policy "Amniotic Membrane and Amniotic Fluid Injections for Ophthalmic Indications."

The following list of products is considered investigational for all indications (may not be all-inclusive):
AlloSkin™
Amnio-maxx™
Amniocore™

Amniocyte plus™
AmnioExcel®
Amniorepair™
Amniotext™
ArthroFlex™ (FlexGraft)
Avance™ Nerve Graft
AxoGuard® Nerve Connector (Axogen/AxioGuard®)
BioDexCel®
BioDfence™
Bionextpatch®
Carepatch®
Cogenex
CollaCare®
CollaCare® Dental
Collamend™
Conexa™
Corecyte™
Coretext™
CorMatrix®
Corplex™
Cryo-cord™
Cymetra®
Dermacyte®
Derm-maxx™
DermaSpan™
ENDURAgen™
ExpressGraft™
FlexiGraft®
HMatrix®
MatriDerm®
Mediskin®
MemoDerm™
Miroderm® biologic wound matrix
NeoForm Dermis™
NeuraGen™ Nerve Guide
NeuroMatrix™
NeuroMend™
NeuraWrap™ Nerve Protector
Pelvicol®/Pelvisoft®
Permacol™
Phasix™
Polycyte™
Procenta®
Puros® Dermis
RegenePro™
Repliform®
Repriza™
Strattice™
Surfactor®
SurgiMend®
TenoGlide™
TenSIX™ Acellular Dermal Matrix
TissueMend
TruSkin™
Veritas® Collagen Matrix
Xcellerate®
XCM Biologic/Medeor Matrix XenMatrix™ AB

Policy Guidelines

Breast Reconstruction

For individuals who are undergoing breast reconstruction who receive allogeneic ADM products, the evidence incudes a randomized controlled trial (RCT) and systematic reviews. Relevant outcomes are symptoms, morbid events, functional outcomes, quality of life, and treatment-related morbidity. A recent systematic review found no difference in overall complication rates with ADM allograft compared to 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, including but not limited to when the use of ADM allows a single-stage reconstruction, the available evidence may be considered sufficient to permit conclusions about health outcomes that may inform patient decision making about reconstruction options. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome. Clinical input indicated that the various acellular dermal matrix (ADM) products used in breast reconstruction have similar efficacy. The products listed are those that have been identified for use in breast reconstruction. Additional ADM products may become available for this indication.

Tendon Repair

For individuals who are undergoing tendon repair who receive Graftjacket ADM, the evidence incudes 1 RCT. Relevant outcomes are symptoms, morbid events, functional outcomes, quality of life, and treatment-related morbidity. One RCT identified found improved outcomes with Graftjacket ADM allograft for rotator cuff repair. Although these results were positive, additional study with a larger number of patients is needed to evaluate consistency of the effect. The evidence is insufficient to determine the effects of the technology on health outcomes.

Surgical Repair of Hernias or Parastomal Reinforcement

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

Diabetic Lower-Extremity Ulcers

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

For individuals who have diabetic lower-extremity ulcers who receive other ADM products, cryopreserved skin allograft, or xenogenic skin substitutes, the evidence includes RCTs. Relevant outcomes are disease-specific survival, symptoms, change in disease status, morbid events, and quality of life. Additional study with a larger number of subjects is needed to compare the effect of other human ADM products, cryopreserved skin allograft (TheraSkin) and xenogenic skin substitutes (eg, Oasis Wound Matrix, PriMatrix) to the standard of care. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have non-healing diabetic lower-extremity ulcers who receive a patch or flowable formulation of HAM (ie, AmnioBand Membrane, Biovance, EpiFix, Grafix), the evidence includes RCTs. The relevant outcomes are symptoms, morbid events, functional outcomes, and QOL. The RCTs evaluating amniotic and placental membrane products for the treatment of non-healing (<20% healing

with ≥2 weeks of standard care) diabetic lower-extremity ulcers have compared HAM with standard care or with an established advanced wound care product. These trials used wound closure as the primary outcome measure, and some used power analysis, blinded assessment of wound healing, and ITT analysis. For the HAM products that have been sufficiently evaluated (ie, AmnioBand Membrane, Biovance, EpiCord, EpiFix, Grafix), results have shown improved outcomes compared with standard care, and outcomes that are at least as good as an established advanced wound care product. Improved health outcomes in the RCTs are supported by multicenter registries. The evidence is sufficient to determine that the technology results in a meaningful 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 disease-specific survival, symptoms, change in disease status, morbid events, and quality of life. RCTs have demonstrated the efficacy of Apligraf living cell therapy and xenogenic Oasis Wound Matrix over the standard of care. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

