Protocol

Bio-Engineered Skin and Soft Tissue Substitutes

(701113)

Medical Benefit		**Effective Date**: 07/01/14	**Next Review Date**: 03/15
Preauthorization	Yes	**Review Dates**: 03/12, 03/13, 03/14	

The following Protocol contains medical necessity criteria that apply for this service. It is applicable to Medicare Advantage products unless separate Medicare Advantage criteria are indicated. If the criteria are not met, reimbursement will be denied and the patient cannot be billed. ***Preauthorization is required.*** *Please note that payment for covered services is subject to eligibility and the limitations noted in the patient's contract at the time the services are rendered.*

Description

Bio-engineered 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. Bio-engineered skin and soft tissue substitutes are being evaluated for a variety of conditions, including breast reconstruction and to aid healing of lower-extremity ulcers and severe burns. Acellular dermal matrix products are also being evaluated in the repair of a variety of soft tissues.

Background

Bio-engineered skin and soft tissue substitutes may be either acellular or cellular. Acellular products (i.e., cadaveric human dermis with cellular material removed) contain a matrix or scaffold composed of materials such as collagen, hyaluronic acid, and fibronectin. 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. Bio-engineered skin and soft tissue substitutes have the potential to improve rates of healing and reduce secondary complications.

Other situations in which bio-engineered skin products might substitute for living skin grafts include certain postsurgical states such as 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 situation in which artificial skin products may substitute for auto- or allografts. Certain primary dermatologic conditions that involve large areas of skin breakdown, such as bullous diseases, may also be conditions in which artificial skin products can be considered as substitutes for skin grafts. Acellular dermal matrix (ADM) products are also being evaluated in the repair of other soft tissues including rotator cuff repair, following oral and facial surgery, hernias, and a variety of other conditions.

Regulatory Status

There are a large number of artificial skin products that are commercially available or in development. The following summary of commercially available skin substitutes describes those products that have substantial

relevant evidence on efficacy. Information on other artificial skin and soft tissue substitutes that are available in the U.S. may be found in a 2012 Technology Assessment from the Agency for Healthcare Research and Quality. (1)

Acellular Dermal Matrix

Allograft ADM products derived from donated human skin tissue are supplied by U.S. AATB-compliant tissue banks using the standards of the American Association of Tissue Banks (AATB) and U.S. Food and Drug Administration's (FDA) guidelines. The processing removes the cellular components (i.e., epidermis and 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 it as banked human tissue and therefore, does not require FDA approval.

- AlloDerm® (LifeCell Corporation) is an ADM (allograft) tissue-replacement product that is created from native human skin and processed so that the basement membrane and cellular matrix remain intact. Originally, AlloDerm required refrigeration and rehydration prior to use. It is currently available in a ready-to-use product that is stored at room temperature. An injectable micronized form of AlloDerm (Cymetra) is also available.
- AlloMax™ Surgical Graft (Bard Davol) is an acellular non-cross-linked human dermis allograft. (AlloMax was previously marketed as NeoForm™.)
- FlexHD® (Ethicon) is an acellular hydrated dermis derived from donated human allograft skin. The Musculoskeletal Transplant Foundation acquires and processes the tissue.
- DermaMatrix™ (Synthes) is an ADM (allograft) derived from donated human skin tissue. DermaMatrix Acellular Dermis is processed by the Musculoskeletal Transplant Foundation® (MTF®).
- GraftJacket® Regenerative Tissue Matrix (KCI) is an acellular regenerative tissue matrix that has been processed from screened donated human skin supplied from U.S. tissue banks. The allograft is minimally processed to remove the epidermal and dermal cells, while preserving dermal structure.

PriMatrix™ (TEI Biosciences) is a xenogeneic ADM processed from fetal bovine dermis. It is indicated through FDA's 510(k) process for partial- and full-thickness wounds; diabetic, pressure, and venous stasis ulcers; surgical wounds; and tunneling, draining, and traumatic wounds.

