Policy

DEPARTMENT: Utilization Management	**POLICY #:** UM.045
TITLE: Skin Substitute Grafts/Cellular and Tissue-Based Products	**VERSION:** 1.0
REVIEW APPROVED BY: Stefanie Caswell	**REVIEW APPROVAL DATE: 1/6/25**
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RELATED DEPARTMENTS:	
DEPENDENCIES: N/A	

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Purpose

This policy outlines the coverage criteria for skin substitutes. To qualify as a skin substitute graft/CTP the product must be:

1. A non-autologous human cellular or tissue product (e.g., dermal or epidermal, cellular and acellular, homograft or allograft), OR non-human cellular and tissue product (i.e., xenograft), OR biological product (synthetic or xenogeneic) applied as a sheet, allowing scaffold for skin growth, intended to remain on the recipient and grow in place or allow recipient's cells to grow into the implanted graft material AND
2. Supported by high-certainty evidence to demonstrate the product's safety, effectiveness, and positive clinical outcomes

Definitions, Abbreviations, and Acronyms

Acronym	Meaning
DME	Durable Medical Equipment
DFU	Diabetic Foot Ulcer
VLU	Venous Leg Ulcer
SOC	Standard of Care
AHRQ	Agency for Healthcare Research and Quality (AHRQ)

Policy

This policy has been developed to parallel information noted in alignment with two primary sources:

- L36377 Skin Substitute Grafts/Cellular and Tissue-Based Products for the Treatment of Diabetic Foot Ulcers and Venous Leg Ulcers
    - This LCD is not applicable in all states. For those states, the language of the LCD is being adopted in this policy.
- Technology Assessment Program: Skin Substitutes for Treating Chronic Wounds by the Agency for Healthcare Research and Quality (AHRQ)

  https://www.cms.gov/Medicare/Coverage/DeterminationProcess/downloads/id109TA.pdf

All skin substitutes require a prior authorization to determine the appropriateness of their use. This class of wound care is developing, and the research is in some instances limited and

emerging. This policy seeks to clarify the appropriate use cases for skin substitutes as defined by the research available.

Clinical Indications

Based on the findings from the literature review performed by AHRQ, there are the majority of studies available for review examined treatment options for diabetic foot ulcers. In L36377 Skin Substitute Grafts/Cellular and Tissue-Based Products for the Treatment of Diabetic Foot Ulcers and Venous Leg Ulcers, some additional indications have been noted for venous leg ulcers. The literature review from AHRQ notes that their review "did not identify sufficient evidence for pressure ulcers and arterial leg ulcers."

As such, skin substitutes are not proven effective for the treatment of pressure ulcers or arterial ulcers and are therefore not covered to be used for these wounds. There may be other indications for skin substitutes, such as burns, and these less common applications are not covered in this policy. Skin substitutes for use in conditions not outlined in this policy are still subject to prior authorization and appropriate guidance will be applied in the review of those instances.

Coverage Criteria- Diabetic Foot Ulcers and Venous Leg Ulcers

Application of a skin substitute graft/CTP in the treatment of DFUs and VLUs is considered reasonable and necessary:

1. The presence of a chronic, non-infected DFU having failed to achieve at least 50% ulcer area reduction with documented standard of care (SOC) treatment (outlined below) for a minimum of 4 weeks with documented compliance.
2. The presence of a chronic, non-infected VLU having failed to respond to documented SOC treatment (outlined below) for a minimum of 4 weeks with documented compliance. SOC treatment includes:
    - Comprehensive patient assessment (history, exam, vascular assessment) and diagnostic tests as indicated as part of the implemented treatment plan.
    - For patients with a DFU: assessment of Type 1 or Type 2 diabetes and management history with attention to certain comorbidities (e.g., vascular disease, neuropathy, osteomyelitis), review of current blood glucose levels/hemoglobin A1c (HbA1c), diet and nutritional status, activity level, physical exam that includes assessment of skin, ulcer, and vascular perfusion, and assessment of off-loading devices or use of appropriate footwear.
    - For patients with a VLU: assessment of clinical history (that includes prior ulcers, body mass index, history of pulmonary embolism or superficial/deep venous thrombosis, number of pregnancies, and physical inactivity), physical exam (edema, skin changes and vascular competence), evaluation of venous reflux,

perforator incompetence, and venous thrombosis. The use of a firm strength compression garment (>20 mmHg) or multi-layered compressive dressing is an essential component of SOC for venous stasis ulcers.