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

For individuals who have lower-extremity ulcers due to venous insufficiency who receive a patch or flowable formulation of HAM, the evidence includes two RCTs. The relevant outcomes are symptoms, morbid events, functional outcomes, and QOL. The evidence on HAM for the treatment of lower-extremity venous ulcers includes two multicenter RCTs with EpiFix. One RCT reported larger percent wound closure at four weeks but the percentage of patients with complete wound closure did not differ between EpiFix and the SOC. A second multicenter RCT reported a significant difference in complete healing at 12 weeks, but the interpretation is limited by methodologic concerns. Well-designed and well-conducted RCTs that compare HAM with the SOC for venous insufficiency ulcers are needed. The evidence is insufficient to determine the effects of the technology on health outcomes.

Dystrophic Epidermolysis Bullosa

For individuals who have dystrophic epidermolysis bullosa who receive OrCel, the evidence includes case series. Relevant outcomes are disease-specific survival, symptoms, change in disease status, morbid events, and quality of life. OrCel was approved under a humanitarian drug exemption for use in patients with dystrophic epidermolysis bullosa undergoing hand reconstruction surgery, to close and heal wounds created by the surgery, including those at donor sites. Outcomes have been reported in small series (eg, 5 patients). The evidence is insufficient to determine the effects of the technology on health outcomes.

Deep Dermal Burns

For individuals who have deep dermal burns who receive bioengineered skin substitutes (ie, 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, there are few skin substitutes approved, and the evidence is limited for each product. Epicel (living cell therapy) has received 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 a meaningful improvement in the net health outcome.

Peripheral Nerve Repair
There is insufficient scientific evidence in the peer-reviewed medical literature to support the efficacy of either acellular, allogeneic nerve grafts or nerve conduits for bridging defects resulting from peripheral nerve injuries. The published literature for processed, acellular nerve grafts consists of small case series and registry data, and for nerve conduits, a small randomized trial and small case series. Study limitations include non-standardized assessment of clinical outcomes, lack of comparator groups, small group size and lack of long-term follow-up.

Billing/Coding/Physician Documentation Information

This policy may apply to the following codes. Inclusion of a code in this section does not guarantee that it will be reimbursed. For further information on reimbursement guidelines, please see Administrative Policies on the Blue Cross Blue Shield of North Carolina web site at www.bcbsnc.com. They are listed in the Category Search on the Medical Policy search page.

Applicable service codes:
Application of skin replacements and skin substitutes is reported with CPT codes 15040-15278.
Nerve repair with allograft is reported with CPT codes 64910, 64912, 64913
Codes 15040-15261 are specific to autografts and tissue-cultured autografts.
Codes 15271-15278 are specific to skin substitute grafts.
Code 15777 is a specific add-on code for use of these materials as an implant.

There are specific HCPCS codes for some of these products. If no specific HCPCS code exists for the product, an unlisted code such as Q4100 would be used.

HCPCS modifiers:
JC: skin substitute used as a graft
JD: skin substitute not used as a graft

Product specific codes:
Q4100 - Q4108, Q4110 - Q4118, Q4121 - Q4128, Q4130, Q4132, Q4133 - Q4143, Q4145, Q4148, Q4150, Q4151, Q4153 - Q4157, Q4159, Q4160, Q4162, Q4163, Q4168 - Q4171, Q4173, Q4174, Q4177, Q4178, Q4181, Q4183 - Q4192, Q4194, Q4198, Q4199, Q4201, Q4202, Q4205, Q4206, Q4208 – Q4222, Q4224 – Q4242, Q4244 – Q4250, Q4254-Q4271, Q4279, Q4285 - Q4299, Q4300 - Q4304, C1832, C9349, C9352 - C9356, C9358, C9360, C9361, C9363, C9364, A2001- A2025, A4100

Billing for skin substitute application procedures are required to also include the appropriate high cost or low cost skin substitute products.