Amniotic Membrane

Amniotic membrane is harvested immediately after birth, cleaned, sterilized, and either fresh frozen or dehydrated. Human amniotic membrane is considered to be minimally processed and not significantly changed in structure from the natural material; FDA classifies it as banked human tissue and therefore, it does not require FDA approval. EpiFix® and Amniofix® (both from MiMedix) are commercially available sources of dehydrated human amniotic membrane. EpiFix® is provided in sheets and Amniofix® is an injectable form of micronized amniotic membrane. Other amniotic membrane products are AmnioClear® (Musculoskeletal Transplant Foundation®), AmnioGraft® (Bio-Tissue), and BioDfense™ and BioDDryFlex® (both from BioD).

Collagen Scaffold

OASIS™ Wound Matrix (Cook Biotech) is a xenogeneic collagen scaffold derived from porcine small intestinal mucosa. It was cleared by the FDA's 510(k) process in 2000 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.

Living Cell Therapy

Apligraf® (Organogenesis) is a bilayered living cell therapy composed of an epidermal layer of living human

keratinocytes and a dermal layer of living human fibroblasts. Apligraf® is supplied as needed, in one size, with a shelf-life of 10 days. It was FDA-approved in 1998 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® (Shire Regenerative Medicine) is composed of cryopreserved human-derived fibroblasts and collagen derived from newborn human foreskin and cultured on a bioabsorbable mesh. Dermagraft has been approved by the FDA for repair of diabetic foot ulcers.

Epicel® (Genzyme Biosurgery) is a cultured epithelial autograft 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 greater than or equal to 30%. It may be used in conjunction with split-thickness autografts or alone in patients for whom split-thickness autografts may not be an option due to the severity and extent of their burns.

OrCel™ (Forticell Bioscience) (formerly called 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 (PMA) for healing donor site wounds in burn victims and under a humanitarian device exemption (HDE) for use in patients with recessive dystrophic epidermolysis bullosa undergoing hand reconstruction surgery to close and heal wounds created by the surgery, including those at donor sites.

Biosynthetic

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 three-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 (Integra LifeSciences) is a bovine, collagen/glycosaminoglycan dermal replacement covered by a silicone temporary epidermal substitute. It is FDA-approved for use in postexcisional treatment of life-threatening full-thickness or deep partial-thickness thermal injury where sufficient autograft is not available at the time of excision or not desirable because of the physiologic condition of the patient. Integra™ Matrix Wound Dressing and Integra™ meshed Bilayer Wound Matrix are substantially equivalent skin substitutes that are FDA-510(k) approved for other indications.

TransCyte™ (Advanced Tissue Sciences) consists of human dermal fibroblasts grown on nylon mesh, combined with a synthetic epidermal layer and was approved by FDA in 1997. TransCyte is intended to be used 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.

Related Protocol

Autologous Platelet-Derived Growth Factors as a Treatment of Wound Healing and Other Conditions

Policy (Formerly Corporate Medical Guideline)

Breast reconstructive surgery using allogeneic acellular dermal matrix products* (i.e., AlloDerm®, AlloMax™, DermaMatrix™, FlexHD®, GraftJacket®) may be considered **medically necessary**:

- when there is insufficient tissue expander or implant coverage by the pectoralis major muscle and additional coverage is required,
- when there is viable but compromised or thin post-mastectomy skin flaps that are at risk of dehiscence or necrosis, or

- the infra-mammary fold and lateral mammary folds have been undermined during mastectomy and re-establishment of these landmarks is needed.

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

- Apligraf®**
- Dermagraft®**

Treatment of chronic, non-infected, partial- or full-thickness lower extremity skin ulcers due to venous insufficiency, which have not adequately responded following a one-month period of conventional ulcer therapy, using the following tissue-engineered skin substitutes may be considered **medically necessary**.

