

Corporate Medical Policy

Bioengineered Skin

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Description of Procedure or Service

Bioengineered skin or graftskin (living skin equivalent) is used to treat chronic wounds, burns, and rare skin conditions such as recessive dystrophic epidermolysis bullosa. These products promote the growth of new skin, or serve as a temporary cover until other grafts can be placed. Bioengineered skin consists of a dermal layer and/or an epidermal layer which is embedded into a cellular matrix forming the skin substitute.

It is thought that bioengineered skin accelerates wound healing by introducing living cells, which are "smart", to reestablish the condition needed for repair.

Skin ulcers are a diverse and complex group of disorders with a variety of apparent causes. They are a source of major disability, morbidity, and carry an increased risk of mortality. Skin ulcers can result from venous insufficiency, diabetic neuropathy and/or peripheral arterial disease, pressure sores, acute surgical wounds such as those caused by excision of skin cancer, and/or burn injuries.

Management of skin wounds is designed with attention to each patient's particular set of characteristics and causal factors. Treatment strategies incorporate common principles that apply to the management of all wounds. While there is no universally agreed upon standard of care, there are a number of accepted components of what is considered optimal local care. Principles of good wound care include optimized tissue perfusion, a moist wound environment, antimicrobial therapy where appropriate, aggressive wound debridement, pressure relief, and adequate nutrition.

Treatment for each category of ulcers has components that are indication-specific and should be used in addition to the common principles of good wound care. For example, venous ulcers combine good wound care with compression treatment. This decreases the venous pressure and improves the blood return to the heart. Diabetic neuropathic ulcers often require extensive debridement, weight off-loading, and aggressive control of blood glucose. Diabetic ulcers can be particularly difficult to heal and may require additional interventions for healing.

In the absence of complications, most acute wounds tend to heal within 8 weeks or so with standard care. However, a minority of wounds will not heal and become refractory. Refractory skin wounds are characterized by lack of healing, prolonged treatment courses, and frequent recurrences. In some cases of prolonged non-healing ulcers, skin grafting can be attempted.

Bioengineered skin has been shown to improve the management and healing in the treatment of severe burns. Bioengineered skin is used when there is limited amount of the patient's own skin to use for grafts or they are too ill to have more wound sites created.

Another use for bioengineered skin is for a condition called epidermolysis bullosa. Epidermolysis bullosa (EB) is a rare disease that is usually inherited. These patients suffer from extremely fragile skin with recurrent painful blister formation that can develop into open sores or ulcers. An exacerbation of this disease can be caused by just minor skin friction or trauma.

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Tissue-engineered skin substitutes have emerged as a potential alternative to skin grafting in cases of refractory, non-healing skin ulcers and burns. Various manufacturers produce bio-engineered skin substitutes including, but not limited to Apligraf[®], Integra[®], Epicel[®], Dermagraft[®], AlloDerm[®], OrCel[®], and TransCyte. Each product is different and requires FDA approval for specific indications.

Apligraf[®] (graftskin) is a culture-derived human skin equivalent (HSE). Like human skin it has 2 layers. The upper epidermal layer is made of living human keratinocytes. The bottom dermal layer consists of human fibroblasts combined with bovine collagen to produce a matrix of proteins. This living skin construct is similar in cell proliferation to human skin.

Integra is a bilayered (two layers) membrane system made of a porous matrix of fibers that cross-link bovine tendon collagen and glycosaminoglycan. The epidermal substitute layer is made of a thin poly silicone layer to control moisture.

Epicel[®] uses autologous keratinocytes from a patient's healthy skin tissue that are cultured to form cultured epidermal autografts (CEA). The autografts are processed into sheets that are attached to a petrolatum-gauze backing using stainless steel surgical clips. The autograft is applied directly to the burn wound.

Dermagraft[®] is a single layer biosynthetic dermal substitute made of human fibroblasts. The fibroblasts are obtained from neonatal foreskin and cultured on a bioabsorbable polyglactin mesh for several weeks. Matrix proteins are secreted during the culture period that includes human dermal collagens and soluble factors which creates a three-dimensional matrix that is used as a dermal replacement or temporary skin substitute.

OrCel[®] (formally known as composite cultured skin) is a living skin equivalent. This bilayered cellular matrix is made of human dermal cells cultured in bovine collagen sponge. The absorbable matrix is used as a wound dressing.

Alloderm[®] is skin tissue donated from cadavers to make an acellular dermal matrix that has been freeze dried after processing. It is used to serve as a scaffold for normal tissue remodeling. The collagen framework provides strength to the skin and contains no cells that can cause rejection or irritation. Alloderm has been researched as a support mechanism for breast reconstruction, difficult hernia repairs and after parotidectomy to avoid Frey's syndrome.

Transcyte[®] is a bilaminar skin substitute made of human fibroblasts cultured on a silicone-covered nylon mesh and combined with a synthetic epidermal layer. This biosynthetic skin substitute is cryopreserved and used for temporary wound coverage.

EZ Derm[™] is a porcine (pig) derived xenograft (non-human skin graft) of collagen that has been chemically crosslinked with aldehyde (non-human skin graft) to provide strength and durability. This skin substitute has the reliability of a long shelf life at room temperature. It is designed as a biosynthetic temporary wound covering.