BCBSNC may request medical records for determination of medical necessity. When medical records are requested, letters of support and/or explanation are often useful, but are not sufficient documentation unless all specific information needed to make a medical necessity determination is included.

Scientific Background and Reference Sources

Consultant Review - 1/94

Physician Advisory Group - 3/95

BCBSA Medical Policy Reference manual (Growth Factors for Wound Healing S9055)

MPAG Review - 3/99

Specialty Matched Consultant Advisory Panel - 10/2000

Medical Policy Advisory Group - 10/2000

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Schonfeld WH, Villa KF, Fastenau JM, Mazonson PD, Falanga V. An economic assessment of Apligrar (Graftskin) for the treatment of hard-to-heal venous leg ulcers. Wound Repair Regen. 2000 Jul-Aug;8(4):251-7.

Specialty Matched Consultant Advisory Panel - 9/2002

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Specialty Matched Consultant Advisory Panel - 7/2004

Specialty Matched Consultant Advisory Panel - 6/2006

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Specialty Matched Consultant Advisory Panel - 6/2008

Senior Medical Director Review - 1/15/2009

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Medical Director review 5/2011

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Policy Implementation/Update Information

1/94	Original Policy Issued.
3/95	Reviewed: Remains investigational

9/95	Reaffirmed: Remains investigational
10/96	Reaffirmed
3/99	Reaffirmed
8/99	Reformatted, Description of procedure changed, Medical Term Definitions added.
10/00	Specialty Matched Consultant Advisory Panel review. No change recommended in criteria. System coding changes. Medical Policy Advisory Group. No change in criteria. Approve.
10/02	Name changed from Keratinocyte Allografts to Bioengineered Skin for the Treatment of Skin Ulcers. Description section expanded. Changed from investigational to covered for certain indications. Specialty Matched Consultant Advisory Panel review.
4/03	Date of Last Review changed to 10/2002 when review was done by the Specialty Matched Consultant Advisory Panel and policy was updated. Date of Next Review changed to 2 years later - 10/2004.
9/03	Added Dermagraft as a covered product with specific criteria. Sources added. Added codes J7342 and J7350. Removed code 15350.
12/03	Billing/Coding section updated for consistency.
9/9/04	Policy name changed from Bioengineered Skin for the Treatment of Skin Ulcers to Bioengineered Skin. Specialty Matched Consultant Advisory Panel review 7/14/2004. Added information in Description of Procedure or Service section to include burns. Added statement in Policy section indicating "BCBSNC will provide coverage for bioengineered skin for the treatment of burns when it is determined to be medically necessary because the medical criteria and guidelines shown below have been met." In section regarding When Bioengineered Skin is Covered, added "C. Bioengineered skin may be considered medically necessary in the treatment of burns when all of the following criteria are met. 1.When the product has full FDA approval. and 2.When the product is used within the scope of the FDA indications." Removed reference to Biobrane in that it is a biosynthetic wound dressing for burns and does not apply to this policy. Added HCPCS code Q0183. References added. Notification given 9/9/2004. Effective date 11/11/2004.
1/6/05	First quarter 2005 HCPCS codes J7343, J7344 added to Billing/Coding section of policy.
1/5/06	Added new 2006 CPT codes 15150, 15151, 15152, 15155, 15156, 15157, 15170, 15171, 15175, 15176, 15300, 15301, 15320, 15321, 15330, 15331, 15335, 15336, 15340 15341, 15360, 15361, 15365, 15366,15420, 15421, 15430, 15431, and HCPCS code J7341 to "Billing/Coding" section. Deleted CPT codes 15342 and 15343.
7/24/06	Specialty Matched Consultant Advisory Panel review 6/20/2006. Updated "Description of Procedure or Service" section to include information regarding specific products. Added "rare skin conditions" to the "Policy" statement. The following changes were made to the "When Bioengineered Skin is Covered" section. Removed the statement "The ulcers are not infected". Changed the wording regarding "standard wound care" to "clinically appropriate therapy". Under B. changed statement from indicating 4 applications to "Applications will be limited to no more than 6 pieces per wound when the above criteria are met." Added additional indication under C. "rare skin conditions such as recessive dystrophic epidermolysis bullosa". Added the following product names under "When Bioengineered Skin is Not Covered"; "EZ Derm®, Mediskin®, Alloderm®, Oasis®,

