CLINICAL MEDICAL POLICY	
Policy Name:	Skin Replacement Therapy for Chronic Non-healing Wounds in the Outpatient Setting
Policy Number:	MP-032-MD-PA
Responsible Department(s):	Medical Management
Provider Notice/Issue Date:	06/10/2024; 07/01/2023; 02/01/2023; 03/01/2022; 02/13/2021; 02/17/2020; 03/18/2019; 04/15/2018
Effective Date:	07/01/2024; 08/01/2023; 03/01/2023; 04/01/2022; 03/15/2021; 03/16/2020; 03/18/2019; 04/15/2018; 05/01/2017
Next Annual Review:	12/2024
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Products:	Highmark Wholecare℠ Medicaid
Application:	All participating hospitals and providers
Page Number(s):	1 of 30

Policy History

Date	Activity
07/01/2024	Provider Effective date
04/09/2024	PARP Approval
04/17/2024	QI/UM Committee review
04/17/2024	Annual Review: Per PA DHS TAG determination, HCPCS codes Q4158 and A2019 have been changed from an Option #4 to an Option #1, the codes have been added to the PA Fee Schedule. Added codes Q4158 and A2019 to Procedure Codes under Coding Requirements section.
08/01/2023	Provider Effective date
06/14/2023	PARP Approval
05/17/2023	QI/UM Committee review
05/17/2023	Urgent Revision: Per PA DHS TAG determination, updated coverage determination for FlexHD/AllopatchHD (Q4128), & AmnioBand/Guardian (Q4151). FlexHD/AllopatchHD (Q4128), & AmnioBand/Guardian (Q4151) are now set as an Option #3, and will require a Program Exception for approval. Added HCPCS codes Q4128 and Q4151 to the 'Coding Requirements' section. Removed Q4151 from 'Noncovered Procedure Codes' section. Updated the 'Reference List of Skin Replacement Products' and 'Reference Sources' sections.
03/01/2023	Provider Effective date

01/12/2023	PARP Approval
12/21/2022	QI/UM Committee review
12/21/2022	Annual Review: No changes to clinical stance. Updated 'Summary of Literature' and 'Reference Sources' sections.
04/01/2022	Provider Effective date
02/07/2022	PARP Approval
12/15/2021	QI/UM Committee review
12/15/2021	Annual Review: No changes to clinical criteria. Removed CMS guidance on PRP injections covered under clinical trial information, CMS has updated this stance and is now covering PRP injections. PRP will remain experimental/investigational by Highmark Wholecare. Updated Summary of Literature and Reference Sources sections. Adjusted the Description for the following Procedure Codes (per AMA guidance): Q4132, Q4133, Q4165, Q4122, Q4137, Q4148, Q4156, Q4158, Q4162, Q4163.
03/15/2021	Provider Effective Date
10/17/2016	Initial policy developed

Disclaimer

Highmark Wholecare ℠ 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 Wholecare℠ may provide coverage under the medical-surgical benefits of the Company's Medicaid products for medically necessary skin replacement products when used in the treatment of chronic, non-healing wounds.

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 warrants individual consideration, based upon review of applicable medical records.

(Current applicable Pennsylvania HealthChoices Agreement Section V. Program Requirements, B. Prior Authorization of Services, 1. General Prior Authorization Requirements.)

Definitions

Prior Authorization Review Panel (PARP) – A panel of representatives from within the Pennsylvania Department of Human Services who have been assigned organizational responsibility for the review, approval and denial of all PH-MCO Prior Authorization policies and procedures.

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

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.

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.

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

Ankle-Brachial Index (ABI) –This is 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.

Bio-engineered Skin and Soft Tissues – Tissues that may be derived from human tissue (autologous or allogeneic), non-human tissue (xenographic), synthetic material, or a composite of these materials.

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

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.

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 (i.e., blood glucose control, tobacco use).

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

Procedures

This medical policy addresses the use of skin replacement products (i.e., skin substitutes) for the treatment of chronic non-healing wounds. The goal of skin replacement treatment is to provide temporary wound coverage, complete wound closure, reduced time to heal, decreased pain, minimized post-operative contracture, and improvement in overall quality of health.

1. The following general information is required for ALL medically necessary skin replacement therapy indications:
   A. The ordering provider must be a physician licensed by the state of Pennsylvania with full scope of practice for the treatment of the systemic disease process that is responsible for causing the chronic non-healing wound; AND

B. 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 notate the identity of the physician who is responsible for care related to the condition; AND
C. The individual's condition is defined as having a Failure of Response. A Failure of Response is defined as an ulcer or skin deficit that has failed to respond to clearly documented appropriate wound care, the wound 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
D. There must be evidence of adequate arterial blood supply (e.g., ankle-brachial index of 0.65 or greater in the affected limb); AND
E. There must be an evaluation and provision for adequate nutritional status, including pre-albumin and albumin levels.

2. In addition to the general information above, ALL of the following wound-specific medical necessity criteria must be met:
   A. **Diabetic Foot Ulcers (DFU) Indication(s)**:
      1) 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
      2) There must be documentation of the patient's compliance with all conservative wound care measures; AND
      3) The foot ulcer must extend through the dermis but without tendon, muscle, joint capsule, or bone exposure; AND
      4) Diabetes is well managed, and the HbA1C is within an acceptable range; AND
      5) The diabetic foot ulcer is free of infection; AND
      6) The 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. **Venous leg ulcers (VLU) Indications**:
      1) The presence of a venous stasis ulcer which has not responded to documented appropriate therapy for greater than four weeks. The therapy should include the use of compression therapy using multilayer dressings or compression stockings with greater than 20 mmHg pressure or pneumatic compression; AND
      2) There must be documentation that the patient has been compliant with wound care measures.

      Note: Please see the '*Informational*' section below to view the skin replacement products that are considered medically necessary.

3. The following medical record documentation requirements are applicable for all wound types:
   - 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.
   - Documentation that specifically states the reason that the wound has failed to heal with standard wound care.
   - Documentation that demonstrates that the criteria listed in this policy have been met, along with appropriate diagnoses and response to treatment(s).

- Clear documentation of the wound(s) 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.

4. In a course of treatment, repeat application of skin substitutes/replacements are not indicated when prior applications were unsuccessful. Contraindications include presence of ANY of the following:
    - Edema
    - Venous hypertension
    - Lymphedema
    - Active cellulitis
    - Osteomyelitis
    - Foreign body
    - Malignant process
    - Tunneling/tracts
    - Eschar
    - Necrotic material

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

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

6. When skin replacement therapy is not medically necessary
    - For conditions other than those listed above because the scientific evidence has not been established.
    - For the use of a skin replacement product for indications not approved by the FDA or in accordance with the manufacturers package guidelines.
    - For the use of autologous platelet rich plasma (PRP), which is considered experimental/investigational.
    - Simultaneous use of more than one skin replacement product for the same wound.

   Note: Please see the '*Informational*' section below to view the skin replacement products that are not covered.

7. Post-payment Audit Statement
   The medical record must include documentation that reflects the medical necessity criteria and is subject to audit by Highmark Wholecare℠ at any time pursuant to the terms of your provider agreement.

8. Place of Service
   The proper place of service for the placement of skin replacement products can be outpatient/provider office.

9. Related Policy
   - MP-007-MD-PA Hyperbaric Oxygen Therapy (HBOT)

Governing Bodies Approval

The U.S. Food and Drug Administration (FDA) regulates skin substitutes based on the skin substitute's composition and origin, under one of the following categories:

- Human- and human/animal-derived products are regulated through the premarket approval (PMA) process. PMA is the most stringent type of device marketing application required by the FDA. The applicant must receive FDA approval of its PMA application prior to marketing the device. PMA approval is based on a determination by the FDA that there is sufficient valid scientific evidence to ensure that the device is safe and effective for its intended use(s).

- Animal-derived products and synthetic products are regulated through the 510(k) process. The 510(k) process requires applicants to demonstrate that the device to be marketed (i.e., a Class II device) is "substantially equivalent" to a pre-existing legally marketed device (predicate) in terms of safety and effectiveness. The predicate must have been approved either via PMA or 510(k). This process is usually used when manufacturers make small changes to a previously approved device that are thought to improve effectiveness without compromising safety, thus allowing for expedited approval without costly and lengthy scientific studies confirming safety and effectiveness.

- Human-derived products are regulated as human cells, tissue, and cellular and tissue-based products (HCT/Ps). This regulation describes the rules concerning the use of HCT/Ps for human medical purposes. The final rule, 21 CFR Part 1271, became effective on April 4, 2001, for human tissues intended for transplantation that are regulated under section 361 of the PHS Act and 21 CFR Part 1270. HCT/Ps are regulated by the Center for Biologics Evaluation and Research (CBER). CBER is responsible for regulating biological and related products including blood, vaccines, allergenics, tissues, and cellular and gene therapies. Establishments producing HCT/Ps must register with the FDA and list their HCT/Ps. HCT/Ps establishments are not required to demonstrate the safety or effectiveness of their products, and the FDA does not evaluate the safety or effectiveness of these products.