Oasis[®] is an acellular skin substitute made from porcine small intestine. The matrix is composed of submucosa acellular collagen and acts as a wound covering. It accommodates the remodeling of host tissue by providing an acellular dermal scaffold for tissue growth.

PriMatrix[™] (formerly known as DressSkin) is an acellular collagen dermal tissue matrix made from fetal bovine skin. It is cell-friendly, strong and vascularizes quickly to provide a scaffold for new tissue development. It was developed to be used in the management of skin ulcers, second-degree burns, surgical wounds, and trauma wounds.

TissueMend[®] is an acellular soft tissue matrix (scaffold) made from fetal bovine dermis. Fetal dermis has minimal hair and hair follicles and has highly regenerative capabilities. Over time parallel collagen fibers develop and new tissue becomes integrated with the host matrix at the margins of the original wound. It assists the repair and reinforcement of soft tissue. It is indicated for wounds with poor tissue quality and insufficient tendon length such as rotator cuff repair as reinforcement.

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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.

*****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 **Apligraf®** bioengineered skin 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.

BCBSNC will provide coverage for **Alloderm®** bioengineered skin for the use in breast reconstruction when it is determined to be medically necessary because the medical criteria and guidelines shown below have been met.

BCBSNC will provide coverage for bioengineered skin for the treatment of burns and rare skin conditions when it is determined to be medically necessary because the medical criteria and guidelines shown below have been met.

Benefits Application

Please refer to certificate for availability of benefits. This policy relates only to the services or supplies described herein. Benefits may vary according to benefit design, therefore certificate language should be reviewed before applying the terms of the policy.

When Bioengineered Skin is covered

- A. The application of **Apligraf®** for the following indications:
1. Treatment of venous ulcers when **all** of the following criteria are met:
 - a. When used in conjunction with standard therapy,
 - b. The ulcers have not healed by at least 50% after clinically appropriate therapy,
 - c. The ulcers intended for treatment are partial or full thickness venous stasis ulcers, and
 - d. The patient has adequate arterial blood supply to the involved limb.
 2. Treatment of chronic diabetic neuropathic foot ulcers when **all** of the following criteria are met:
 - a. When used in conjunction with clinically appropriate diabetic foot ulcer care,
 - b. The ulcers have persisted for three weeks or longer,
 - c. The ulcers have not healed by 50% after 3 weeks of standard treatment,
 - d. The patient has adequate arterial blood supply to the involved foot,
 - e. The ulcers intended for treatment are full-thickness neuropathic diabetic foot ulcers, but do not go down to the tendon, muscle, capsule, or bone.

*****Applications will be limited to no more than 4 applications per wound when the above criteria is met.**

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- B. The application of **Dermagraft**[®] for the following indications:
1. Treatment of full-thickness diabetic foot ulcers when **all** of the following criteria are met:
 - a. When used in conjunction with clinically appropriate diabetic foot ulcer care protocols,
 - b. The ulcers have persisted for six weeks or longer,
 - c. The ulcers have not healed by 50% after 3 weeks of standard treatment,
 - d. The ulcers intended for treatment are full-thickness neuropathic diabetic foot ulcers, but do not extend down to the tendon, muscle, joint capsule, or bone,
 - e. The patients have adequate blood supply to the involved foot.
- ***Applications will be limited to no more than 8 weekly applications per wound when the above criteria are met.
- C. Alloderm (an acellular allograft) may be considered medically necessary for use in breast reconstruction surgery.
- D. Bioengineered skin may be considered medically necessary in the treatment of burns and rare skin conditions such as recessive dystrophic epidermolysis bullosa 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.

When Bioengineered Skin is not covered

- A. For indications other than those listed above. Other Graftskin products have not been proven medically effective and are therefore considered investigational for all other applications. BCBSNC does not pay for investigational services.
- B. **Apligraf**[®] is contraindicated for use in the following situations:
1. The wounds are infected.
 2. The patient has a known allergy to bovine collagen.
 3. The patient has a known hypersensitivity to components in the product's agarose shipping medium.
- No more than 4 applications of Apligraf[®] will be approved per wound.
- The application of Apligraf[®] has not been proven medically effective and is therefore considered **investigational** for all other applications including, but not limited to burns, pressure sores and acute surgical wounds. BCBSNC does not pay for investigational services.
- C. **Dermagraft**[®] is contraindicated for use in the following situations:
1. Ulcers that have signs of clinical infection
 2. Ulcers that have sinus tracts.
 3. Patients with known hypersensitivity to bovine products.
 4. For any indications other than those listed above in the "Covered" section of the policy.
- D. **EZ Derm**[®], **Mediskin**[®]
- 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.

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- F. **Oasis[®], Surgis[®]**
- G. **Acticoat[®]**
- H. **GraftJacket**
- I. **PriMatrix[™](formerly known as DressSkin)**
- J. **TissueMend[®]**
- K. **Celladerm[®]**

Policy Guidelines

Currently there is insufficient evidence to determine the efficacy for uses of certain bioengineered skin other than those indicated above as covered.