3. An implemented treatment plan to be continued throughout the course of treatment demonstrating all the following:
    - Debridement as appropriate to a clean granular base.
    - Documented evidence of offloading for DFUs.
    - Documented evidence of sustained compression dressings for VLUs.
    - Infection control with removal of foreign body or focus of infection.
    - Management of exudate with maintenance of a moist environment.
    - Documentation of smoking history, and counselling on the effect of smoking on wound healing. Treatment for smoking cessation and outcome of counselling (if applicable).
4. The skin substitute graft/CTP is applied to an ulcer that has failed to heal or has stalled in response to documented SOC treatment. Documentation of response to treatment requires measurements of the initial ulcer, pre-SOC ulcer measurements, weekly SOC ulcer measurements, post-completion SOC ulcer measurements following (at least) 4 weeks of SOC treatment, ulcer measurements at initial placement of the skin substitute graft/CTP, and before each subsequent placement of the skin substitute graft/CTP. Failure to heal or stalled response despite standard of care measures must have preceded the application for a minimum of 4 weeks and established SOC treatment must continue for the course of therapy. Continuous compression therapy for VLUs must be documented for the episode of care.
5. The medical record documentation must include the interventions having failed during prior ulcer evaluation and management. The record must include an updated medication history, review of pertinent medical problems diagnosed since the previous ulcer evaluation, and explanation of the planned skin replacement with choice of skin substitute graft/CTP. The procedure risks and complications must also be reviewed and documented.
6. The patient is under the care of a qualified provider for the treatment of the systemic disease process(es) etiologic for the condition (e.g., venous insufficiency, diabetes, neuropathy) and documented in the medical record.

<u>The following are considered reasonable and necessary (per episode of care):</u>

1. The maximum number of applications of a skin substitute graft/CTP within the episode of skin replacement therapy (defined as 12 to 16 weeks from the first application of a skin substitute graft/CTP) is 8 applications. The mean number of skin substitute graft/CTP

applications associated with wound healing is 4; however, with documentation of progression of wound closure under the current treatment plan and medical necessity for additional applications, up to 8 applications may be allowed. Use of greater than 4 applications requires an attestation from the provider showing that requirements have been met and the additional applications are medically necessary. In absence of this attestation, denial of the additional applications will occur.

2. The usual episode of care for skin substitute grafts/CTP is 12 weeks; however, some wounds may take longer to heal therefore 16 weeks is allotted with documentation that includes progression of wound closure under current treatment plan.
3. The skin substitute graft/CTP must be used in an efficient manner utilizing the most appropriate size product available at the time of treatment.
    - Excessive wastage (discarded amount) should be avoided by utilization of size appropriate packaging of the product consistent with the wound size. The graft must be applied in a single layer without overlay of product or adjacent skin in compliance with the correct label application techniques for the skin substitute graft/CTP.
4. Only skin substitute grafts/CTP with labeled indications for use over exposed muscle, tendon, or bone will be considered reasonable and necessary for those indications.

<u>The following are considered not reasonable and necessary</u>:

1. Greater than 8 applications of a skin substitute graft/CTP within an episode of care (up to 16 weeks).
2. Repeat applications of skin substitute grafts/CTP when a previous application was unsuccessful. Unsuccessful treatment is defined as increase in size or depth of an ulcer, no measurable change from baseline, and no sign of improvement or indication that improvement is likely (such as granulation, epithelialization, or progress towards closure).
3. Application of skin substitute grafts/CTP in patients with inadequate control of underlying conditions or exacerbating factors, or other contraindications (e.g., active infection, progressive necrosis, active Charcot arthropathy of the ulcer extremity, active vasculitis, or ischemia).
4. Use of surgical preparation services (e.g., debridement), with routine, simple, or repeat skin replacement surgery with a skin substitute graft/CTP.
5. All liquid or gel skin substitute products/CTP for ulcer care.
6. Placement of skin substitute grafts/CTP on an infected, ischemic, or necrotic wound bed.