- Human- and human/animal-derived products are regulated as a Humanitarian Use Device (HUD) obtained through a Humanitarian Device Exemption (HDE). In rare instances, certain medical devices intended to be used for humanitarian purposes are evaluated by the FDA through the Humanitarian Device Exemption (HDE) process. A device approved in this manner is designated as a Humanitarian Use Device (HUD). A HUD designation permits the use of certain medical devices when there is no comparable device available to treat or diagnose a disease or condition affecting fewer than 4,000 individuals annually. Because clinical investigation demonstrating the device's efficacy is not feasible (given the low prevalence of the disease in the population), an HDE grants manufacturers an exemption to the usual premarket approval process and allows marketing of the device only for the FDA-labeled HDE indication(s). Under FDA requirements,

an HUD may only be used after institutional review board (IRB) approval has been obtained for the use of the device in accordance with the FDA-labeled indication(s) under the HDE.

CMS

The Centers for Medicare and Medicaid Services (CMS) has published the following guidance:

- National Coverage Determination (NCD) Blood-Derived Products for Chronic Non-Healing Wounds (270.3)
- Local Coverage Determination (LCD) Application of Bioengineered Skin Substitutes to Lower Extremity Chronic Non-Healing Wounds (L35041)
- Local Coverage Article (LCA) Billing and Coding: Application of Bioengineered Skin Substitutes to Lower Extremity Chronic Non-Healing Wounds (A54117)
- Local Coverage Determination (LCD) Platelet Rich Plasma (L39068)
- Local Coverage Article (LCA) Billing and Coding: Platelet Rich Plasma (A58808)

Platelet Rich Plasma (PRP)

The PRP procedure is considered experimental/investigation by Highmark Wholecare and therefore not medically necessary. However, effective for services performed on or after April 13, 2021, CMS will cover autologous PRP for the treatment of chronic non-healing diabetic wounds under section 1862(a)(1)(A) of the Social Security Act (the Act) for a duration of 20 weeks, when prepared by devices whose FDA-cleared indications include the management of exuding cutaneous wounds, such as diabetic ulcers.

The Pennsylvania Department of Human Services Technology Assessment Group (TAG) workgroup meets quarterly to discuss issues revolving around new technologies and technologies or services that were previously considered to be a program exception. During this meeting, decisions are made as to whether or not certain technologies will be covered and how they will be covered. TAG's decisions are as follow:

- Option #1: Approved - Will be added to the Fee Schedule
- Option #2: Approved as Medically Effective - Will require Program Exception
- Option #3: Approved with (or denied due to) Limited/Minimal Evidence of Effectiveness - Will require Program Exception
- Option #4: Denied - Experimental/Investigational

Skin Replacement Therapy Product	TAG Determination	Determination Date
Gamma Graft (Q4111)	Option #4	May 2010
Graftjacket Xpress (Q4113)	Option #4	December 2014
Epifix (Q4186)	Option #2	January 2016
Oasis Wound Matrix (Q4102)	Option #3	May 2016
Oasis Ultra TRI-LAYER Wound Matrix (Q4124)	Option #4	May 2016
Oasis Burn Matrix (Q4103)	Option #3	May 2016
TheraSkin (Q4121)	Option #3	May 2016
Integra & Omnigraft (Q4105)	Option #4	January 2017
Marigen (Kerecis Omega3 Wound Grafting) (Q4158)	Option #1	November 2023
Grafix Core (Q4132)	Option #3	October 2019
Grafix Prime (Q4133)	Option #3	October 2019
FlexHD or AllopatchHD (Q4128)	Option #3	February 2023
AmnioBand or Guardian (Q4151)	Option #3	February 2023
Kerecis Omega3 MariGen Shield	Option #1	November 2023

Program Exception
Epifix (Q4186), Oasis Wound Matrix (Q4102), Oasis Burn Matrix (Q4103), TheraSkin (Q4121), Grafix Core (Q4132), Grafix Prime (Q4133), FlexHD/AllopatchHD (Q4128), & AmnioBand/Guardian (Q4151) all require a Program Exception. The ordering physician must provide a supporting statement indicating why the requested therapy is medically necessary, and the alternative options have been or are likely to be ineffective, adversely affect patient compliance, or cause an adverse reaction.

Summary of Literature

Chronic wounds of the lower extremity are known to be a condition linked to high prevalence, high cost, and poor clinical outcome. Wounds become chronic when they are persistent and unresponsive to initial therapy even with appropriate medical care. The most common types of lower extremity chronic wounds are described by their specific etiology, including vascular (e.g., arterial, venous, mixed ulcers, pressure ulcers), or neuropathic (e.g., diabetic ulcers).

Initially, a chronic wound may be treated by regularly cleaning the wound and covering it with proper wound dressings and bandages. If the wound still has not healed after a certain period of time despite proper wound care, other treatments may be offered. Other forms of wound care treatment are debridement, compression stockings and compression bandages, antibiotics, hyperbaric oxygen therapy, Ultrasound and electromagnetic therapy, negative pressure wound therapy, or skin replacement therapy (IQWiG, 2006).

Skin replacement therapy is considered as a treatment option if a wound is so large that it cannot close on its own. In this procedure, skin is taken from another part of the patient's body – usually the thigh – and transplanted onto the wound. There are also grafts that are made from human cell products and synthetic materials. Studies have shown that these increase the chances of poorly healing venous leg ulcers closing faster (IQWiG, 2006).

Skin grafts may be recommended for:

- Areas where there has been infection that caused a large amount of skin loss
- Burns
- Cosmetic reasons or reconstructive surgeries where there has been skin damage or skin loss
- Skin cancer surgery
- Surgeries that need skin grafts to heal
- Venous ulcers, pressure ulcers, or diabetic ulcers that do not heal
- Very large wounds
- A wound that the surgeon has not been able to close properly (Icahn School of Medicine at Mount Sinai, 2021)

A patient's own tissue, called an autograft, can often be used for a surgical reconstruction procedure. Autograft tissue is the safest and fastest-healing tissue that can be used. However, harvesting autograft tissue creates a second surgical site from which the patient must recover. The additional recovery time can extend a patient's hospital stay. In addition, the secondary site could be uncomfortable for years after the surgery. Allograft tissue, taken from another person, takes longer to incorporate into the recipient's body, but there is no second surgical site to heal. Also, the surgical time and hospital stay may be shorter when allograft tissue is used. Allograft tissue transplants are not rejected by the body as with organ

transplants, so that it is not necessary to use drugs to suppress the body's immune response (Hartford Hospital).

Human skin allograft is an alternate option of wound coverage when autograft is not available. Various synthetic skin substitute dressings are now available in the market, and thus use of human skin allograft has decreased. Skin allograft is obtained from a human donor (deceased or healthy) and used as a temporary cover for burn wounds. It can be classified into the following:

- Viable:
    - Fresh (freshly harvested from donor or refrigerated)
    - Cryopreserved
- Nonviable:
    - Lyophilized (glycerol)
    - Irradiated (gamma irradiation)

Allografts are preserved in a skin bank. After the advent of commercially available biological dressings (various skin substitutes), use of human skin allograft has decreased. Allograft avoids pain and risk of infection from frequent dressing changes. Availability of allograft and risk of infection are the two main constraints in its regular use. Within its indications, human skin allograft is an effective method of burn wound coverage and it cannot be replaced by synthetic skin substitutes at present (Gupta, Mohapatra, Chittoria, et al., 2019).

Skin substitutes are heterogeneous group of wound coverage materials that aid in would closure and replace the functions of the skin, either temporarily or permanently, depending on the product characteristics. These substances are alternatives to the standard wound coverage in circumstances when standard therapies are not desirable. There are several important factors that are taken into consideration in the decision to use the skin substitutes in burn and wound management. These include the depth of burn/wound, availability of donor site, likelihood of wound infection, sites of burn, likelihood of contracture, aesthetic outcome, relative cost, time consumption and experience of the burn surgeons. The skin substitutes provide rapid wound coverage solution that may require less vascularized wound bed, increase in the dermal component of healed wound, reduce or removed inhibitory factors of wound healing, reduced inflammatory response and subsequent scarring. However, these skin substitutes generally necessitate higher cost, expertise and experience (Halim, Khoo, Mohd Yussof, 2010).

The optimal skin substitute will provide for immediate replacement of both the lost dermis and epidermis, with permanent wound coverage. Other features of the ideal skin substitute should have the following features:

- Able to resist infection
- Able to prevent water loss
- Able to withstand the shear forces
- Cost effective
- Widely available
- Long shelf life and easy to store
- Lack of antigenicity
- Flexible in thickness
- Durable with long-term wound stability
- Can be conformed to irregular wound surfaces and
- Easy to be secured and applied (Halim, Khoo, Mohd Yussof, 2010)

A systematic review and meta-analysis was recently published which examined the efficacy of healing diabetic foot ulcers with biologic skin substitutes. Twenty-five studies were identified that assessed the proportion of complete wound closure by 12 weeks. The study found that wounds treated with biologic dressings were 1.67 times more likely to heal by 12 weeks than those treated with standard of care (SOC) dressings ($P < 0.00001$). Five studies assessed the proportion of complete wound closure by 6 weeks. Wounds treated with biologic dressings were 2.81 times more likely to heal by 6 weeks than those treated with SOC dressings ($P = 0.0001$). Descriptively, 29 of 31 studies assessed the time to healing favored biologic dressings over SOC dressings. This systematic review provided supporting evidence that biologic skin substitutes are more effective than SOC dressings at healing diabetic foot ulcers by 12 weeks. Future studies must address the relative benefits of different skin substitutes as well as the long-term implications of these products and their financial considerations (Gordon, Alfonso, Nicholson, Chiu, 2019).