Surgis®, Acticoat®, and GraftJacket. Removed deleted HCPCS code Q0183. References added.

1/17/07 Added the following new 2007 HCPCS codes, J7345 and J7346 to "Billing/Coding" section. Deleted HCPCS code, J7350.

4/23/07 Added CPT codes 15400 and 15401 to "Billing/Coding" section.

01/14/08 Added information to the "Description" section regarding "Primatrix™ (formerly known as DressSkin) and TissueMend®". "Primatrix, DressSkin, and TissueMend" added to "Key Words". Added new 2008 HCPCS codes; "J7347, J7348, and J7349" to "Billing/Coding" section. Removed HCPCS code J7345.

7/28/08 Specialty Matched Consultant Advisory Panel review 6/23/08. Added "Celaderm® is an allograft that contains active keratinocytes made from epithelial cells of the foreskin. Although metabolically active they are not capable of proliferating. The product has not received FDA approval at this time." to the "Description section. Added to "Alloderm" under the "When Not Covered" section "is considered investigational for all indications including but not limited to breast reconstruction and recurrent hernia repair." and added "Celladerm®" to the list. Updated the rationale in the "Policy Guidelines" section. References added.

1/5/09 Added new HCPCS codes: Q4100, Q4101. Q4102, Q4103, Q4104, Q4105, Q4106, Q4107, Q4108, Q4109, Q4110, Q4111, Q4112, Q4113, and Q4114 to the "Billing/Coding" section. Removed deleted HCPCS codes: J7340, J7341, J7342, J7343, J7344, J7346, J7347, J7348, and J734.

2/2/09 Reviewed with Senior Medical Director 1/20/09. The investigational status of Alloderm for the use in breast reconstruction has changed and now may be medically necessary when specific criteria is met. "Policy" statement updated. Added the following statement to the "Description" section; "Alloderm has been researched as a support mechanism for breast reconstruction, difficult hernia repairs and after parotidectomy to avoid Frey's syndrome." Added the following indications to the "When Covered" section: "C. Alloderm (an acellular allograft) may be considered medically necessary for use in breast reconstruction surgery." Reference to breast reconstruction with Allograft was removed in the "When Not Covered" section and reworded to indicate; "E. Alloderm® is considered investigational for all indications except those addressed in the "When Covered" section including but not limited to parotidectomy and recurrent hernia repair or other major abdominal cavity reconstruction." Revised "Policy Guidelines" section and added the following statement; "The use of Alloderm in breast reconstruction can be particularly useful in women who have insufficient tissue expander or implant coverage by the pectoralis major muscle and additional coverage is require, or when there is viable but compromised or thin post-mastectomy skin flaps that are at risk of dehiscence or necrosis or when the infra-mammary fold and lateral mammary folds have been undermined during mastectomy and re-establishment of these landmarks are needed.". References added.

