Bioengineered Skin and Skin Replacement Therapy in the Outpatient Setting

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Disclaimer

Highmark Health Options medical policy is intended to serve only as a general reference resource regarding coverage for the services described. This policy does not constitute medical advice and is not intended to govern or otherwise influence medical decisions.

POLICY STATEMENT

Highmark Health Options may provide coverage under medical surgical benefits of the Company's Medicaid products for medically necessary bioengineered skin and skin replacement therapy.

This policy is designed to address medical necessity guidelines that are appropriate for the majority of individuals with a particular disease, illness or condition. Each person's unique clinical circumstances warrant individual consideration, based upon review of applicable medical records.

The qualifications of the policy will meet the standards of the National Committee for Quality Assurance (NCQA) and the Delaware Department of Health and Social Services (DHSS) and all applicable state and federal regulations.

DEFINITIONS

Highmark Health Options (HHO) – Managed care organization serving vulnerable populations that have complex needs and qualify for Medicaid. Highmark Health Options members include individuals and families with low income, expecting mothers, children, and people with disabilities. Members pay nothing to very little for their health coverage. Highmark Health Options currently services Delaware Medicaid: Delaware Healthy Children Program (DHCP) and Diamond State Health Plan Plus LTSS (DSHP Plus LTSS) members.

Acellular Products – Skin products that contain a matrix or scaffold composed of materials such as collagen, hyaluronic acid, and fibronectin.

Allograft – Skin or tissue harvested from another human being (e.g., cadaver) used as a temporary skin replacement and must be replaced by either an autograft or the ingrowth of the patient's own skin.

Ankle-Brachial Index (ABI) – A numeric value of the ratio of the blood pressure at the ankle to the blood pressure in the upper arm (brachium) by Doppler ultrasound. Compared to the arm, lower blood pressure in the leg is an indication of blocked arteries

Autograft – A sample of the patient's own healthy skin, as pinch or mesh grafts, is harvested and placed in the ulcer in split- or full-thickness grafts; alternatively, the patient's cells may be grown in a laboratory to form a thin film (cultured keratinocyte autograft, or cultured epidermal autograft), which can take 3 to 4 weeks.

Autologous/Autografts Skin Grafts – Permanent skin coverings that use skin from other parts of the patient's body.

Bio-engineered Skin – 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 utilized in the treatment for breast reconstruction, healing of lower extremity ulcers and severe burns. Acellular dermal matrix (ADM) products are utilized in the repair of a variety of soft tissues.

Cellular Products – Skin products that contain living cells such as fibroblasts and keratinocytes with a matrix.

Chronic Wound – A wound that does not respond to standard wound treatment for at least a 30-day period during organized comprehensive therapy.

Failed Response – An ulcer or skin deficit that has failed to respond to documented appropriate wound care measures, has increased in size or depth, or has not changed in baseline size or depth, and has no indication that improvement is likely.

Lower Extremity – Anatomically defined as the hip, thigh, leg, ankle, and foot.

Standard Treatment of Chronic Lower Extremity Ulcers – Therapies that primarily include infection and edema control, mechanical off-loading, mechanical compression or limb elevation, debridement of necrotic or infected tissue, and management of concomitant medical issues (e.g., blood glucose control, tobacco use).

Xenograft – Skin or tissue is harvested from an animal with similar skin structure (usually pigs or cows)

PROCEDURES

A prior authorization is required for both procedure and skin graft codes.

This medical policy addresses the use of skin replacement products for the treatment of chronic non-healing wounds. The goal of this treatment is to provide temporary wound coverage, complete wound closure, reduced time to heal, lessen pain, minimize post-operative contracture, and improve overall quality of health.

The following general information is required for all covered indications:

- The ordering provider must be a physician licensed by the state with full scope of practice for the treatment of the systemic disease process that is responsible for causing the chronic non-healing wound; AND
- In the situation when the performing provider is NOT the physician caring for the systemic disease, the performing provider must document in the medical record that he/she is aware of the systemic condition and notates the identity of the physician who is responsible for care related to the condition; AND
- The patient's wound has a failure of response (an ulcer or skin deficit that has failed to respond to clearly documented appropriate wound care, has a wound that has increased in size or depth, or has not changed in baseline size or depth, and there is no indication that improvement is expected); AND
- There must be evidence of adequate arterial blood supply (e.g., ankle-brachial index of 0.65 or greater in the affected limb; AND
- There must be an evaluation and provision for adequate nutritional status, including pre-albumin and albumin levels.