PRP

Autologous PRP is the fraction of blood plasma from a patient's peripheral blood that contains higher than baseline concentrations of platelets including concentrated growth factors and cytokines. PRP contains Platelet-Derived Growth Factor (PDGF), Fibroblast Growth Factor (FGF), Insulin Growth Factor (IGF), Vascular Endothelial Growth Factor (VEGF), Transforming Growth Factor-β, and Hepatocyte Growth Factor (HGF), all of which have been shown to stimulate healing. PRP preparations are being offered typically in a point-of-care setting, delivered as a preparation of aqueous suspension obtained by centrifugation of whole blood or as a gel. PRP is most commonly applied to the wound bed with dressing, but can be injected in the wound bed (AHRQ, 2020).

The contents of the platelet in PRP are either released through spontaneous activation upon exposure to collagen in the wounds,3 pre-released as PRP lysate by freeze-thawing disruption of platelet membrane,4 or pre-released by activation with degranulation triggered by thrombin and/or calcium chloride.5 PRP has attracted significant interest because platelets possess various growth factors that are critical for tissue repair and regeneration, and they have antibacterial properties in traumatic injuries. (AHRQ, 2020).

Several agencies have concluded that the effectiveness of growth factors for this condition have not been adequately established to warrant recommendation for use (AHRQ, 2020) (CMS, 2013). The available studies have mixed results, with only some trials reporting improvement with PRP, and other trials reporting improvement. Additional studies are needed in order 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 for venous leg ulcers, and two trials with people 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.

Coding Requirements

Procedure Codes

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 (list separately in addition to code for primary procedure)
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 procedure)
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 to 75 sq. cm (list separately in addition to code for primary procedure)
15157	Tissue cultured skin autograft, face, scalp, eyelids, mouth, neck, ears, orbits, genitalia, hands, feet, and/or multiple digits; each additional 1% of body area of infants and children, or part thereof (list separately in addition to code for primary procedure)
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 wound surface area, or part thereof (list separately in addition to code of 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 wound 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 up to 100 sq. cm; first 100 sq. cm wound surface area, or 1% of body 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 up 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 matrix) for soft tissue reinforcement (i.e., breast trunk). (list separately in addition to code for primary procedure)
HCPCS Code	**Description**
A2019	Kerecis Omega3 MariGen Shield, per square centimeter
Q4100	Skin substitute, not otherwise specified
Q4101	Apligraf, per sq. cm
Q4102*	Oasis wound matrix, per sq. cm
Q4103*	Oasis burn matrix, per sq cm

Q4104	Integra bilayer matrix wound dressing (BMWD), per sq. cm
Q4106	Dermagraft, per sq. cm
Q4107	GRAFTJACKET, per sq. cm
Q4108	Integra matrix, per sq. cm
Q4114	Integra flowable wound matrix, injectable, 1 cc
Q4116	AlloDerm, per sq. cm
Q4121*	TheraSkin, per sq. cm
Q4128*	FlexHD, AllopatchHD, OR MatrixHD
Q4132*	Grafix Core and GrafixPL Core, per sq cm
Q4133*	Grafix PRIME, GrafixPL PRIME, Stravix and StravixPL, per sq cm
Q4151*	AmnioBand or Guardian, per sq cm
Q4152	DermaPure, per sq. cm
Q4154	Biovance, per sq. cm
Q4158	Kerecis Omega3, per square centimeter
Q4164	Helicoll, per sq. cm
Q4165	Keramatrix or Kerasorb, per sq cm
Q4186*	Epifix, per sq cm

*= TAG Determination

Non-covered Procedure Codes

All requests for the codes listed below require Medical Director approval

HCPCS Code	Description
Q4105*	Integra dermal regeneration template (DRT) or Integra Omnigraft dermal regeneration matrix, per sq. cm
Q4110	PriMatrix, per sq. cm
Q4111*	GammaGraft, per sq. cm
Q4112	Cymetra, injectable, 1cc
Q4113*	GRAFT JACKET XPRESS, injectable, 1cc
Q4115	AlloSkin, per sq. cm
Q4117	HYALOMATRIX, per sq. cm
Q4118	MatriStem micromatrix, 1 mg
Q4122	DermACELL, DermACELL AWM or DermACELL AWM Porous, per sq cm
Q4123	AlloSkin RT, per sq. cm
Q4124*	OASIS ultra tri-layer wound matrix, per sq. cm
Q4125	ArthroFlex, per sq. cm
Q4126	MemoDerm, DermaSpan, TranZgraft or IntéguPly, per sq cm
Q4127	Talymed, per sq. cm
Q4134	HMatrix, per sq. cm
Q4135	Mediskin, per sq. cm
Q4136	E-Z Derm, per sq. cm
Q4137	AmnioExcel, AmnioExcel Plus or BioDExcel, per sq cm
Q4138	BioDfence Dryflex, per sq. cm
Q4139	AmnioMatrix or BioDMatrix, injectable, 1 cc
Q4140	BioDFence, per sq. cm
Q4141	AlloSkin AC, per sq. cm
Q4142	XCM biologic tissue matrix, per sq. cm
Q4143	Repriza, per sq. cm
Q4145*	EpiFix, injectable, 1 mg
Q4146	Tensix, per sq. cm
Q4147	Architect, Architect PX, or Architect FX, extracellular matrix, per sq. cm
Q4148	Neox Cord 1K, Neox Cord RT, or Clarix Cord 1K, per sq cm

Q4149	Excellagen, 0.1 cc
Q4150	AlloWrap DS or dry, per sq. cm
Q4153	Dermavest and Plurivest, per sq. cm
Q4155	Neox Flo or Clarix Flo, 1mg
Q4156	Neox 100 or Clarix 100, per sq cm
Q4157	Revitalon, per sq. cm
Q4159	Affinity, per sq. cm
Q4160	Nushield, per sq. cm
Q4161	bio-ConneKt wound matrix, per sq. cm
Q4162	WoundEx Flow, BioSkin Flow, 0.5 cc
Q4163	WoundEx, BioSkin, per sq cm
0232T	Injection(s), platelet rich plasma, any tissue, including image guidance, harvesting and preparation when performed
G0460	Autologous platelet rich plasma for chronic wounds/ulcers, including phlebotomy, centrifugation, and all other preparatory procedures, administration, and dressings, per treatment
P9020	Platelet rich plasma, each unit
P9022	Red blood cells, washed, each unit
S9055	Procuren or other growth factor preparation to promote wound healing

*= TAG Decision

Diagnosis Codes

ICD-10 Code	Description
E08.621	Diabetes mellitus due to underlying condition with foot ulcer
E09.621	Drug or chemical induced diabetes mellitus with foot ulcer
E10.621	Type 1 diabetes mellitus with foot ulcer
E11.621	Type 2 diabetes mellitus with foot ulcer
E13.621	Other specified diabetes mellitus with foot ulcer
E13.622	Other specified diabetes mellitus with other skin ulcer
I70.231	Atherosclerosis of native arteries of right leg with ulceration of thigh
I70.232	Atherosclerosis of native arteries of right leg with ulceration of calf
I70.233	Atherosclerosis of native arteries of right leg with ulceration of ankle
I70.234	Atherosclerosis of native arteries of right leg with ulceration of heel and midfoot
I70.235	Atherosclerosis of native arteries of right leg with ulceration of other part of foot
I70.238	Atherosclerosis of native arteries of right leg with ulceration of other part of lower leg
I70.241	Atherosclerosis of native arteries of left leg with ulceration of thigh
I70.242	Atherosclerosis of native arteries of left leg with ulceration of calf
I70.243	Atherosclerosis of native arteries of left leg with ulceration of ankle
I70.244	Atherosclerosis of native arteries of left leg with ulceration of heel and midfoot
I70.245	Atherosclerosis of native arteries of left leg with ulceration of other part of foot
I70.248	Atherosclerosis of native arteries of left leg with ulceration of other part of lower leg
I70.291	Other atherosclerosis of native arteries of extremities, right leg
I70.292	Other atherosclerosis of native arteries of extremities, left leg
I70.293	Other atherosclerosis of native arteries of extremities, bilateral legs
I70.331	Atherosclerosis of unspecified type of bypass graft(s) of the right leg with ulceration of thigh
I70.332	Atherosclerosis of unspecified type of bypass graft(s) of the right leg with ulceration of calf