- Apligraf®**
- Oasis™ Wound Matrix***

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

- OrCel™ (for the treatment of mitten-hand deformity when standard wound therapy has failed and when provided in accordance with the Humanitarian Device Exemption [HDE] specifications of the FDA)****

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

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

*Banked Human Tissue

**FDA PMA approved

***FDA 510(k) cleared

****FDA-approved under a humanitarian device exemption (HDE)

All other uses of bio-engineered skin and soft tissue substitutes listed above are considered **investigational**.

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

- ACell® UBM Hydated Wound Dressing
- ACell® UBM Lyophilized Wound Dressing
- AlloPatch HD™
- AlloSkin™
- AlloSkin™ RT
- Amniofix®
- Aongen™ Collagen Matrix
- ArthroFlex™ (FlexGraft)
- Atlas Wound Matrix
- Avagen Wound Dressing
- Avaulta Plus™
- Biobrane®
- BioDfence/BioDfactor
- CellerateRX®
- Collagen Sponge (Innocoll)
- Collagen Wound Dressing (Oasis Research)
- Collaguard®
- CollaSorb™
- CollaWound™
- Collexa®
- Collieva®
- Conexa™
- Coreleader Colla-Pad
- CorMatrix®
- CRXa™
- Cymetra®
- Dermadapt™ Wound Dressing
- DressSkin
- Durepair Regeneration Matrix®
- Endoform Dermal Template™
- ENDURAgen™
- EpiFix®
- Excellagen
- E-Z Derm™
- FortaDerm™ Wound Dressing
- GammaGraft

- Grafix® core
- Grafix® prime
- GraftJacket® Xpress, injectable
- HA Absorbent Wound Dressing
- Helicoll
- Hyalomatrix® (Laserskin®)
- Hyalomatrix® PA
- hMatrix®
- Integra™ Flowable Wound Matrix
- Integra™ Bilayer Wound Matrix
- Jaloskin®
- MatriDerm®
- MatriStem® Burn Matrix
- MatriStem® Micromatrix
- MatriStem® Wound Matrix
- Matrix Collagen Wound Dressing
- Matrix HD™
- MediHoney®
- Mediskin®
- MemoDerm™
- Oasis® Burn Matrix
- Oasis® Ultra Tri-Layer Matrix
- Permacol™
- PriMatrix™
- Primatrix™ Dermal Repair Scaffold
- Puros® Dermis
- Repliform®
- Repriza™
- SIS Wound Dressing II
- SS Matrix™
- Stimulen™ Collagen
- StrataGraft
- Strattice™ (xenograft)
- Suprathel®
- SurgiMend®
- Talymed®
- TenoGlide™
- TheraForm™ Standard/Sheet
- TheraSkin®Unite™
- Unite® Biomatrix
- Veritas® Collagen Matrix

Benefit Application

For general business, the existence of Legislative Mandates, such as New York Sate Legislation regarding reconstruction after a mastectomy, may impact whether a service could be considered investigational.

Medicare Advantage

For Medicare Advantage porcine (pig) skin dressings may be **medically necessary** as an occlusive dressing for burns, donor sites of a homograft, and decubiti and other ulcers. The following are examples of products that are derived from porcine, and because FDA approval is integral to the uses they are deemed reasonable and necessary for, it should be considered:

- Oasis™ Wound Matrix (medically necessary indications below)
- Permacol™

AlloDerm® Regenerative Tissue Matrix is considered **medically necessary** for the following indications:

- Abdominal wall reconstruction
- Breast reconstruction after mastectomy for breast cancer

It is contraindicated for use in any patient who is sensitive to any of the antibiotics listed on the package or polysorbate 20.

Poor general medical condition or any pathology that would limit the blood supply and compromise healing should be considered when selecting patients for implanting AlloDerm® Regenerative Tissue Matrix as such conditions may compromise successful implantation.

Apligraf® will be considered **medically necessary** for the following:

- When used with standard therapeutic compression for venous stasis ulcers (VSUs):
  - Only for ulcers that have failed to respond to documented conservative measures of greater than four (4) weeks in duration, that have at minimum included regular dressing changes, debridement of necrotic tissue and standard therapeutic compression. A “failed response” is defined as an ulcer that has increased in size or depth, or for which there has been no change in baseline size or depth and no sign of improvement or indication that improvement is likely, such as granulation, epithelialization, or progress

towards closing. Documentation of response, or lack thereof, requires measurement of the ulcer at baseline, following cessation of conservative or conventional management. Documentation should also include measurement of the ulcer immediately prior to the placement of Apligraf®.