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.

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 code: 15150, 15151, 15152, 15155, 15156, 15157, 15170, 15171, 15175, 15176, 15300, 15301, 15320, 15321, 15330, 15331, 15335, 15336, 15340 15341, 15360, 15361, 15365, 15366, 15400, 15401, 15420, 15421, 15430, 15431, Q4100, Q4101, Q4102, Q4103, Q4104, Q4105, Q4106, Q4107, Q4108, Q4109, Q4110, Q4111, Q4112, Q4113, Q4114, Q4115, Q4116.

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.

Medical Term Definitions

Not applicable.

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)

Policy: Bioengineered Skin

MPAG Review - 3/99

Specialty Matched Consultant Advisory Panel - 10/2000

Medical Policy Advisory Group - 10/2000

BCBSA TEC Assessment, Volume 16, No 12, November 2001

Brem H, Balledux J, Bloom T, et al. Healing of diabetic foot ulcers and pressure ulcers with human skin equivalent. *Arch Surg.* 2000;135:627-34.

Paquette D, Falanga V. Leg ulcers. *Clinics in Geriatric Medicine.* 2002;18(1).

Veves A, Falanga V, Armstrong DG, Sabolinski ML. Graftskin, a human skin equivalent, is effective in the management of noninfected neuropathic diabetic foot ulcers: a prospective randomized multicenter clinical trial. *Diabetes Care.* Feb 2001;24(2):290-5.

Falanga V, Sabolinski M. A bilayered living skin construct (APLIGRAF) accelerates complete closure of hard-to-heal venous ulcers. *Wound Repair Regen.* 1999 Jul-Aug;7(4):201-7.

Brem H, Balledux J, Sukkariéh T, Carson P, Falanga V. Healing of venous ulcers of long duration with a bilayered living skin substitute: results from a general surgery and dermatology department. *Dermatol Surg* Nov 2001;27(11):915-9.

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

Gentzkow GD, Iwasaki SD, Hershon KS, Mengel M, et al. Use of Dermagraft, a cultured human dermis, to treat diabetic foot ulcers. *Diabetes Care.* 1996 April;19(4):350-354

Pollak RA, Edington H, Jensen J, Kroeker, et al. A human dermal replacement for the treatment of diabetic foot ulcers. *Wounds: A Compendium of Clinical Research and Practice.* 1997 November/December;9(6):175-182.

Gentzkow GD, Jensen JF, Pollak RA, Kroeker RO, et al. Improving healing of diabetic foot ulcers after grafting with a living human dermal replacement. *Wounds: A Compendium of Clinical Research and Practice.* 1999 May/June;11(3):77-84

Demling, RH., DeSanti, L. (1999, May). Management of partial thickness facial burns (comparison of topical antibiotics and bio-engineered skin substitutes). *Burns*, 25:3, 256-61. Retrieved 5/10/2004 from http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=10323611.

ECRI. (2001,December). Bioengineered composite skin substitute for donor sites in burn victims. Target database. Retrieved on 5/10/2004 from http://www.target.ecri.org/summary/detail.aspx?doc_id=1726&q=bioengineered+skin&anm=wynneb.

Specialty Matched Consultant Advisory Panel - 7/2004

Specialty Matched Consultant Advisory Panel - 6/2006

TEI Biosciences. (2007). PriMatrix™: Dermal repair scaffold. Retrieved 12/3/07 from <http://www.tei-bio.com/PriMatrix.aspx>.

Stryker Corporation. Product Overview Orthobiologics: TissueMend Soft Tissue Repair Matrix. Retrieved 12/3/07 from <http://strykercorp.com/jointreplacements/sites/orthobiologics/tissuemend/index.php>.

BCBSA Medical Policy Reference Manual [Electronic Version]. 7.01.113, 12/3/07.

Specialty Matched Consultant Advisory Panel - 6/2008

Senior Medical Director Review - 1/15/2009

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Dermagraft® Prescribing Information. Retrieved 9/2/09 from http://www.dermagraft.com/html/1_info/prescribinginformation.html

Marston WA, Hanft J, Norwood P, Pollak R, for the Dermagraft Diabetic Foot Ulcer Study Group. The efficacy and safety of Dermagraft in improving the healing of chronic diabetic foot ulcers. *Diabetes Care*. 2003;26:1701-1705.

U.S. Food & Drug Administration (FDA). DERMAGRAFT® - P000036. Retrieved 9/2/09 from http://www.accessdata.fda.gov/cdrh_docs/pdf/P000036c.pdf

Senior Medical Director Review - 9/2009

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 bio-synthetic 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.

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- 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 are 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 required, 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)

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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)

Medical policy is not an authorization, certification, explanation of benefits or a contract. Benefits and eligibility are determined before medical guidelines and payment guidelines are applied. Benefits are determined by the group contract and subscriber certificate that is in effect at the time services are rendered. This document is solely provided for informational purposes only and is based on research of current medical literature and review of common medical practices in the treatment and diagnosis of disease. Medical practices and knowledge are constantly changing and BCBSNC reserves the right to review and revise its medical policies periodically.