I70.333	Atherosclerosis of unspecified type of bypass graft(s) of the right leg with ulceration of ankle
I70.334	Atherosclerosis of unspecified type of bypass graft(s) of the right leg with ulceration of heel and midfoot
I70.335	Atherosclerosis of unspecified type of bypass graft(s) of the right leg with ulceration of other part of foot
I70.338	Atherosclerosis of unspecified type of bypass graft(s) of the right leg with ulceration of other part of lower leg
I70.341	Atherosclerosis of unspecified type of bypass graft(s) of the left leg with ulceration of thigh
I70.342	Atherosclerosis of unspecified type of bypass graft(s) of the left leg with ulceration of calf
I70.343	Atherosclerosis of unspecified type of bypass graft(s) of the left leg with ulceration of ankle
I70.344	Atherosclerosis of unspecified type of bypass graft(s) of the left leg with ulceration of heel and midfoot
I70.345	Atherosclerosis of unspecified type of bypass graft(s) of the left leg with ulceration of other part of foot
I70.348	Atherosclerosis of unspecified type of bypass graft(s) of the left leg with ulceration of other part of lower leg
I83.011	Varicose veins of right lower extremity with ulcer of thigh
I83.012	Varicose veins of right lower extremity with ulcer of calf
I83.013	Varicose veins of right lower extremity with ulcer of ankle
I83.014	Varicose veins of right lower extremity with ulcer of heel and midfoot
I83.015	Varicose veins of right lower extremity with ulcer other part of foot
I83.018	Varicose veins of right lower extremity with ulcer other part of lower leg
I83.021	Varicose veins of left lower extremity with ulcer of thigh
I83.022	Varicose veins of left lower extremity with ulcer of calf
I83.023	Varicose veins of left lower extremity with ulcer of ankle
I83.024	Varicose veins of left lower extremity with ulcer of heel and midfoot
I83.025	Varicose veins of left lower extremity with ulcer other part of foot
I83.028	Varicose veins of left lower extremity with ulcer other part of lower leg
I83.211	Varicose veins of right lower extremity with both ulcer of thigh and inflammation
I83.212	Varicose veins of right lower extremity with both ulcer of calf and inflammation
I83.213	Varicose veins of right lower extremity with both ulcer of ankle and inflammation
I83.214	Varicose veins of right lower extremity with both ulcer of heel and midfoot and inflammation
I83.215	Varicose veins of right lower extremity with both ulcer other part of foot and inflammation
I83.218	Varicose veins of right lower extremity with both ulcer of other part of lower extremity and inflammation
I83.221	Varicose veins of left lower extremity with both ulcer of thigh and inflammation
I83.222	Varicose veins of left lower extremity with both ulcer of calf and inflammation
I83.223	Varicose veins of left lower extremity with both ulcer of ankle and inflammation
I83.224	Varicose veins of left lower extremity with both ulcer of heel and midfoot and inflammation
I83.225	Varicose veins of left lower extremity with both ulcer other part of foot and inflammation
I83.228	Varicose veins of left lower extremity with both ulcer of other part of lower extremity and inflammation

I87.011	Post thrombotic syndrome with ulcer of right lower extremity
I87.012	Post thrombotic syndrome with ulcer of left lower extremity
I87.013	Post thrombotic syndrome with ulcer of bilateral lower extremity
I87.031	Post thrombotic syndrome with ulcer and inflammation of right lower extremity
I87.032	Post thrombotic syndrome with ulcer and inflammation of left lower extremity
I87.033	Post thrombotic syndrome with ulcer and inflammation of bilateral lower extremity
I87.311	Chronic venous hypertension (idiopathic) with ulcer of right lower extremity
I87.312	Chronic venous hypertension (idiopathic) with ulcer of left lower extremity
I87.313	Chronic venous hypertension (idiopathic) with ulcer of bilateral lower extremity
I87.331	Chronic venous hypertension (idiopathic) with ulcer and inflammation of right lower extremity
I87.332	Chronic venous hypertension (idiopathic) with ulcer and inflammation of left lower extremity
I87.333	Chronic venous hypertension (idiopathic) with ulcer and inflammation of bilateral lower extremity
L89.152	Pressure ulcer of sacral region, stage 2
L89.153	Pressure ulcer of sacral region, stage 3
L89.154	Pressure ulcer of sacral region, stage 4
L89.212	Pressure ulcer of right hip, stage 2
L89.213	Pressure ulcer of right hip, stage 3
L89.214	Pressure ulcer of right hip, stage 4
L89.222	Pressure ulcer of left hip, stage 2
L89.223	Pressure ulcer of left hip, stage 3
L89.224	Pressure ulcer of left hip, stage 4
L89.312	Pressure ulcer of right buttock, stage 2
L89.313	Pressure ulcer of right buttock, stage 3
L89.314	Pressure ulcer of right buttock, stage 4
L89.322	Pressure ulcer of left buttock, stage 2
L89.323	Pressure ulcer of left buttock, stage 3
L89.324	Pressure ulcer of left buttock, stage 4
L89.42	Pressure ulcer of contiguous site of back, buttock and hip, stage 2
L89.43	Pressure ulcer of contiguous site of back, buttock and hip, stage 3
L89.44	Pressure ulcer of contiguous site of back, buttock and hip, stage 4
L89.512	Pressure ulcer of right ankle, stage 2
L89.513	Pressure ulcer of right ankle, stage 3
L89.514	Pressure ulcer of right ankle, stage 4
L89.522	Pressure ulcer of left ankle, stage 2
L89.523	Pressure ulcer of left ankle, stage 3
L89.524	Pressure ulcer of left ankle, stage 4
L89.612	Pressure ulcer of right heel, stage 2
L89.613	Pressure ulcer of right heel, stage 3
L89.614	Pressure ulcer of right heel, stage 4
L89.622	Pressure ulcer of left heel, stage 2
L89.623	Pressure ulcer of left heel, stage 3
L89.624	Pressure ulcer of left heel, stage 4
L89.892	Pressure ulcer of other site, stage 2
L89.893	Pressure ulcer of other site, stage 3
L89.894	Pressure ulcer of other site, stage 4

L97.111	Non-pressure chronic ulcer of right thigh limited to breakdown of skin
L97.112	Non-pressure chronic ulcer of right thigh with fat layer exposed
L97.113	Non-pressure chronic ulcer of right thigh with necrosis of muscle
L97.114	Non-pressure chronic ulcer of right thigh with necrosis of bone
L97.121	Non-pressure chronic ulcer of left thigh limited to breakdown of skin
L97.122	Non-pressure chronic ulcer of left thigh with fat layer exposed
L97.123	Non-pressure chronic ulcer of left thigh with necrosis of muscle
L97.124	Non-pressure chronic ulcer of left thigh with necrosis of bone
L97.211	Non-pressure chronic ulcer of right calf limited to breakdown of skin
L97.212	Non-pressure chronic ulcer of right calf with fat layer exposed
L97.213	Non-pressure chronic ulcer of right calf with necrosis of muscle
L97.214	Non-pressure chronic ulcer of right calf with necrosis of bone
L97.221	Non-pressure chronic ulcer of left calf limited to breakdown of skin
L97.222	Non-pressure chronic ulcer of left calf with fat layer exposed
L97.223	Non-pressure chronic ulcer of left calf with necrosis of muscle
L97.224	Non-pressure chronic ulcer of left calf with necrosis of bone
L97.311	Non-pressure chronic ulcer of right ankle limited to breakdown of skin
L97.312	Non-pressure chronic ulcer of right ankle with fat layer exposed
L97.313	Non-pressure chronic ulcer of right ankle with necrosis of muscle
L97.314	Non-pressure chronic ulcer of right ankle with necrosis of bone
L97.321	Non-pressure chronic ulcer of left ankle limited to breakdown of skin
L97.322	Non-pressure chronic ulcer of left ankle with fat layer exposed
L97.323	Non-pressure chronic ulcer of left ankle with necrosis of muscle
L97.324	Non-pressure chronic ulcer of left ankle with necrosis of bone
L97.411	Non-pressure chronic ulcer of right heel and midfoot limited to breakdown of skin
L97.412	Non-pressure chronic ulcer of right heel and midfoot with fat layer exposed
L97.413	Non-pressure chronic ulcer of right heel and midfoot with necrosis of muscle
L97.414	Non-pressure chronic ulcer of right heel and midfoot with necrosis of bone
L97.421	Non-pressure chronic ulcer of left heel and midfoot limited to breakdown of skin
L97.422	Non-pressure chronic ulcer of left heel and midfoot with fat layer exposed
L97.423	Non-pressure chronic ulcer of left heel and midfoot with necrosis of muscle
L97.424	Non-pressure chronic ulcer of left heel and midfoot with necrosis of bone
L97.511	Non-pressure chronic ulcer of other part of right foot limited to breakdown of skin
L97.512	Non-pressure chronic ulcer of other part of right foot with fat layer exposed
L97.513	Non-pressure chronic ulcer of other part of right foot with necrosis of muscle
L97.514	Non-pressure chronic ulcer of other part of right foot with necrosis of bone
L97.521	Non-pressure chronic ulcer of other part of left foot limited to breakdown of skin
L97.522	Non-pressure chronic ulcer of other part of left foot with fat layer exposed
L97.523	Non-pressure chronic ulcer of other part of left foot with necrosis of muscle
L97.524	Non-pressure chronic ulcer of other part of left foot with necrosis of bone
L97.811	Non-pressure chronic ulcer of other part of right lower leg limited to breakdown of skin
L97.812	Non-pressure chronic ulcer of other part of right lower leg with fat layer exposed
L97.813	Non-pressure chronic ulcer of other part of right lower leg with necrosis of muscle
L97.814	Non-pressure chronic ulcer of other part of right lower leg with necrosis of bone
L97.821	Non-pressure chronic ulcer of other part of left lower leg limited to breakdown of skin
L97.822	Non-pressure chronic ulcer of other part of left lower leg with fat layer exposed
L97.823	Non-pressure chronic ulcer of other part of left lower leg with necrosis of muscle
L97.824	Non-pressure chronic ulcer of other part of left lower leg with necrosis of bone