- Only when adequate treatment of the underlying disease process(es) contributing to the ulcer, e.g., hypertension, is provided and documented in conjunction with the treatment; and
- Only for ulcers that are free of infection, redness, drainage, underlying osteomyelitis, surround cellulitis, sinus tracts or tunnels, eschar or any necrotic material that could interfere with the adherence of Apligraf® and wound healing.

- When used with standard diabetic foot ulcer (DFU) care for neuropathic DFUs:
  - Only if the patient has the current medical diagnosis of either Type I or Type II diabetes mellitus;
  - Only if the patient does not have a current HbA1C reading exceeding 12%;
  - Only for full thickness ulcers of greater than three weeks in duration, which extend through the dermis but without tendon, muscle, capsule or bone exposure;
  - Only when adequate treatment of the underlying disease process(es) contributing to the ulcer, e.g., diabetes is provided and documented in conjunction with treatment; and
  - Only for ulcers located on the foot or toes that are free of infection, redness, drainage, underlying osteomyelitis, surrounding cellulitis, tunnels and tracts, eschar or any necrotic material that could interfere with the adherence of Apligraf®, and the process of wound healing.
- For both VSUs and DFUs all of the following must also be satisfied and documented:
  - The patient must have adequate circulation/oxygenation to support tissue growth/wound healing as evidenced by physical examination (presence of acceptable peripheral pulses and/or Doppler toe signals and/or ankle-brachial index [ABI] of 0.65 or greater in limb undergoing the procedure);
  - DET treatment must be used in conjunction with following standard conservative measures:
    - Use of pressure-reducing footwear;
    - A non-weight bearing regiment;
    - Debridement of necrotic and callused tissue when necessary; and
    - Acceptable methods of wound care, such as saline moistened dressings.

The patient must be competent and/or have the support system required to participate in follow-up care associated with treatment of the wound with Apligraf®.

The use of Apligraf® on ulcers with any of the following conditions is considered **not medically necessary**:

- cellulitis;
- osteomyelitis;
- necrotic ulcer;
- draining wound;
- bone exposed- wound bed; or
- clinically significant wound healing impairment due to uncontrolled diabetes.

(See additional guidelines after GRAFTJACKET® Regenerative Matrix below)

GRAFTJACKET® Regenerative Tissue Matrix-Ulcer Repair will be considered **medically necessary** for the following indications:

- augmentation of repairs of large rotator cuff tears or ruptured calcaneal tendons;
- treatment of neuropathic diabetic foot ulcers (DFU) with all the following conditions:

- patient has a current medical diagnosis of either Type I or Type II diabetes mellitus; and
- patient does not have a current HbA1C reading exceeding 12%; and
- full thickness ulcers of greater than three weeks duration that extend through the dermis but without tendon, muscle, capsule or bone exposure; and
- underlying disease process(es) contributing to the ulcer, e.g., diabetes, is adequately treated and documented; and
- ulcers are located on the foot or toes and are free of infection, redness, drainage, underlying osteomyelitis, surrounding cellulitis, tunnels or tracts, eschar or any necrotic material that could interfere with the adherence of GRAFTJACKET® Regenerative Tissue Matrix-Ulcer Repair and the process of wound healing; and
- patient must have adequate arterial blood supply as evidenced by ankle-brachial index (ABI) of 0.65 or greater in the limb undergoing the procedure.

GRAFTJACKET® Regenerative Tissue Matrix-Ulcer Repair must be used in conjunction with the following standard conservative measures:

- pressure-reducing footwear;
- non-weight bearing regimen;
- debridement of necrotic and callused tissue when necessary; and
- acceptable standard methods of wound care, such as saline moistened dressings.