Covered Products- DFU & VLU

The appropriateness of skin substitutes is based on the supporting evidence that the skin substitute is appropriate. Not all skin substitutes have been shown effective in the research to treat chronic wounds. Below is a list of indications and non-covered indications for products for which value has been established for certain conditions. Only those products listed below will be covered and only for those indications noted:

Product	Indications	Non-Covered Indications based on lack of research to support use
Affinity	DFU	VLU Pressure Injuries Arterial Wounds
AmnioBand, guardian	DFU VLU	Pressure Injuries Arterial Wounds
Apligraf (GraftSkin)	DFU VLU	Pressure Injuries Arterial Wounds
DermACELL, awm, porous	DFU	VLU Pressure Injuries Arterial Wounds
Derma-Gide	DFU	VLU Pressure Injuries Arterial Wounds
Dermagraft	DFU VLU	Pressure Injuries Arterial Wounds
Epicord	DFU	VLU Pressure Injuries Arterial Wounds
Epifix	DFU VLU	Pressure Injuries Arterial Wounds
FlexHD or AllopatchHD	DFU	VLU Pressure Injuries Arterial Wounds
Grafix stravix prime pl	DFU	VLU Pressure Injuries Arterial Wounds
GraftJacket	DFU	VLU Pressure Injuries Arterial Wounds
Integra or Omniograft dermal	DFU	VLU

regeneration template		Pressure Injuries Arterial Wounds
Kerecis Omega3/ Kerecis omega3, MariGen shield	DFU	VLU Pressure Injuries Arterial Wounds
NuShield	DFU	VLU Pressure Injuries Arterial Wounds
Oasis wound matrix	DFU	VLU Pressure Injuries Arterial Wounds
PriMatrix	DFU	VLU Pressure Injuries Arterial Wounds
Theraskin	DFU	VLU Pressure Injuries Arterial Wounds

Non-Covered Products- DFU & VLU

Some skin substitutes have not been shown effective at treating chronic wounds. These will not be covered for any condition unless additional and more supportive research is released supporting their use:

Skin Substitutes **(Per sq cm unless otherwise stated)**	**Evidence** **(Published, peer reviewed literature to support use in chronic DFU/VLU)**	**Comment**
Ac5 advanced wound system (ac5)	No literature found	
Acesso dl, Acesso tl	No literature found	
Activate matrix	No literature found	
AlloDerm	Evidence in breast surgery and hernia repair	Insufficient evidence for DFU/VLU
Allogen, per cc	No literature found	

Alloskin, Alloskin ac	Evidence in burn and orthopedics.	Insufficient evidence for DFU/VLU
Allowrap DS or DRY	Literature in tarsal tunnel, thoracic outlet syndrome, proctectomy, and burns.	Insufficient evidence for DFU/VLU
American amnion, American amnion AC, American Amnion, Tri-Layer	No literature found	
Amnio bio or axobiomembrane	No literature found	
Amnio quad-core	No literature found	
Amnio Wound	No literature found	
Amnioamp-MP	No literature found	
Amnioarmor	No literature found	
AmnioBand particulate, 1 mg	No literature found	
Amniocore, Amniocore pro, Amniocore pro+	No literature found	
Amniocyte plus, per 0.5cc	No literature found	
Amnioexcel, Amnioexcel plus or biodexcel	Small RCT	Insufficient evidence (see LCD section Amnioexcel)
Amniomatrix or Biodmatrix, injectable, 1 cc	No literature found	
Amnio-maxx or amnio-maxx lite	No literature found	
Amniorepair or Altiply	No literature found	
Amniotext patch	Case report	Insufficient evidence

Amniotext, per cc	No literature found	
Amnio-tri-core amniotic	No literature found	
Amniowrap2	No literature found	
Amniply, for topical use only	No literature found	
Apis	Retrospective comparative study of 47 wounds, case series	Insufficient evidence (see section on Apis)
Architect ecm px fx	No literature found	
Artacent ac, 1 mg	No literature found	
Artacent am	Observational study (n=26)	Insufficient evidence
Artacent cord	No literature found	
Artacent wound	Observational study (n=26)	Insufficient evidence
Arthroflex	Evidence for rotator cuff repair	Insufficient evidence for DFU/VLU
Ascent, 0.5 mg	No literature found	
Axolotl ambient or axolotl cryo, 0.1mg	Case report	Insufficient evidence
Axolotl graft or axolotl dualgraft	Case report, literature in Mohs surgery	Insufficient evidence
Barrera SL or barrera dl	No literature found	
Bellacell HD or Surederm	Literature for breast surgery	Insufficient evidence for DFU/VLU
Bio-connekt wound matrix	No literature found	
BioDFence dryflex	No literature found	
Bionextpatch	No literature found	