L97.912	Non-pressure chronic ulcer of unspecified part of right lower leg with fat layer exposed
L97.913	Non-pressure chronic ulcer of unspecified part of right lower leg with necrosis of muscle
L97.914	Non-pressure chronic ulcer of unspecified part of right lower leg with necrosis of bone
L97.922	Non-pressure chronic ulcer of unspecified part of left lower leg with fat layer exposed
L97.923	Non-pressure chronic ulcer of unspecified part of left lower leg with necrosis of muscle
L97.924	Non-pressure chronic ulcer of unspecified part of left lower leg with necrosis of bone

Informational

The table below lists skin substitute products, which are represented by a specific HCPCS code, and their approved indications. This list does not include all FDA-approved/regulated skin substitute products. This list does not imply coverage for all products.

Reference List of Skin Replacement Products

Skin Substitute	Indication(s)
Medically Necessary:	
Apligraf	Apligraf received premarket FDA approval in 1998 for the treatment of venous leg ulcers (VLU) and in 2001 for the treatment of diabetic foot ulcers. Clinical trials for Apligraf has proven to be effective when used for treatment of VLUs and diabetic foot ulcers (Novartis, 2002). There is not sufficient data to use Apligraf in the treatment of pressure sores, dermatological survey wounds and burns (Novartis, 2002).
Alloderm	AlloDerm has been widely used in several applications for many years. There is an injectable form of AlloDerm marketed as Cymetra, basically a micronized form. AlloDerm is used as a dermal substitute in deep partial- and full-thickness burn wounds, facilitating subsequent autologous split-thickness skin graft take.
AllopatchHD/Flex HD	AlloPatch (acellular dermal matrix derived from the reticular layer) is human allograft skin minimally processed to remove epidermal and dermal cells and is packaged in an ethanol solution. The process utilized preserves the extracellular matrix of the dermis with the intent to address specific and non-specific inflammatory responses. AlloPatch is used for the replacement of damaged or inadequate integumental tissue or for the repair, reinforcement, or supplemental support of soft tissue defects. Zelen et al (2017): Acellular dermal matrices can successfully heal wounds. This study's goal was to compare clinical outcomes of a novel, open-structure human reticular acellular dermis matrix (HR-ADM) to facilitate wound closure in non-healing diabetic foot ulcers (DFUs) versus DFUs treated with standard of care (SOC). Weekly application of HR-ADM is an effective intervention for promoting closure of non-healing DFUs.
AmnioBand or Guardian	AmnioBand is a minimally processed human allograft (dehydrated human placental membrane comprised of amnion and chorion) which retains the structural properties of the extracellular matrix. The resulting dehydrated allograft serves as a wound covering. For use as wound care scaffold for the replacement of damaged or inadequate integumental tissue such as diabetic foot ulcers, venous leg ulcers, pressure ulcers, or for other homologous use. Serena et al (2022): This randomized controlled trial evaluated the safety and effectiveness of weekly and biweekly applications of dehydrated human amnion and chorion allograft (dHACA) plus standard of care compared to standard of care alone on chronic venous leg ulcers. The adverse event rate was 63.5 percent. Among the 38 adverse events, none were graft or procedure related, and all were resolved with appropriate treatment. DHACA and standard of care, either applied weekly or biweekly, significantly healed more venous leg ulcers than standard of care alone, suggesting that the use of aseptically processed dHACA is advantageous and a safe and effective treatment option in the healing of chronic venous leg ulcers.

Skin Substitute	Indication(s)
TheraSkin	A biologically active, cryopreserved human skin allograft with both epidermis and dermis layers. Similar to living skin equivalent (LSE) and provides a supply of living cells, fibroblasts, and keratinocytes and a fully developed extracellular matrix (Snyder, et al., 2012). TheraSkin is regulated by the FDA as an HCT/P (human cells, tissues, and cellular and tissue-based products) under 21 CFR part 1270/1271 and section 361 of the Public Health Service Act. TheraSkin is indicated for non-healing or chronic wounds, pressure ulcers diabetic foot ulcers, venous stasis ulcers and burns.
Oasis (Wound Matrix, Ultra tri-layer wound matrix)	A porcine-derived decellularized intestinal mucosa matrix, intended for the management of pressure ulcers, venous ulcers, diabetic ulcers, chronic vascular ulcers, tunneled/undetermined wounds, surgical wounds, trauma wounds, and draining wounds. Oasis is not indicated for the use in 3rd degree burns.
Biovance	Biovance is a is an amniotic membrane allograft derived from the placenta of a healthy, full-term human pregnancy, intended for the treatment of acute and chronic wounds including burns, diabetic ulcer, pressure ulcers and surgical wounds. Smiell et al. (2015) reported a multicenter registry study of Biovance d-HAM for the treatment of various wound types, including diabetic foot wounds, pressure ulcers, and venous ulcers. The study showed effectiveness of d-HAM in a real-world setting.
DermaPure	DermaPure is a single layer decellularized dermal allograft derived from split thickness grafts harvested from human cadaver tissue donors, DermaPure is used for the treatment of acute and chronic wounds such as diabetic foot ulcers, venous stasis ulcers, and additional wounds that are refractory to more conservative care (CMS, 2014). In a 2017 analysis, Kimmel and Gittleman evaluated the use of DermaPure, a decellularized human skin allograft, in the treatment of a variety of challenging wounds. This retrospective observational analysis reviewed a total of 37 patients from 29 different wound clinics. Each patient received one application of DermaPure which was followed until complete closure. A statistical analysis was performed with the end point being complete healing. All wounds on average had a duration of 56 weeks and healed in an average time of 10 weeks. Individual wound categories included diabetic foot ulcers, which healed in 8 weeks; venous leg ulcers, which healed in 11 weeks; and surgical/traumatic wounds, which healed in 11 weeks.
DermaSpan Acellular Dermal Matrix	DermaSpan (Zimmer Biomet® Sports Medicine) is an acellular dermal matrix derived from human allograft tissue. It is intended for use in various practices, including orthopedics, plastic surgery, and general surgery, for repair and replacement of damaged or inadequate skin tissue (wound coverage). Intended use is for the repair or replacement of damaged or inadequate integument tissue (wound coverage).
EpiFix	EpiFix amniotic membrane allograft (MiMedx Group, Inc., Kennesaw, GA) is a biologic human amniotic membrane processed through Surgical Biologic's proprietary Purion® process, which combines cleaning, dehydration and sterilization to produce a safe, technically sterilized tissue allowing for storage at room temperature. Used in the treatment of partial and full-thickness wounds including, but not limited to: diabetic foot ulcers, venous leg ulcers, arterial ulcers, pressure ulcers, and inflammatory ulcers. In a multi-center RCT, Bianchi and colleagues (2018) evaluated the efficacy of EpiFix allograft as an adjunct to multi-layer compression therapy for the treatment of non-healing full-thickness venous leg ulcers. The authors stated that these results may not be generalized to other amniotic membrane products seeing that scientific papers have been published describing differences among the products. They noted that it must also be recognized that all patients received a high level of care in a wound care center. For ethical reasons, per study protocol, patients receiving standard care were allowed to exit the study and receive advanced wound care treatments if their wound did not reduce by a minimum of 40 % within 8 weeks of study enrollment.
Grafix Core and Grafix Prime	Grafix Core and Grafix Prime are extracellular matrix containing growth factors for acute and chronic wounds, including diabetic foot ulcers and burns.Grafix Core is an allograft containing endogenous mesenchymal stem cells indicated for the treatment of deep