The patient must be competent and/or have the support system required to participate in follow-up care associated with treatment of the wound with GRAFTJACKET® Regenerative Tissue Matrix-Ulcer Repair.

The use of GRAFTJACKET® Regenerative Tissue Matrix-Ulcer Repair on ulcers with any of the following conditions is considered **not medically necessary**:

- cellulitis
- osteomyelitis
- necrotic ulcer
- draining wound
- bone exposed wound bed
- clinically significant wound healing impairment due to uncontrolled diabetes, poor nutrition and/or general medical condition
- autoimmune connective tissue disease.

GRAFTJACKET® matrix is contraindicated for use in any patient who is sensitive to any of the antibiotics listed on the package or polysorbate 20.

For *Apligraf®, GRAFTJACKET® Regenerative Tissue Matrix-Ulcer Repair and TheraSKIN®,* these additional guidelines apply:

A single application for any particular ulcer is usually all that is required to affect wound healing in those wounds that are likely to be helped by this therapy (for Apligraf®, GRAFTJACKET® Regenerative Tissue Matrix-Ulcer Repair). Treatment is usually expected to last no more than twelve (12) weeks and to involve a maximum of five applications (Apligraf®), two applications (GRAFTJACKET® Matrix) or five applications (TheraSKIN®*)* for any ulcer that initially qualifies for treatment. The following situations are **not medically necessary**:

- Use of more than the applications noted above for the same ulcer
- Re-application within three weeks for the same ulcer (within one week for Apligraf® and TheraSKIN®)

- Re-application where initial application has resulted in no decrease in size or depth or increase in granulation tissue, epithelialization, or progress towards closing
- Re-treatment within one year following the last successful application
- Re-treatment of an ulcer following the unsuccessful treatment where it consisted of two failed applications.

GRAFTJACKET® XPRESS Flowable Soft Tissue Scaffold is considered **investigational**.

Dermagraft® use is considered **medically necessary** in the following conditions:

When used with standard diabetic foot ulcer care for neuropathic diabetic foot ulcers (DFUs):

- Only if patient has a current medical diagnosis of Type I or Type II of diabetes mellitus;
- Only if the patient does not have a current HbA1C reading exceeding 12%;
- Only for full thickness ulcers that have been in existence for greater than six weeks;
- Only for ulcers which have failed to respond to documented conservative treatment measures of greater than six weeks;
- Only for ulcers located on the foot or toes that are free of infection, redness, drainage, underlying osteomyelitis, surrounding cellulitis, sinus tracts or tunnels, eschar or any necrotic material that could interfere with the adherence of Dermagraft®, and process of wound healing;
- Only for ulcers which extend through the dermis but without tendon, muscle, capsule or bone exposure;
- The patient must have adequate arterial blood supply as evidenced by ankle-brachial index (ABI) of 0.65 or greater in limb undergoing the procedure.

Dermagraft® treatment must be used in conjunction with following standard conservative measures:

- Use of pressure-reducing footwear;
- A non-weight bearing regimen;
- Debridement of necrotic and callused tissue when necessary;
- Acceptable methods of wound care, such as saline moistened dressings; and
- The patient must be competent and/or have the support system required to participate in follow-up care associated with treatment of the wound with Dermagraft®.

The use of Dermagraft® on ulcers with any of the following conditions is considered **not medically necessary**:

- cellulitis;
- osteomyelitis;
- necrotic ulcer;
- draining wound;
- bone exposed-wound bed; or
- clinically significant wound healing impairment due to uncontrolled diabetes.

Dermagraft® is contraindicated for use in patients with known hypersensitivity to bovine products, as it may contain trace amounts of bovine proteins from the manufacturing medium and storage solution. It should not be used on wounds that have signs of clinical infections.

As long as reasonable healing progress is noted, reapplication may continue to a maximum of eight applications in 12 weeks. Continued reapplication of Dermagraft® when the treatment is unsuccessful after two applications as evidenced by increased wound size over two successive weeks is **not medically necessary**. Retreatment of the same ulcer using Dermagraft® within one year following the last successful or unsuccessful treatment is considered **not medically necessary**.