Breast reconstructive surgery using ONE of the following allogeneic ADM products may be considered medically necessary for any ONE of the following indications:

a. Product(s):
   - AlloDerm®; or
   - AlloMax™; or
   - AlloMend®; or
   - DermaMatrix™; or
   - DermACELL®; or
   - FlexHD®; or
   - GraftJacket®

b. Indication(s):
   - When there is 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
   - The infra-mammary fold and lateral mammary folds have been undermined during mastectomy and re-establishment of these landmarks is needed.

Breast reconstruction surgery using one of the allogeneic ADM products not meeting the criteria as indicated in this policy is considered not medically necessary.

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

- AlloPatch®; or
- Apligraf®; or
- Dermagraft®; or
- Integra® Dermal Regeneration Template or
- Oasis® Ultra Tri-Layer Matrix or
- Oasis Wound Matrix

Treatment of chronic, noninfected, full-thickness diabetic lower extremity ulcers not meeting the criteria as indicated in this policy will be considered not medically necessary.

Treatment of chronic, noninfected, 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 any ONE of the following tissue-engineered skin substitutes may be considered medically necessary:

- Apligraf; or
- Oasis™ Wound Matrix or
- Oasis® Ultra Tri-Layer Matrix

Treatment of chronic, non-infected, partial- or full-thickness lower extremity skin ulcers due to venous insufficiency not meeting the criteria as indicated in this policy is considered not medically necessary.

Treatment of dystrophic epidermolysis bullosa using the following tissue-engineered skin substitutes may be considered medically necessary for ALL of the following indications:

a. Product(s):

- OrCel™

b. Indication(s):
   - 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 Food and Drug Administration (FDA).

Treatment of dystrophic epidermolysis bullosa not meeting the criteria as indicated in this policy is considered not medically necessary.

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

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

Treatment of second- and third-degree burns not meeting the criteria as indicated in this policy is considered not medically necessary.

TheraSkin® may be considered medically necessary for any ONE of the following indications:

- In conjunction with standard therapeutic compression for the treatment of chronic, noninfected, partial or full-thickness skin ulcers due to venous insufficiency greater than one (1) month duration and which have not adequately responded following a one (1) month period of conventional ulcer therapy (i.e., standard dressing changes, standard therapeutic compression, etc.); or
- In conjunction with standard diabetic foot ulcer care for the treatment of full-thickness neuropathic diabetic foot ulcers greater than one month duration which have not adequately responded following at least four weeks of conventional ulcer therapy (i.e., surgical debridement, complete off-loading and standard dressing changes, etc.) which can extend through the dermis, including tendon, muscle, joint capsule or bone exposure; or
- Other uses supported by clinical results and clinical literature include pressure sores, skin cancer excision (e.g., Mohs Surgery), large surgical wounds (i.e., club release, etc.), radiation compromised wounds and necrotizing fasciitis.

TheraSkin® not meeting the criteria as indicated in this policy is considered not medically necessary.

ALL other skin and soft tissue substitutes not listed above are considered experimental/investigational and, therefore noncovered because the safety and/or effectiveness cannot be established by the available published peer-reviewed literature.

CHRONIC NONHEALING WOUNDS

In addition to the general information above, the following wound-specific medical necessity criteria must be met:

DIABETIC FOOT ULCERS (DFU)

a. Indication(s):

- Presence of a neuropathic diabetic foot ulcer of greater than four weeks which has failed to respond to documented conservative wound care measures such as surgical debridement, complete off-loading, and standard dressing changes; AND
- There must be documentation of patient compliance with all conservative wound care measures; AND
- The foot ulcer must extend through the dermis but without tendon, muscle, joint capsule, or bone exposure; AND
- The diabetes is well managed, and the HbA1C is within an acceptable range; AND
- The diabetic foot ulcer is free of infection; AND
- Wound must have adequate circulation and presence of acceptable peripheral pulses or as evidenced by ankle-brachial index (ABI) of 0.65 or greater in the limb being treated. An index of greater than 0.45 is needed to heal.