Skin Substitute	Indication(s)
	chronic wounds, limb salvage procedures, tendon repair and burns. Grafix Prime is an allograft containing endogenous mesenchymal stem cells indicated for upper epithelial layer chronic wounds and burns. Fryberg et al (2017) reported the results of a prospective, multicenter, open-label, and single-arm clinical trial to establish clinical outcomes when Grafix Prime viable cryopreserved human placental membrane (vCHPM) is applied weekly to complex diabetic foot ulcers (DFUs) with exposed deep structures. For patients completing the protocol, the primary endpoint, 100% wound granulation by week 16, was met by 96·3% of patients in a mean of 6·8 weeks. Complete wound closure occurred in 59·3% (mean 9·1 weeks). The 4-week percent area reduction was 54·3%. There were no product-related adverse events. Four patients (13%) withdrew, two (6·5%) for non-compliance and two (6·5%) for surgical intervention.
Helicoll	Helicoll (MCT Medical Solutions LLC) is a semi occlusive, self-adhering collagen sheet used for wound treatments, second degree burns, and chronic ulcers. This biodegradable skin substitute is made from animal tissues. Dhanraj (2015) conducted a prospective randomized controlled study to compare Helicoll, a type I pure collagen dressing, to OpSite dressing and to Scarlet Red dressing in the treatment of standardized split-thickness skin grafts (STSG) donor sites. The authors concluded that Helicoll, as a donor site dressing, is successful in providing pain-free mobility with a measurable healing rate. Study limitations include a small study population and only one wound type (STSG donor site) was evaluated.
Keramatrix	Keramatrix (Molecular Biologicals, LLC) is an open-cell wound dressing used for chronic wounds and ulcers. It is comprised of freeze dried acellular, animal-derived keratin protein. Loan et al. (2016) conducted a controlled study that included 40 patients with superficial or partial thickness burn injuries treated with Keramatrix, compared to 40 historical controls who received standard of care treatment. The results indicated a significantly faster mean healing time in the Keramatrix group than in the control group (8.7 days vs. 14.4 days). Davidson et al. (2013) conducted a randomized controlled trial using a standard care alginate (Algisite) dressing side by side with an experimental dressing (Keramatrix) on 26 patients with partial-thickness donor site wounds. The authors concluded that Keramatrix dressing significantly increases the rate of epithelialization of acute, traumatic partial-thickness wounds in older patients.
AmnioBand or Guardian	AmnioBand is a minimally processed human allograft (dehydrated human placental membrane comprised of amnion and chorion) which retains the structural properties of the extracellular matrix. The resulting dehydrated allograft serves as a wound covering. For use as wound care scaffold for the replacement of damaged or inadequate integumental tissue such as diabetic foot ulcers, venous leg ulcers, pressure ulcers, or for other homologous use. Serena et al (2022): This randomized controlled trial evaluated the safety and effectiveness of weekly and biweekly applications of dehydrated human amnion and chorion allograft (dHACA) plus standard of care compared to standard of care alone on chronic venous leg ulcers. The adverse event rate was 63.5 percent. Among the 38 adverse events, none were graft or procedure related, and all were resolved with appropriate treatment. DHACA and standard of care, either applied weekly or biweekly, significantly healed more venous leg ulcers than standard of care alone, suggesting that the use of aseptically processed dHACA is advantageous and a safe and effective treatment option in the healing of chronic venous leg ulcers.
Not Medically Necessary	
Affinity	Affinity (Organogenesis Inc.) is a fluid membrane allograft that is intended for clinical use in wound repair and healing. Intended to be applied as an on-lay graft for acute and chronic wounds, including, but not limited to, neuropathic ulcers, venous stasis ulcers, pressure ulcers, burns, post-traumatic wounds and post-surgical wounds.
AlloSkin	Alloskin is a specialty allograft derived from epidermal and dermal cadaveric tissue and designed for wound care (Snyder, et al., 2012). Alloskin is a 1:1 meshed, biological

Skin Substitute	Indication(s)
	cadaveric dermis, which is decellularized and further processed to provide an acellular tissue allograft. These products have been used in acute and chronic wound therapy.
AlloSkin AC	AlloSkin AC is a meshed dermis-only human skin graft that has been decellularized while preserving the natural biologic components and structure of the dermal matrix. The graft provides a favorable microenvironment for bio-ingrowth to begin revascularization and cellular repopulation.
AlloSkin RT	AlloSkin RT meshed human dermal graft is a sterile skin graft with broad clinical applications for acute and chronic wound therapy.
Allowrap	Allowrap is a human amniotic membrane designed to provide a biologic barrier following surgical repair. There are few published studies addressing the use of Allowrap. Therefore, it is not possible to conclude whether Allowrap has a beneficial effect on health outcomes.
AmnioMatrix or BioDMatrix	AmnioMatrix and BioDMatrix are viable human multipotential placental cryopreserved allografts composed of morselized amniotic membrane and amniotic fluid components recovered from the same human donor (CMS, 2013). There are few published studies addressing the use of Amniomatrix or Biodmatrix. Therefore, it is not possible to conclude whether Amniomatrix or Biodmatrix has a beneficial effect on health outcomes.
AmnioExCel or BioDExCel	AmnioExCel (or BioDExCel) is a sterile, resorbable, noncrosslinked dehydrated human amnion membrane allograft composed of an epithelial layer and a stromal layer specifically processed for repair or replacement of lost or damaged dermal tissue (CMS, 2013). Authors from a prospective, open-label, randomized parallel group clinical trial evaluated dehydrated amniotic membrane allograft (DAMA) and SOC compared to SOC alone for the closure of chronic DFUs. The authors concluded the findings suggested DAMA is safe and effective in the management of DFUs but additional research is needed.
ArthroFLEX®	An acellular dermal matrix intended for supplemental support and covering for soft-tissue repair. Carpenter et al. (2017) conducted a study of a small case series to report the clinical results of interpositional arthroplasty using acellular dermal matrix in 4 patients (age 32 to 42 years) for the treatment of advanced ankle osteoarthritis. The primary findings included relief of pain, with improvement in tibiotalar joint range of motion from a mean of 16.5° preoperatively to a mean of 31° postoperatively. All 4 patients underwent open arthrotomy of the anterior and posterior tibiotalar capsule with plafond exostectomy and debridement of all deleterious tissue within the ankle capsule, and ArthroFlex acellular dermal matrix applied. The follow-up period ranged from 12 to 18 months. The mean pre- and 12-month postoperative Association of Orthopaedic Foot and Ankle Society hindfoot-ankle scale scores were 35 and 88.5, respectively. The authors concluded that these outcomes suggest that interpositional tibiotalar arthroplasty using an acellular dermal matrix is successful in improving function and range of motion and decreasing pain. This study is limited by a small number of participants and lack of a control arm. Larger randomized controlled trials are needed and should include longer follow-up periods, histologic testing, and arthroscopic evaluations to further assess the durability of this procedure. An ECRI report for Arthroflex Decellularized Dermal Allograft indicated that there is a very small amount of evidence available, and it is not possible to determine the safety and efficacy of ArthroFLEX for repair of rotator cuff tears (ECRI, 2017).
Architect Extracellular Collagen Matrix	Architect is a sterile, extracellular equine derived collagen matrix (ECM) that is intended to treat partial or full thickness skin wounds. Architect PX is a partially stabilized ECM comprised of equine pericardium that is indicated for the local management of moderately to heavy exuding wounds. Indicated for the local management of moderately to heavy exuding wounds, including: partial and full thickness wounds, draining wounds, pressure sores/ulcers, venous ulcers, chronic vascular ulcers, diabetic ulcers, trauma wounds (e.g., abrasions, lacerations, partial thickness burns, skin tears), surgical wounds (e.g., donor sites/grafts, post-laser surgery, post-Moh's surgery, podiatric wounds, dehisced surgical incisions). There are few published studies addressing the use of Architect extracellular matrix for wound treatment. Therefore, it is not possible to