Integra®Dermal Regeneration Template will be considered **medically necessary** for the following:

- The treatment is for post excisional treatment of life-threatening full-thickness or deep partial-thickness thermal injuries; or
- The treatment may be used for the repair of scar contractures secondary to third degree burns when other therapies have failed, or when donor sites for repair are not sufficient or desirable due to the physiological condition of the patient. These scars must be documented to be disabling by limiting elasticity and immobilizing the SKIN; and
- Sufficient autograft is not available at the time of excision, or is not desirable due to the physiological condition of the patient; and
- The substitute SKIN product must be applied on the same day as the initial excision of the recipient site; and
- Each piece of this product is for a single use in a single patient only. The device is intended for one-time use.

The use of this product in patients with chemical, radiation, or electrical burns should be limited and based on thorough evaluation of the wound by the surgeon. The wound must be documented to be suitable to excisional therapy and that there is likelihood that a viable wound bed will be created by excision. The product is contraindicated for patients with clinically diagnosed infected wounds.

In the vast majority of patients, only one application of this skin substitute product would be required.

Integra® Bilayer Wound Dressing is considered **investigational**.

OASIS® Wound Matrix and *OASIS® Ultra Tri-Layer Matrix* will be considered **medically necessary** for the following indications:

- Partial and full thickness wounds
- Pressure ulcer
- Venous stasis ulcers (VSUs) – when ALL the following conditions are met:
  - The venous stasis ulcer has been present for greater than one month duration;
  - The venous stasis ulcer has failed to respond to documented conservative measures of at least four weeks duration. A "failed response" is defined as an ulcer that has increased in size or depth, for which there has been no change in baseline size or depth and no sign of improvement or indication that improvement is likely, such as granulation, epithelialization, or progress towards closing;
  - Documentation of response or lack thereof requires measurement of the ulcer at baseline and at completion of at least four weeks of standard conservative management. Documentation should also include measurement of the ulcer immediately prior to the placement of OASIS® Wound Matrix and OASIS® Ultra Tri-Layer Matrix and before each additional weekly placement;
  - Conservative methods of wound care include wound tissue hydration with saline, non-adherent dressings, moisture-donating or absorptive dressing (depending on amount of exudate), and compression wraps.
- Chronic vascular ulcers
  - Ankle Brachial Index (ABI) when applicable must be greater than 0.7 mm HG, in the affected limb being treated.
- Neuropathic diabetic foot ulcers (DFUs) - when ALL the following conditions are met:
  - The patient is currently under management for either Type I or Type II diabetes mellitus;
  - The non-healing diabetic foot ulcer has been present for greater than one month and has a viable wound bed with granulation tissue present;
  - Standard conservative wound care measures have been tried. Conservative measures include removal of mechanical stress, debridement of necrotic tissue if present, and saline moistened dressings;
  - The ulcer is located on the foot or toes and there is no exposed bone, tendon, or fascia.

- Surgical wounds (donor sites/grafts, post-Mohs surgery, post-laser surgery, wound dehiscence).

OASIS® Wound Matrix and OASIS® Ultra Tri-Layer Matrix should be used only in cases where the patient is competent and/or has a support system to participate in the follow-up care associated with its use.

OASIS® Wound Matrix and OASIS® Ultra Tri-Layer Matrix is contraindicated in patients with the following history or conditions and would be considered **not medically necessary**:

- for individuals with rheumatoid arthritis;
- history of radiation therapy to the ulcer site;
- for uncontrolled congestive heart failure;
- for severe arterial disease;
- for persons receiving corticosteroids or immunosuppressive therapies;
- for individuals with a history of collagen vascular disease;
- malnutrition (albumin);
- known allergy to porcine-derived products;
- ulcers that are clinically infected;
- uncontrolled diabetes (HgbA1c > 12%);
- previous organ transplant;
- individuals undergoing hemodialysis;
- wounds with signs of cellulitis, osteomyelitis, or necrotic or avascular ulcer beds;
- for ulcers with exposed bone, tendon, or fascia;
- insufficient blood supply to the ulcer (TcPO2@ < 30 mm Hg, toe or ankle brachial index < 0.7 mm Hg);
- active Charcot joint disease or Sickle Cell disease;
- third degree burns.