8/3/09 Added new HCPCS codes Q4115 and Q4116 to "Billing/Coding" section. (btw)

10/26/09 Added the following statement to the "Description" section; "**Note: This Medical Policy is complex and technical. For questions concerning the technical language and/or specific clinical indications for its use, please consult your physician. Changed the wording in the "When Covered" section under B. Dermagraft from "Applications will be limited to no more than 6 pieces per wound when the above criteria are met." to "Applications will be

limited to no more than 8 weekly applications per wound when the above criteria are met." Reviewed with Senior Medical Director 9/16/09. References added. (btw)

6/22/10 Policy Number(s) removed. (amw)

10/26/10 Added new product information to "Description" section for Cymetra®, C-Qur™, Avaulta Plus™, Collamend, Cuffpatch™, DermaMatrix Acellular Dermis, E-Z Derm™, Integra™ Matrix Wound Dressing, Mediskin®, Oasis™, OrthADAPT™, Pelvicol®, Pelvisoft®, PriMatrix, Strattice™, Surgimend®, Surgisis®, Unite™. These products have been added to the "What is not Covered" section. Updated references. Specialty Matched Consultant Advisory Panel review 9/2010. Added HCPCS codes C9358, C9360, C9363 and C9364 to Billing/Coding section. (mco)

1/4/11 Added new product information for Matristem®, Hyalomatrix®, Endoform Dermal Template™, and Theraskin®. Added the following codes to reflect the 2011 HCPCS coding updates: C9367, G0440, G0411, Q4117, Q4118, Q4119, Q4120, and Q4121. Deleted code Q4109(mco)

1/18/11 Senior Medical Director review 1/2011. Changed title of policy from "Bioengineered Skin" to "Bioengineered Skin and Tissue." Added new product information to "Description" section for CorMatrix® pericardial patch and Veritas® Collagen Matrix. The products were also added to the "When not Covered" section. References updated. Reformatted the "When not Covered" section. (mco)

5/24/11 Medical Director review 5/2011. Under "When Covered" section A-1, replaced the word "venous" with "vascular" and in section A-1-d, added "including restoration by vascular bypass grafting, stenting or other means." In section 2, deleted the words "diabetic" from the criteria for neuropathic foot ulcers. (mco)

7/01/11 Added new code to "Billing/Coding" section: C9365. Added new product to "Not Covered" section: Oasis Ultra Tri-Layer Matrix. (mco)

11/8/11 Specialty Matched Consultant Advisory Panel review 9/2011. Updated "Description" section. "When Covered" section re-formatted. Added new products to the "When not Covered" section and alphabetized product list. FDA indications provided for all products listed in policy. Added C9354 to "Billing/Coding" section. References updated. (mco)

12/30/11 Deleted the following codes from "Billing/Coding" section: 15170, 15171, 15175, 15176, 15330, 15331, 15335, 15336, , 15340, 15341, 15360, 15361, 15365, 15366, 15400, 15401, 15420, 15421, 15430, 15431, C9365, G0440, G0441. Added the following codes to "Billing/Coding" section: 15271, 15272, 15273, 15274, 15275, 15276, 15277, 15278, 15777, C9366, Q4122, Q4123, Q4124, Q4125, Q4126, Q4127, Q4128, Q4129, Q4130. New codes will be effective 1/1/2012. Added new product "Epifix®" to "When not Covered" section. (mco)

3/20/12 New policy criteria as follows: "BCBSNC will provide coverage for Apligraf® bioengineered skin, **Oasis® Wound Matrix** and Dermagraft® for the treatment of skin ulcers when it is determined to be medically necessary because the medical criteria and guidelines shown below have been met." "When Covered" section revised to state, "A.The applications of Apligraf® and ~~Dermagraft®~~ **Oasis Wound Matrix®** are covered for the treatment of vascular ulcers when all of the following criteria are met: 1.When used in conjunction with standard therapy, 2. The ulcers have not healed by at least 50% after clinically appropriate therapy, 3.The ulcers intended for treatment are partial or full

thickness venous stasis ulcers, and 4.The patient has adequate arterial blood supply to the involved limb, including restoration by vascular bypass grafting, stenting or other means." "When not Covered" section updated to include the following statements: "B.Oasis® Wound Matrix is contraindicated in the following situations: 1.The patient has a known allergy to porcine collagen 2.For any indications other than those listed above in the "When Covered" section of the policy." Added the following statement to the "When not Covered" section: "With the exception of products used within the scope of FDA indications for treatment of burns and rare skin conditions such as recessive dystrophic epidermolysis bullosa, FDA approval for a specific use does not define that product as non-investigational." References updated. Medical Director review 3/2012. (mco)