Skin Substitute	Indication(s)
	conclude whether Architect extracellular matrix has a beneficial effect on health outcomes.
Aquacel Ag Advantage	An anti-microbial dressing that combines 2 technologies, including Hydrofiber Technology and Advantage Technology. Based on a review of available peer-reviewed published literature, there is very limited evidence regarding the use of Aquacel Ag+ Extra/Aquacel Ag Advantage dressing for the management of wounds. The lack of definitive conclusions addressing safety, clinical effectiveness, impact on health outcomes, and/or appropriate patient selection lead to no definitive conclusions
Bio-ConneKt Wound Matrix	Bio-ConneKt Wound Matrix (MLM Biologics) is a bioengineered skin substitute derived from equine Type I collagen. Bio-ConneKt is intended for management of moderately to heavily exuding wounds, including partial and full thickness wounds, draining & tunneling wounds, pressure sores/ulcers, venous ulcers, chronic vascular ulcers, diabetic ulcers, trauma wounds, and surgical wounds. There are few published studies addressing the use of Bio-ConnecKt for wound treatment. Therefore, it is not possible to conclude whether Bio-ConnecKt has a beneficial effect on health outcomes.
BioDfence and BioDfence DryFlex	BioDfence and BioDfence DryFlex are membrane allografts derived from the human placental tissues for use as a tissue barrier that covers and protects the underlying tissues. The FDA failed to identify any adverse events associated with BioDfence products. Hayes (2018) concluded that there is insufficient evidence to inform decisions in the safety and efficacy of the BioDfence allograft.
AmnioPro; BioSkin; BioSkin Flow; WoundEx Flow;	The BioFix Allograft Membrane and Allograft Membrane-Plus are dehydrated, decellularized amniotic membranes, intended for homologous use as a wound covering. WoundEx Flow consists of placental connective tissue matrix intended to replace or supplement damaged or inadequate connective tissue. AmnioPro Membrane is a human amniotic tissue allograft consisting of dehydrated and decellularized human amniotic membrane. FlowerPatch is dehydrated amniotic membrane allograft processed from human amniotic tissues. There is insufficient published evidence addressing the use of all dehydrated amniotic membrane human amniotic membranes indicated above. Therefore, it is not possible to conclude whether they have a beneficial effect on health outcomes.
DermACELL	Indications for use include: arterial ulcers, chronic wounds, deep wounds, diabetic foot ulcers, and pressure ulcers.
Dermavest	Dermavest and Plurivest (AediCell) are contiguous particularized sheets that contain a myriad of cell attachment proteins (CAP) including collagen, proteoglycans, polysaccharides, and cytokine/growth factors (GF's) that, combined with the structural aspects of the placental connective tissue matrix, act as a scaffold for cell infiltration and proliferation. There are few published studies addressing the use of Dermavest or Plurivest. Therefore, it is not possible to conclude whether Dermavest or Plurivest has a beneficial effect on health outcomes.
hmatrix PR ADM	Hmatrix PR ADM (Bacterin International, Inc.) is an acellular dermal matrix allograft derived from donated human skin. It is indicated to provide appropriate support and reinforcement for hernia and abdominal wall repairs. There are few published studies addressing the use of hmatrix. Therefore, it is not possible to conclude whether hmatrix has a beneficial effect on health outcomes.
Excellagen	Excellagen is a pharmaceutically formulated fibrillary Type I bovine collagen gel for wound care management. Indicated for the management of wounds including partial and full thickness wounds, pressure ulcers, venous ulcers, diabetic ulcers, chronic vascular ulcers, tunneled/ undermined wounds, surgical wounds (e.g., donor sites/grafts, post-Moh's surgery, post-laser surgery, podiatric, wound dehiscence), trauma wounds (e.g., abrasions, lacerations, second-degree burns, skin tears) and draining wounds. There are few published studies addressing the use of Excellagen for wound treatment. Therefore, it is not possible to conclude whether Excellagen has a beneficial effect on health outcomes.

Skin Substitute	Indication(s)
E-Z Derm	E-Z Derm Biosynthetic Wound Dressing is a porcine-derived xenograft that has been chemically cross-linked with an aldehyde to provide durability and storage. The dermal elements from the original pig dermis are likely all deactivated in the chemical process, unlike the frozen pig dermis which is still available. The studies are limited addressing the use of E-Z Derm for wound care management.
Integra Bilayer Matrix Wound Dressing (BMWD)	An advanced wound care device comprised of a porous matrix of cross-linked bovine tendon collagen and glycosaminoglycan and a semi-permeable polysiloxane (silicone layer). Integra was cleared for marketing under the 510(k) process in August 2002 and is indicated "for the management of wounds including partial and full-thickness wounds, pressure ulcers, venous ulcers, diabetic ulcers, chronic and vascular ulcers, surgical wounds (donor sites/grafts, post-Mohs surgery, post-laser surgery, podiatric, wound dehiscence), trauma wounds (abrasions, lacerations, second-degree burns, and skin tears) and draining wounds. This device is intended for one-time use."
Integra Dermal Regeneration Template (IDRT) and Integra Omnigraft Dermal Regeneration Template:	Omnigraft Dermal Regeneration Matrix (Omnigraft) is an advanced wound care device, comprised of a porous matrix of cross-linked bovine tendon collagen and glycosaminoglycan with a polysiloxane (silicone) layer. In January 2016, the FDA approved the Integra Dermal Regeneration Template (Omnigraft Dermal Regeneration Template) for certain diabetic foot ulcers that last for longer than 6 weeks and do not involve exposure of the joint capsule, tendon or bone, when used in conjunction with standard diabetic ulcer care. The approval was based upon the clinical results of a multi-center, randomized, controlled clinical trial (the Foot Ulcer New Dermal Replacement Study (FOUNDER) Study) (Driver et al, 2015).
Graftjacket Tissue Matrix	Graftjacket tissue matrix is a wound care product derived from cadaveric skin, which undergoes a process that removes the epidermis and dermal cells. Graftjacket tissue matrix is an acellular regenerative tissue matrix that is designed to provide a scaffold for wound repair. Graftjacket tissue matrix is indicated for full-thickness diabetic foot ulcers greater than three week duration that extend through the dermis, but without tendon, muscle, joint capsule or bone exposure.
Mediskin	Mediskin (Brennen Medical, Inc., St. Paul, MN) is a frozen porcine xenograft with a dermal and epidermal layer. The xenograft is 510(k) approved by the FDA as a collagen wound dressing. Per the manufacturer proposed uses include: temporary coverage prior to autograft, partial thickness skin loss, protect meshed autografts, outpatient skin loss, donor sites, skin ulcerations and abrasions. MoInlycke Health Care LLC is the supplier of Mediskin. There are few published studies addressing the use of Mediskin for wound treatment. The use of porcine-derived decellularized fetal skin products (e.g., Mediskin®) has not been established since there are currently no published studies addressing the use of Mediskin.
MemoDerm Acellular Dermal Matrix; DermaSpan; TranZgraft; IntegUPly	A skin substitute that derives from human allograft tissue and is manufactured using a proprietary gamma irradiation sterilization process. It is markets for use for joint surgeries and chronic diabetic foot ulcers.
PriMatrix Dermal Repair Scaffold	PriMatrix (Integra Life Sciences, Inc.) is a bovine derived acellular dermal matrix indicated for the treatment of a variety of wounds. There is insufficient scientific evidence regarding the effectiveness of PriMatrix acellular dermal tissue matrix for wound healing. Available evidence is comprised primarily of small, retrospective studies. A systematic evidence review of wound healing products prepared for the Agency for Healthcare Research and Quality found no studies of PriMatrix of sufficient quality to meet criteria for inclusion in the systematic evidence review (Snyder et al, 2012). In a prospective multi-center study, Kavros et al (2014) evaluated the healing outcomes of chronic diabetic foot ulcers treated with PriMatrix, a fetal bovine acellular dermal matrix. The authors concluded that the findings of this of this multi-center prospective study suggested that PriMatrix used in conjunction with a center's standard of care wound therapy offers a cost-effective

Skin Substitute	Indication(s)
	strategy to heal diabetic foot ulcers over that of other advanced wound therapy products based on 12-week healing outcomes as well as number of applications needed to achieve successful closure. The main drawback of this study was the lack of a direct comparison within the study to standard of care as well as to other advanced therapies. The authors stated that the findings from this study should be expanded to include these clinical efficacy comparisons as well as cost-effectiveness comparisons in order to maximize health benefits per dollar spent for the treatment of diabetic foot ulcers.
GammaGraft	GammaGraft (Promethean LifeSciences, Inc., Pittsburgh, PA) is an irradiated human skin allograft acquired from cadaveric donors. Indications for use include: venous stasis ulcers, diabetic foot ulcers, full thickness ulcers, Moh's surgery sites, skin graft donor sites, partial thickness wounds, and areas of dermabrasion. Sivak et al. (2016) conducted a retrospective review of patients undergoing scalp reconstruction utilizing GammaGraft and subsequent skin grafting with GammaGraft. This study is limited by a small number of patients. Further research with randomized controlled trials is needed to validate these findings. The PA DHS Technology Assessment Group (TAG) made an option #4 coverage decision which indicates a lack of peer-reviewed published literature.
Graftjacket Xpress Flowable Soft Tissue Scaffold	Graftjacket Xpress Flowable Soft-Tissue Scaffold is a micronized (finely ground) decellularized soft tissue scaffold indicated for the repair or replacement of damaged or inadequate integumental tissue, specifically deep, dermal wounds that exhibit tunneling, and extension from the wound base that may extend deep into the tendon and bone. Graftjacket Xpress is a soft tissue graft (reconstituted as a "gel"), which is comprised solely of human dermal tissue, including its native protein and collagen structure and essential biochemical composition. The re-hydrated skin substitute scaffold is placed into the tunnels or tracts and is intended to produce the same or superior clinical outcomes with a minimally invasive procedure. There is a lack of peer-reviewed published medical literature on the effectiveness and safety of the Graftjacket Xpress.
Hyalomatrix PA	Hyalomatrix is a bilayered wound dressing composed of a nonwoven pad made of a benzyl ester of hyaluronic acid, a long-acting derivative of hyaluronic acid, and a semipermeable silicone membrane providing a microenvironment (Snyder, et al., 2012). Hyalomatrix KC Wound Dressing was cleared for marketing under the 510(k) process in July 2001 for "the management of wounds in the granulation phase such as pressure ulcers, venous and arterial leg ulcers, diabetic ulcers, surgical incisions, second degree burns, skin abrasions, lacerations, partial-thickness grafts and skin tears, wounds and burns treated with meshed grafts. Alvarez and colleagues (2017) provided an analysis of a prospective, parallel, and randomized, single-center study involving 16 subjects in an outpatient wound care center setting. The aim of the study was to evaluate the safety and effectiveness of a hyaluronic acid extracellular matrix for the treatment of chronic VLUs. The authors concluded that the findings of this interim analysis indicated that continuation of the present study is needed. They stated that a more reliable power calculation from these findings forecasts that the inclusion of 50 to 60 participant would be needed to achieve the statistical goal ($p < 0.05$) related to the primary end-point.
Integuply	Integuply is an acellular human dermis derived from aseptically processed human allograft skin tissue. It is indicated for the repair or replacement of damaged or inadequate integumental tissue or for other homologous uses of human integument. Typically used in conjunction with a chronic wound care management regimen for the treatment of diabetic ulcers, Charcot foot ulcers, venous ulcers, trauma wounds, pressure ulcers, partial and full thickness wounds, and surgical wounds.
Marigen Omega3 Acellular Dermal Matrix	Marigen is an omega 3, acellular, dermal extracellular matrix xenograft made from fish (piscine) dermis (CMS, 2014). Indicated for the management of wounds including: partial and full-thickness wounds, pressure ulcers, venous ulcers, chronic vascular ulcers, diabetic ulcers, trauma wounds (e.g., abrasions, lacerations, second-degree burns, skin tears), surgical wounds (e.g., donor sites/grafts, post-Moh's surgery, post-laser surgery, podiatric, wound dehiscence), and draining wounds.