b. Product(s):
- Apligraf ®; OR
- AlloPatch Pliable®; OR
- AlloDerm; OR
- Biovance; OR
- Dermagraft; OR
- DermaPure; OR
- Helicoll; OR
- Integra® Bilayer Wound Matrix; OR
- Integra Omnigraft dermal regeneration matrix®; OR
- Kermatrix; OR
- TheraSkin; OR
- Oasis™ wound matrix; OR
- Epifix; OR
- Graftjacket Regenerative Tissue Matrix (RTM); OR
- Grafix; OR
- TheraSkin®

VENOUS LEG ULCERS (VLU)

a. Indication(s):
- The presence of a venous stasis ulcer which has not responded to documented appropriate therapy for greater than four weeks. These therapies would include the use of compression therapy using multilayer dressings or compression stockings with greater than 20 mmHG pressure or pneumatic compression; AND
- There must be documentation that the patient has been compliant with wound care measures.

b. Product(s):
- Apligraf ®; OR
- AlloDerm; OR
- Biovance; OR
- DermaPure; OR
- Integra® Bilayer Wound Matrix; OR
- Oasis™ Wound Matrix; OR
- TheraSkin®

Documentation requirements for all wound types:

- Medical record documentation includes measurements of the initial ulcer, measurements at the completion of at least four weeks of appropriate wound care, and measurements immediately prior to skin replacement product and with each subsequent placement of skin products;
- Medical record documentation that specifically states the reason that the wound has failed to heal with standard wound care;
- Medical record documentation that demonstrates that the medical policy criteria have been met, along with appropriate diagnoses and response to treatment(s);
- Medical record has clear descriptions of the wound(s) relative to the location, stage, size duration, and presence or lack of infection. There must be a wound description pre- and post-treatment with each skin replacement application.
- Documentation of the amount of skin replacement product used and amount wasted.
- Timing, frequency, and number of reapplications of bioengineered skin substitutes should be appropriate for the material used and clinical condition of the patient.

In a course of treatment, repeat application of skin substitutes/replacements are not indicated when prior application was unsuccessful.

CONTRAINDICATIONS

Presence of any of the following:

- Edema, venous hypertension, or lymphedema
- Active cellulitis, osteomyelitis, foreign body, or malignant process
- Tunneling and tracts, eschar, and necrotic material

LENGTH of Coverage

A single application of skin replacement products is usually all that is necessary in order to effect wound healing in wounds that are likely to be improved by this therapy. The use of more than two applications for the same ulcer within six months is considered not medically necessary. Requests for additional skin replacement applications will be reviewed on a case-by-case basis with supporting medical record documentation.

Retreatment within one year following successful initial treatment (up to two applications) is not considered medically necessary.

WHEN SERVICES ARE NOT COVERED

- For conditions other than those listed above, scientific evidence has not been established.
- Services are not covered for the use of a skin replacement product for indications not approved by the FDA or in accordance with the manufacturer's package guidelines.
- Services are not covered for the use of Autologous Platelet Rich Plasma (PRP) and are considered experimental/investigation and therefore considered not medically necessary.
- Simultaneous use of more than one product for the episode of the wound is not covered.

POST-PAYMENT AUDIT STATEMENT

The medical record must include documentation that reflects the medical necessity criteria and is subject to audit by Highmark Health Options at any time pursuant to the terms of your provider agreement.