6/29/12 C9368 and C9369 added to "Billing/Coding" section. Added new products to "When not Covered" section: Grafix® CORE and Grafix® PRIME. (mco)

7/10/12 Revised the FDA information for product EZ Derm™ to state: "FDA 510(k) approved xenograft for the treatment of partial-thickness burns and venous, diabetic, and pressure ulcers."(mco)

10/16/12 Specialty Matched Consultant Advisory Panel review 9/2012. Added new products to the "When not Covered" section: AmnioFix®, Axogen/AxioGuard, DermaCell™, DuraGen®, Neox™1K/Neox™100, NuCell™/NuShield™, Restore Orthobiologic Soft Tissue Implant, SpinalMend™, TissueMend, Unite®Biomatrix, XCM Biologic, DermaSpan™ and DuraGen® Dural Graft and DuraGen® Plus. (mco)

1/1/13 Description section updated to remove non-covered product information. Non-covered product information is now specifically addressed in the "When not Covered" section. "When not Covered" section updated to include new products: hMatrix®, C-QUR Edge™, C-QUR V-Patch™ and C-QUR Lite™ V-Patch. Also added the following statement to the "When not Covered" section: "**With the exception of products used within the scope of FDA indications for treatment of burns and rare skin conditions such as recessive dystrophic epidermolysis bullosa, FDA approval for a specific use does not define that product as non-investigational."** Deleted C9366, C9368, C9369 and added Q4131, Q4132, Q4133, Q4134, Q4135, Q4136 to Billing/Coding section. Medical Director review 12/2012. (mco)

2/26/13 References updated. Added the following statement to the Description section and to the "When not Covered" section: "Dermagraft had been FDA approved by a Humanitarian Device Exemption (HDE) for the treatment of dystrophic epidermolysis bullosa. The manufacturer has since withdrawn Dermagraft from HDE status." (mco)

10/15/13 Specialty Matched Consultant Advisory Panel review 9/2013. Medical Director review 9/2013. References updated. New products added to the "When not Covered" section. (mco)

12/31/13 C5271, C5272, C5273, C5274, C5275, C5276, C5277, C5278, Q4137, Q4138, Q4139, Q4140, Q4141, Q4142, Q4143, Q4145, Q4146, Q4147, Q4148, Q4149 added to Billing/Coding section. New products added to the "When not Covered" section. (mco)

4/1/14 Description section updated. Added the following statement to the "When Covered" section: "D. Breast reconstructive surgery using allogeneic acellular dermal matrix products (i.e., AlloDerm®, AlloMax™, DermaMatrix™, FlexHD®, GraftJacket®) may be

considered medically necessary." "When Covered" section re-formatted. Updated "When not Covered" section to include new products and to remove products that are now considered medically necessary for use in breast reconstruction surgery. Deleted code C9367 from Billing/Coding section. Policy Guidelines updated. References updated. Medical Director review 3/2014. (mco)

10/28/14 Specialty Matched Consultant Advisory Panel review 9/2014. Medical Director review 9/2014. (mco) (td)

12/30/14 Added Codes Q4150, Q4151, Q4152, Q4153, Q4154, Q4155, Q4156, Q4157, Q4158, Q4159, Q4160 and C9349 to the Billing/Coding section effective 1/1/15. (td)

2/24/15 References updated. Policy Statement updated to include Epifix® coverage if meets medical necessity criteria. When Covered section updated to include Epifix considered medically necessary for the treatment of chronic, non-infected full-thickness diabetic or neuropathic lower extremity ulcers. When Not Covered section updated to include additional products and to remove Epifix. Medical Director review 2/2015. (td)

3/10/15 When Covered section revised to cover 5 applications for Epifix. Policy Statement unchanged. (td)

7/1/15 When Not Covered section revised to add the trade name PuraPly. The trade name for the product has been changed from "Fortaderm" to "PuraPly" effective July 1, 2015. References updated. Billing/Coding section updated to include code C9356. (td)

10/30/15 Specialty Matched Consultant Advisory Panel review 9/30/2015. Medical Director review 9/2015. (td)