The application of OASIS® Wound Matrix and OASIS® Ultra Tri-Layer Matrix to human wounds requires reapplication every five to seven days. Once correctly applied, the wound should be assessed every five to seven days and if appropriate, additional applications of Oasis® should be performed.

If wounds/ulcers managed with OASIS® Wound Matrix or OASIS® Ultra Tri-Layer Matrix do not evidence a measurable response after twelve weeks of applications, future applications are considered **not medically necessary**.

Primatrix™ Dermal Repair Scaffold will be considered **medically necessary** for the following:

- Partial thickness wounds
- Full thickness wounds with or without exposed bone and/or exposed tendon – when ALL the following conditions are met:
  - The wound has been determined and documented to be full thickness with or without exposed underlying structures.
  - The wound has been adequately debrided of necrotic and/or non-viable tissue and results in a bleeding wound bed.
  - PriMatrix is adequately applied and secured in a manner that maintains contact with the wound bed.
  - A moist wound environment is maintained but excessive fluid/exudates accumulation is managed by means of appropriate dressing.
  - The patient must have adequate arterial blood supply to support tissue growth.
- Pressure ulcers

- Diabetic ulcers – when ALL the following conditions are met:
  - The type 1 or type 2 diabetic is under current medical management; and
  - The diabetic foot ulcer has been present for a minimum of 30 days duration.
  - The diabetic foot ulcer must have failed to respond to documented conservative measures including aggressive sharp or surgical debridement of necrotic tissue, saline moistened dressings and a non-weight bearing regime. Medical record documentation will contain evidence that the conservative measures have failed as evidenced by an ulcer that has increased in size and/or depth or that there has been no change in baseline size or depth with no sign of improvement or no indication that improvement is likely.
  - The patient must have adequate arterial blood supply to support tissue growth.
  - The ulcer must be free of infection and underlying osteomyelitis.
- Venous ulcers – when ALL the following conditions are met:
  - The venous stasis ulcer has been present for greater than two months duration and has been refractory to the conservative treatment measures described below for greater than one month.
  - The venous stasis ulcer must have failed to respond to documented conservative measures including aggressive sharp or surgical debridement of necrotic tissue, saline moistened dressings and compression dressing. Medical record documentation will contain evidence that the conservative measures have failed as evidenced by an ulcer that has increased in size and/or depth or that there has been no change in baseline size or depth with no sign of improvement or no indication that improvement is likely.
  - PriMatrix is applied in conjunction with adequate compression dressing.
  - The patient must have adequate arterial blood supply to support tissue growth.
- Surgical wounds (donor sites/grafts, post-Mohs surgery, podiatric, wound dehiscence)
- Trauma wounds
- Tunneled/undermined wounds
- Draining wounds.

Primatrix™ Dermal Repair Scaffold is contraindicated and therefore will be considered **not medically necessary** for the following:

- Patients with a known history of hypersensitivity to collagen or bovine products.
- Use in third-degree burns.

Reapplication is required. Once correctly applied, the wound should be assessed every five to seven days and if appropriate, additional applications of PriMatrix™ Dermal Repair Scaffold should be performed. Treatment courses in studies provided by the manufacturer typically varied between seven and thirteen weeks duration and involved a maximum of five applications no less than two weeks apart.

TheraSKIN® will be considered **medically necessary** for the same VSU and DFU criteria as *Apligraf®* above, except conservative measures would have been required for six (6) weeks VSUs.