PLACE OF SERVICE: OUTPATIENT

CODING REQUIREMENTS

CPT code	Description
15150	Tissue cultured skin autograft, trunk, arms, legs; first 25 sq cm or less.
15151	Tissue cultured skin autograft, trunk, arms, legs; additional 1 sq cm to 75sq cm (list separately in addition to code for primary procedures).
15152	Tissue cultured skin autograft, trunk, arms, legs; each additional 100 sq cm, or each additional 1% of body area of infants and children, or part thereof (list separately in addition to code for primary procedures).
15155	Tissue cultured skin autograft, face, scalp, eyelids, mouth, neck, ears, orbits, genitalia, hands, feet, and/or multiple digits; first 25 sq cm or less.
15156	Tissue cultured skin autograft, face, scalp, eyelids, mouth, neck, ears, orbits, genitalia, hands, feet, and/or multiple digits; additional 1 sq cm or 75 sq cm (list separately in addition to code for primary procedures).
15157	Tissue cultured skin autograft, face, scalp, eyelids, mouth, neck, ears, orbits, genitalia, hands, feet, and/or multiple digits; each additional 100 sq cm, or each additional 1% of body area of infants and children, or part thereof (list separately in addition to code for primary procedures).
15271	Application of skin substitute graft to trunk, arms, legs, total wound surface area up to 100 sq cm; first 25 sq cm or less wound surface area.
15272	Application of skin substitute graft to trunk, arms, legs, total wound surface area up to 100 sq cm; each additional 25 sq cm or less wound surface area, or part thereof (list separately in addition to code for primary procedure).
15273	Application of skin substitute graft to trunk, arms, legs, total wound surface area greater than or equal to 100 sq cm; first 100 sq cm or less wound surface area, or 1% of body area of infants and children.
15274	Application of skin substitute graft to trunk, arms, legs, total wound surface area greater than or equal to 100 sq cm; each additional 100 sq cm wound surface area, or part thereof, or each additional 1% of body area of infants and children, or part thereof (list separately in addition to code for primary procedure).
15275	Application of skin substitute graft to face, scalp, eyelids, mouth, neck, ears, orbits, genitalia, hands, feet, and/or multiple digits, total wound surface area up to 100 sq cm; first 25 sq cm or less wound surface area.
15276	Application of skin substitute graft to face, scalp, eyelids, mouth, neck, ears, orbits, genitalia, hands, feet, and/or multiple digits, total wound surface area up to 100 sq cm; each additional 25 sq cm wound surface area or part thereof (list separately in addition to code for primary procedure).
15277	Application of skin substitute graft to face, scalp, eyelids, mouth, neck, ears, orbits, genitalia, hands, feet, and/or multiple digits, total wound surface area greater than or equal to 100 sq cm; first 100 sq cm or less wound surface area, or 1% of body area of infants and children.
15278	Application of skin substitute graft to face, scalp, eyelids, mouth, neck, ears, orbits, genitalia, hands, feet, and/or multiple digits, total wound surface area greater than or equal to 100 sq cm; each additional 100 sq cm wound surface area, or part thereof, or each additional 1% of body area of infants and children, or part thereof (list separately in addition to code for primary procedure).
15777	Implantation of biologic implant (e.g., acellular dermal matric) for soft tissue reinforcement (i.e., breast, trunk) (list separately in addition to code for primary procedure).
19357	Tissue expander placement in breast reconstruction, including subsequent expansion(s).
19361	Breast reconstruction; with latissimus dorsi flap.

19364	Breast reconstruction; with free flap (e.g., ftram, diep, siea, gap flap).
19367	Breast reconstruction; with single-pedicled transverse rectus abdominis myocutaneous (tram) flap.
19368	Breast reconstruction; with single-pedicled transverse rectus abdominis myocutaneous (tram) flat, requiring separate microvascular anastomosis (supercharging).
19369	Breast reconstruction, with bepedicled transverse rectus abdominis myocutaneous (tram) flat.
19380	Revision of reconstructed breast (e.g., significant removal of tissue, re-advancement and/or re-inset of flaps in autologous reconstruction or significant capsular revision combined with soft tissue excision in implant-based reconstruction).

COVERED DIAGNOSIS CODES

Codes						
E08.621	E09.621	E10.621	E11.621	E13.621	E13.622	I70.231
I70.232	I70.233	I70.234	I70.235	I70.238	I70.241	I70.242
I70.243	I70.244	I70.245	I70.248	I70.291	I70.292	I70.29
I70.331	I70.332	I70.333	I70.334	I70.335	I70.338	I70.341
I70.342	I70.343	I70.344	I70.345	I70.348	I83.011	I83.012
I83.013	I83.014	I83.015	I83.018	I83.021	I83.022	I83.023
I83.024	I83.025	I83.028	I83.211	I83.212	I83.213	I83.214
I83.215	I83.218	I83.221	I83.222	I83.223	I83.224	I83.225
I83.228	I87.011	I87.012	I87.013	I87.031	I87.032	I87.033
I87.311	I87.312	I87.313	I87.331	I87.332	I87.333	L89.152
L89.153	L89.154	L89.212	L89.213	L89.214	L89.222	L89.223
L89.224	L89.312	L89.313	L89.314	L89.322	L89.323	L89.324
L89.42	L89.43	L89.44	L89.512	L89.513	L89.514	L89.522
L89.523	L89.524	L89.612	L89.613	L89.614	L89.622	L89.623
L89.624	L89.892	L89.893	L89.894	L97.111	L97.112	L97.113
L97.114	L97.121	L97.122	L97.123	L97.124	L97.211	L97.212
L97.213	L97.214	L97.221	L97.222	L97.223	L97.224	L97.311
L97.312	L97.313	L97.314	L97.321	L97.322	L97.323	L97.324
L97.411	L97.412	L97.413	L97.414	L97.421	L97.422	L97.423
L97.424	L97.511	L97.512	L97.513	L97.514	L97.521	L97.522
L97.523	L97.524	L97.811	L97.812	L97.813	L97.814	L97.821
L97.822	L97.823	L97.824	L97.912	L97.913	L97.914	L97.922
L97.923	L97.924					