12/30/15 Billing/Coding section updated to include codes: Q4161, Q4162, Q4163, Q4164, Q4165; effective 1/1/16. When Covered section updated to include additional products. (td)

7/26/16 Description section extensively revised. Specific products removed from the Policy statement which is revised to read: **BCBSNC will provide coverage for bioengineered skin and soft tissue substitutes when it is determined to be medically necessary because the medical criteria and guidelines shown below have been met.** "When Covered" section reformatted and new products added. Policy Guidelines section extensively revised. Deleted the following products from the "investigational" list: AmnioBand, Biovance, Grafix CORE, Grafix PRIME and Neox 1K. Rationale added for individual indications. (an)

8/30/16 Corrected typo in Description section. No other change to policy. (an)

10/25/16 Specialty Matched Consultant Advisory Panel review 9/28/2016. Policy accepted as written. (an)

12/30/16 Amnioband®/Guardian added back to the list of Investigational products. Added codes *Q4166, Q4167, Q4168, Q4169, Q4170, Q4171, Q4172, Q4173, Q4174, Q4175* to the Billing/Coding section. (an)

2/24/17 Minor change to Description section. AlloMend added to list of products covered for breast reconstructive surgery. AlloPatch added to list of products covered for chronic, noninfected, full-thickness diabetic lower-extremity ulcers. List of investigation/ noncovered products was extensively revised. All amniotic membrane and amniotic fluid

injection deleted from this list—refer to policy titled: **Amniotic Membrane and Amniotic Fluid Injections**. Policy Guidelines section updated. Billing/Coding section updated. (an)

4/28/17 Note regarding application limit for Epifix was removed from this policy and moved to policy titled "Amniotic Membrane and Amniotic Fluid Injections." (an)

5/26/17 DermACELL ™ added back to the list of Investigational products. (an)

6/30/17 In the When Covered section, the bullet points under breast reconstructive surgery were deleted. The following statement was added to the Policy Guidelines section for Breast Reconstruction: Clinical input indicated that the various acellular dermal matrix (ADM) products used in breast reconstruction have similar efficacy. The products listed are those that have been identified for use in breast reconstruction. Additional ADM products may become available for this indication. CellerateRX® (CRXa™) removed from the list of investigational products. (an)

7/28/17 DermACELL ™ removed from the list of Investigational products. Allogeneic acellular dermal matrix products, including Dermacell, may be considered medically necessary for breast reconstructive surgery. (an)

9/15/17 NeoForm Dermis and Avance Nerve Graft added to list of investigational products. Integra Omnigraft deleted from investigational product list and added to bullet point under "Treatment of chronic, noninfected, full-thickness diabetic lower extremity ulcers". Specialty Matched Consultant Advisory Panel review 8/30/2017. (an)

12/15/17 New codes added to Billing/Coding section, effective 1/1/2018: Q4176, Q4179, Q4180, Q4182. (an)

3/29/18 FlexHD® Pliable™ and Cortiva® added to list of covered products. Integra Flowable Wound Matrix moved from the Investigational products list to the "When Covered" section. The following statement from the "Not Covered" section was also added to the "When Covered" section: *With the exception of products used within the scope of FDA indications for treatment of burns and rare skin conditions such as recessive dystrophic epidermolysis bullosa, FDA approval for a specific use does not define that product as non-investigational.* Reference added. (an)

9/7/18 Specialty Matched Consultant Advisory Panel review 8/22/2018. No change to policy statement. (an)

2/12/19 Added information regarding peripheral nerve grafting to Description Section. Added NeuraGen**™** Nerve Guide and NeuraWrap**™** Nerve Protector to list of investigational products. Rationale added to Policy Guidelines section. Codes added to Billing/Coding section: 64910, 64912, 64913, C9352, C9353, C9355, C9361. Medical Director review 1/2019. **Notification given 2/12/2019 for effective date 4/16/2019.** (an)

4/16/19 Reference added. Deleted information regarding NuCel/NuShield/NuShield Orthopaedics Spine. This is an amniotic membrane product. (an)