EpiFix® is considered **medically necessary** in the wound management for patients with neuropathic diabetic foot ulcers (DFUs) when all the following criteria are met:

When used with standard diabetic foot ulcer care for neuropathic DFUs:

- patient has a medical diagnosis of either Type I or Type II diabetes mellitus
- HbA1c reading 12% or lower
- Ulcer is partial or full thickness of greater than four weeks in duration, with documented failure of prior treatment to heal it

- Ulcer extends through the dermis, with or without tendon, muscle, capsule or bone exposure
- Ulcer exhibits no signs of infection

Adequate circulation to the affected extremity is present, as evidenced by one of the following during the past 60 days:

- TcPO2 with results ≥ 30 mm HG; or
- ABI with results of ≥ 0.7 and ≤ 1.2; or
- Doppler arterial waveforms which are triphasic or biphasic at the ankle of the affected leg.

Conservative measures that must be in place:

- Debridement of necrotic tissue;
- Non-weight bearing regimen;
- Use of pressure-reducing footwear.

The use of EpiFix® on ulcers with any one of the following conditions is considered **not medically necessary**:

- Osteomyelitis
- Cellulitis
- Necrotic tissue
- Draining wound
- Exposed bone
- Active infection at wound site
- Patients who are currently receiving radiation therapy or chemotherapy
- Patients with an allergy to Gentamycin or Streptomycin
- Patients whose index diabetic foot ulcer is greater than 25 cm2
- Treatment of the ulcer greater than twelve (12) weeks.

Treatment with EpiFix® occurs weekly, and is expected to last up to twelve (12) weeks. Reapplication of EpiFix® within one week for the same ulcer is considered **not medically necessary**.

Re-treatment within one year following the last successful application with EpiFix® is considered **not medically necessary**.

Re-treatment of an ulcer following the unsuccessful treatment where it consisted of two (2) failed EpiFix® applications is considered **not medically necessary**.

Medicare Advantage Policy Guidelines

Other than the specific products discussed above, this is general information regarding biologic products for wound treatment and surgical interventions.

Types of wound coverings, skin substitutes, or other tissue substitutes:

1. Dermal and/or epidermal, (substitute) tissue of human origin or non-human origin, with or without bioengineered or processed elements, with or without metabolically active elements, solid or injectable;
2. Allograft skin for temporary wound closure;
3. Xenograft, skin (dermal), for temporary wound closure;
4. Tissue cultured epidermal autograft;
5. Tissue cultured allogeneic skin substitute;

6. Tissue cultured allogeneic dermal substitute; and
7. Biologic Wound Dressings.

The Food and Drug Administration (FDA) distinguishes between products according to function (wound management, e.g., wound dressings and wound treatment, e.g., bioactive skin substitutes.) The former (Class II) requires 510(k) pre-market notification for FDA clearance while the latter (Class III) requires pre-market approval.

Human tissue products (acellular) require no FDA clearance or approval and are intended for homologous use only. [Title 21 Code of Federal Regulations (CFR), Section 1271.10(a) 2005]

Medicare Advantage considers Class II or Human Tissue products **investigational** unless otherwise specified in the biologic product criteria above.

Medicare Advantage will consider the use of Class III products **medically necessary** when used in keeping with the FDA's approved indications for those products unless otherwise specified in the criteria above.

Also refer to the general business policy statements above when otherwise not specifically addressed in this Medicare Advantage section and not contradictory to these general statements. For example, general business policy statements and regulatory status sections above provide some FDA information for the following which are not discussed separately in this Medicare Advantage criteria section: Epicel®, OrCel™, TransCyte™, and for Dermagraft® for wounds related to dystrophic epidermolysis bullosa.

Services that are the subject of a clinical trial do not meet our Technology Assessment Protocol criteria and are considered investigational. *For explanation of experimental and investigational, please refer to the Technology Assessment Protocol.*

It is expected that only appropriate and medically necessary services will be rendered. We reserve the right to conduct prepayment and postpayment reviews to assess the medical appropriateness of the above-referenced procedures. **Some of this Protocol may not pertain to the patients you provide care to, as it may relate to products that are not available in your geographic area.**

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We are not responsible for the continuing viability of web site addresses that may be listed in any references below.

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