REIMBURSEMENT

Participating facilities will be reimbursed per their Highmark Health Options contract.

Summary of Literature
Chronic wounds of the lower extremity are known to be a condition associated with high prevalence, high cost, and poor clinical outcome. Wounds become chronic when they are unresponsive to initial therapy or persistent in the face of appropriate care. The most common types of chronic wounds of the lower extremity are described by their etiology:

- Vascular (e.g., arterial, venous, or mixed ulcers)
- Pressure ulcers
- Neuropathic (e.g., diabetic ulcers)

Skin grafting has evolved from the initial autograft and allograft preparations to biosynthetic and tissue engineered human skin equivalents. There are a large number of potential applications for these products, and one large category is non-healing wounds. Non-healing wounds encompass diabetic neuropathic ulcers, vascular insufficiency ulcers, and pressure ulcers. These types of wounds are known to heal inadequately with standard wound care, leading to prolonged morbidity and increased risk of mortality.

Numerous clinical trials have been published for many commercially available skin replacement products for several medical conditions including non-healing wounds, pressure ulcer, inflammatory ulcers, and burns. In addition, there are ongoing and unpublished trials.

In 2015, the United Kingdom's National Institute for Health and Care Excellence (NICE) published clinical guidelines on the prevention and management of diabetic foot problems. NICE recommends that clinicians consider dermal or skin substitutes as an adjunct to standard care when treating diabetic foot ulcers, only when healing has not progressed and on the advice of the multidisciplinary foot care service.

Autologous platelet-derived growth factors are referred to as platelet rich plasma (PRP), autologous platelet gel, or platelet releasate, and several PRP preparations available today that are FDA approved. There are PRP preparations intended to be used to mix with bone graft materials to enhance bone grafting properties in orthopedic practices. There are two preparations that can be prepared at the bedside for immediate application (i.e., AutoGel and SafeBlood), specifically for wound healing. Proc uren® (Cytomedix, Inc.) was another product used for chronic wound healing, however, it is no longer manufactured or commercially available.

Platelet-derived growth factor has been suggested for adjunctive use in the management of chronic non-healing wounds. It is not clearly understood how PRP works, but some practitioners speculate that if the acute healing pathways can be activated, the body can be induced to repair damage. Therefore, an injection into the injury site is thought to stimulate an acute injury and may possibly induce an acute healing process.

Several agencies have concluded that the effectiveness of growth factors for this condition have not been adequately established to warrant recommendation for use (AHRQ, 2011) (CMS, 2013). The available studies have mixed results with some trials reporting improvement with PRP and other trials reporting improvement. Additional studies are needed to truly resolve these issues.

In 2012, a Cochrane analysis was completed to address autologous PRP used for healing chronic wounds. There were nine eligible random controlled trials (RCT) with a total of 325 participants, and 44% were women. Four RCTs recruited patients with mixed chronic wounds, three RCTs recruited patients for venous leg ulcers and two trials used patients with diabetic foot ulcers. The median length of treatment was 12 weeks. The authors reported that there were no statistically significant differences in groups treated with PRP compared to the groups that were not treated with PRP. In conclusion, there is no evidence to suggest that autologous PRP is of value for treating chronic wounds, and well-designed, adequately powered clinical trials are needed.

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POLICY UPDATE HISTORY

03/22/2023	Approved in Medical Policy Committee
03/28/2023	Approved QI/UM