9/10/19 Specialty Matched Consultant Advisory Panel 8/20/19. (eel)

10/1/19 Coding section updated with new codes effective 10/1/19. Added codes Q4222 and Q4226. (eel)

6/30/20 Coding section updated with new code effective 7/1/20. Added code C1849. (eel)

9/8/20 Policy name changed from **Bioengineered Skin and Tissue** to **Skin and Soft Tissue Substitutes**. Description, Policy guidelines, Coding and References sections updated. "When not covered" section reworded for clarity with "Skin and soft tissue substitutes are not covered when application site is infected or member has an allergy to the product." added. Added amniotic membrane products into policy for wound and burn applications. Clarified this policy does not apply to amniotic ophthalmic indications. "When covered" section completely reworded for clarity. Updated list of products considered always investigational. (eel)

10/1/20 Coding section updated with new codes effective 10/1/20. Added codes Q4249, Q4250, Q4254 and Q4255. (eel)

12/31/20 When not covered section revised for clarification. Added "The Plan may compare the cost -effectiveness of alternatives when determining which products will be covered" to When not covered section. Medical Director review. (bb)

3/9/21 Description updated for clarification. Coverage criteria added for Dural reconstruction/repair to When covered section. DuraGen® and Durepair Regeneration Matrix® removed from When not covered section. References added. Medical Director review. (bb)

6/1/21 When covered section "Dural Reconstruction/Repair" updated for clarity and added **spinal** to criteria. Medical Director review. (bb)

8/10/21 Added information to When Skin and Soft Tissue Substitutes are covered.Criteria to include clarification of 2nd and 3rd degree burn products. Also added PuraPly® and StrataGraft® to products that are covered. (jm)

9/7/21 Removed Stratagraft from the When Not Covered section "for all indications". References updated. Specialty Matched Consultant Advisory Panel 8/2021. Medical Director review 8/2021. (jd)

12/30/21 The following codes were added to the Billing/Coding section: A2001, A2002, A2003, A2004, A2005, A2006, A2007, A2008, A2009, A2010, Q4199 effective 1/1/2022. (tt)

3/31/22 The following codes were added to the Billing/Coding section: A2011, A2012, A2013, A4100, Q4224, Q4225, Q4256, Q4257, Q4258 effective 4/1/2022. (tt)

5/3/22 Updated information to When Skin and Soft Tissue Substitutes are covered. Criteria to include clarification of 2nd degree burn products: "Kerecis* (formerly known as MariGen™*). (tt)

5/31/22 The following reimbursement policy was added to related policies section: Facility Billing Requirements. Added the following statement to Billing/Coding section: "Billing for skin substitute application procedures required to also include the appropriate high cost or low-cost skin substitute products." (tt)

6/14/22 The following codes were added to the Billing/Coding section: Q4259, Q4260, Q4261 effective 7/1/2022.

9/13/22 References updated. Specialty Matched Consultant Advisory Panel review 8/2022. Medical Director review 8/2022. No changes to policy statement. (tt)

9/30/22 The following codes were added to the Billing/Coding section: A2014, A2015, A2016, A2017, A2018 effective 10/1/2022. (tt)

12/30/22 Billing/Coding section updated to add Q4236, Q4262, Q4263, Q4264; and remove C1849, effective 1/1/2023. (tt)

3/31/23 Billing/Coding section updated to add A2019, A2020, A2021, Q4265, Q4266, Q4267, Q4268, Q4269, Q4270, and Q4271, effective 4/1/2023. (tt)

7/18/23 Added HCPCS code C1832 to Billing/Coding section. (tt)

8/29/23 References updated. Specialty Matched Consultant Advisory Panel review 8/2023. Medical Director review 8/2023. No changes to policy statement. (tt)

9/29/23 Added HCPCS codes A2002, A2023, A2024, A2025, Q4285, Q4286 to Billing/Coding section, effective 10/1/2023. (tt)

12/29/23 Added HCPCS codes Q4279, Q4287 - Q4299, and Q4300 - Q4304 to Billing/Coding section, effective 1/1/2024. (tt)