Skin Substitute	Indication(s)
MatriDerm	MatriDerm (MedSkin Solutions Dr. Suwelack AG) is a dermal substitute composed of bovine collagen and elastin that is intended to serve as a scaffold for skin restoration.
MatriStem Wound Matrix and MatriStem MicroMatrix	MatriStem (ACell Inc.) products consist of collagens, carbohydrates, and proteins derived from the urinary bladder tissue of pigs. MatriStem is intended for surgical wound care, pelvic floor support or reconstruction, burns, and wound healing. Intended for the management of topical wounds including: partial and full-thickness wounds, pressure ulcers, venous ulcers, diabetic ulcers, chronic vascular ulcers, tunneled/undermined wounds, surgical wounds (e.g., donor sites/grafts, post-Moh's surgery, post-laser surgery, podiatric, wound dehiscence), trauma wounds (e.g., abrasions, lacerations, second-degree burns, and skin tears), and draining wounds. Frykberg et al (2016) reported on an interim analysis of a prospective, multicenter clinical study is to assess the application of MatriStem MicroMatrix (MSMM) and MatriStem Wound Matrix (MSWM) (porcine urinary bladder derived extracellular matrix) compared with Dermagraft (DG) (human fibroblast-derived dermal substitute) for the management of non-healing diabetic foot ulcers (DFUs). A Hayes report for MatriStem Urinary Bladder Matrix Products concluded that the evidence from small studies suggest a potential benefit in wound management, but longer follow-ups and larger studies are needed to confirm these benefits (Hayes, 2017).
Neox 100 Wound Matrix, Neox 1k Wound Matrix and Neox Flo	Neox Wound Allografts (Amniox® Medical, Inc.) are comprised of two products, Neox CORD 1K Wound Allograft which is a cryopreserved human umbilical cord and amniotic membrane; and NEOX 100 Wound Allograft which is a cryopreserved human amniotic membrane indicated for minor and superficial dermal wounds. Neox Flo is a particulate form of Neox. Used in the treatment of partial- and full-thickness wounds including: diabetic foot ulcers, venous leg ulcers, arterial ulcers, and pressure ulcers. There are few published studies addressing the use of Neox Flo and therefore, there is no evidence to conclude beneficial health outcomes.
NuShield	NuShield (NuTech) is a protective patch derived from amniotic membrane and is indicated as an adhesion barrier, wound covering, and acts as an adjunct to soft tissue healing, and is intended for use in spinal surgery and as a protective barrier for tendons and nerves following tendon repair. Intended to be applied as an on-lay graft for acute and chronic wounds, including, but not limited to, neuropathic ulcers, venous stasis ulcers, pressure ulcers, burns, post-traumatic wounds and post-surgical wounds. There are few published studies addressing the use of Nushield. Therefore, it is not possible to conclude whether Nushield has a beneficial effect on health outcomes.
PuraPly; PuraPly Antimicrobial Wound Dressing	PuraPly is a dressing made of porcine intestinal collagen matrix that is coated with polyhexamethylene biguanide hydrochloride (PHMB) antimicrobial agent. It is intended for wound care management. There are few published studies addressing the use of PuraPly or PuraPly Antimicrobial for wound treatment. Therefore, it is not possible to conclude whether PuraPly or PuraPly Antimicrobial has a beneficial effect on health outcomes. According to Hayes (2020), There is insufficient quantity of published, peer-reviewed, human clinical data to evaluate PuraPly AM Wound Matrix for treatment of wounds in a health technology assessment (HTA).
Repriza	Repriza is a prehydrated, ready-to-use, acellular dermal matrix derived from human allograft tissue. Repriza is a surgical implant and does not have any other use outside of the surgical setting. There is no indications that are specific to VLUs or DFUs. Also, there are few published studies addressing the use of Reprize. Therefore, it is not possible to conclude whether Reprize has a beneficial effect on health outcomes.
Revitalon	Revitalon is a human tissue allograft made of donated amniotic membrane derived from the inner lining of donated placenta. Revitalon can be used as a covering for full-thickness wounds, damaged membranes, and as a dressing for burns. It is comprised of native human amnion and chorion consisting of collagen types I, III, IV, V, VI, laminin, fibronectin, nidogen, and proteoglycans. Indicated for the management of wounds including: diabetic ulcers and venous ulcers. There are few published studies addressing the use of Revitalon

Skin Substitute	Indication(s)
	for wound treatment. Therefore, it is not possible to conclude whether Revitalon has a beneficial effect on health outcomes.
Stravix and Stravix PL	Stravix is a cryopreserved human placental tissue composed of umbilical amnion and Wharton's jelly. Stravix retains the native collagen and hyaluronic acid-rich extracellular matrix (ECM), endogenous growth factors, and endogenous cells including epithelial cells, fibroblasts, and mesenchymal stem cells (MSCs) found in placental tissue.
Talymed	Talymed is a wound care management product composed of shortened fibers of poly-N-acetyl glucosamine (pGlcNAc) isolated from microalgae. It is indicated for the management of a range of serious, complex wounds. Kelechi et al. (2012) conducted a randomized controlled investigator blinded pilot study to evaluate the efficacy, safety, and tolerability of Talymed among patients with venous leg ulcers (VLUs) compared to treatment with standard care plus pGlcNAc or to standard care alone. It was concluded that the results of this pilot study suggest that the pGlcNAc advanced wound-healing technology is well tolerated and effective. This study was limited by the small sample size and patients unblinded to treatment allocation. Further research with randomized controlled trials is needed to validate these findings.
TenSIX Acellular Dermal Matrix	TenSIX is an acellular dermal matrix with natural histomorphology preserved. TenSIX is derived from aseptically processed cadaveric human skin tissue that is terminally sterilized.
TranZgraft Acellular Dermal Matrix (Memoderm)	TranZgraft (AZIYO® Biologics) is an acellular collagen matrix intended for repair of sports related injuries, including tendons and ligaments. There are few published studies addressing the use of TranZgraft. Therefore, it is not possible to conclude whether this product has a beneficial effect on health outcomes.
Unite Biomatrix	Unite Biomatrix is a non-reconstituted collagen dressing used to maintain the wound bed in the healing phase thereby allowing for health granulation tissue and wound closure. Unite Biomatrix may be applied to discrete areas of the wound that have not yet healed satisfactorily. Unite Biomatrix is packaged in a solution and is available pre-fenestrated or non-fenestrated. Unite Biomatrix differs from other skin products in that it is composed of decellularized equine pericardial implants. The use of equine-derived decellularized collagen products has not been established as shown by the lack of evidence on the subject.
XCM Biologic Tissue Matrix	XCM Biologic Tissue Matrix is a sterile non-crosslinked 3-D derived from porcine dermis. It is indicated for the use in general surgical procedures for the reinforcement and repair of soft tissue where weakness exists. A systematic review and meta-analysis was conducted to evaluate the clinical and patient-centered outcomes of XCM Biologic tissue matrix compared with other mucogingival procedures (Atieh, 2016). The authors reported limited evidence that may improve aesthetic satisfaction, reduce postoperative morbidity, and shorten operating time. Further long-term randomized controlled trials are required to endorse the supposed advantages of XCM.
Kerecis Omega3/ Kerecis Omega3 MariGen Shield	Kerecis Omega3 Wound is a decellularized intact fish skin developed for the management of chronic wounds, such as diabetic wounds, pressure ulcers, and vascular ulcers, as well as surgical wounds, trauma wounds and other wounds which are commonly treated in the private office and wound care centers. The fish skin sheets contain fat, protein, elastin, glycans and other natural skin elements and are provided in different sizes.

Reimbursement

Participating facilities will be reimbursed per their Highmark Wholecare℠ contract.

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