Biovance, Biovance Tri-Layer or biovance 3L	Observational study, case series	Insufficient evidence
Carepatch	No literature found	
Celera dual layer or celera dual membrane	No literature found	
Cellesta cord, Cellesta or Cellesta Duo	No literature found	
Cellesta flowable amnion per 0.5cc	No literature found	
Cocoon membrane	No literature found	
Cogenex amniotic membrane	No literature found	
Cogenex flowable amnion, per 0.5cc	No literature found	
Coll-e-derm	No literature found	
Complete aa, Complete aca, Complete sl, Complete ft	No literature found	
Corecyte, for topical use only, per 0.5cc	No literature found	
Coretext or protext, per cc	No literature found	
Corplex	No literature found	
Corplex P, per cc	No literature found	
Cryo-cord	No literature found	
Cygnus	No literature found	
Cygnus dual	No literature found	
Cygnus, matrix	Lab study	Insufficient evidence

Cymetra, injectable, 1 cc	No literature found	
Cytal (formerly Matristem)	One RCT and 2 case series	Insufficient evidence
Dermabind dl, Dermabind ch, Dermabind sl	No literature found	
DermaBind tl or Amniobind	No literature found	
Dermacyte amniotic membrane allograft	Case report, Retrospective comparative report (n=18)	Insufficient evidence
Dermapure	Retrospective review (n=37), Observational study (n=20)	Insufficient evidence
Dermavest, plurivest	Case series, Lab study	Insufficient evidence
Derm-maxx	No literature found	
Emerge matrix	No literature found	
Enverse	No literature found	
Epieffect	No literature found	
EpiFix injectable, 1 mg	No literature found	
Esano a, Esano aaa, Esano ac, Esano aca	No literature found	
Excellagen, 0.1cc	Lab paper	Insufficient evidence
EZ-derm	Evidence in burns	Insufficient evidence for DFU/VLU
Floweramnioflo, 0.1 cc	No literature found	
Floweramniopatch	No literature found	
Flowerderm	No literature found	
Fluid flow or fluid gf, 1 cc	No literature found	
Gammagraft	Bench/ case report	Insufficient evidence

Genesis amniotic membrane	No literature found	
Grafix core, grafixpl core	Prospective study in 31 complex wounds achieving 59% closure. Retrospective report (n=441) Case series for VLU	Insufficient evidence
Grafix plus	No literature found	
GraftJacket Xpress, injectable, 1 cc	Lab study	Insufficient evidence
Helicoll	Literature for split-thickness graft donor sites.	Insufficient evidence for DFU/VLU
Hmatrix	Evidence in breast surgery, head and neck, and hand/arm reconstruction, and abdominal wall closure.	Insufficient evidence for DFU/VLU
Hyalomatrix	Evidence in burns, trauma, skin cancer. Evidence in ulcer management includes case series and a review article	Insufficient evidence
Impax, Impax dual layer membrane, Impax dual later amniotic graft	No literature found	
Innovaburn or Innovamatrix xl	Review paper	Insufficient evidence
Innovamatrix ac, Innovamatrix fs	No literature found	

Innovamatrix pd 1mg	No literature found	
Integra bilayer dermal matrix wound dressing	No literature found	
Integra flowable wound matrix, injectable, 1 cc	No literature found	
Integra Meshed Bilayer Wound Matrix	No literature found	
Interfyl, 1 mg	Literature on soft tissue reconstruction	Insufficient evidence for DFU/VLU
Keramatrix or Kerasorb	No literature found	Insufficient evidence
Keroxx (2.5G/CC), 1 cc	No literature found	
Lamellas xt, Lamellas	No literature found	
Matriderm	One RCT and case series	Insufficient evidence for DFU/VLU
Matrion	No literature found	
Matristem micromatrix, 1 mg, MAtristem wound matrix, Matristem burn matrix	One RCT and 2 case series	Insufficient evidence for DFU/VLU
Mediskin	Evidence for split-thickness graft donor sites.	Insufficient evidence for DFU/VLU
Membrane graft or membrane wrap	No literature found	
Membrane wrap-hydro	No literature found	
Memoderm, Dermaspan, Tranzgraft, or Integuply	Case report	Insufficient evidence
Mgl-complete	No literature found	

Microlyte, Matrix	Prospective observational study in 35 chronic wounds with 91% healing or improved at 12 weeks.	Insufficient evidence
Miro3d	No literature found	
Miroderm	Prospective pilot study in 7 wounds, and prospective observational study of 38 ulcers.	Insufficient evidence
Mirragen adv wnd matrix	Bench papers/ case series, small RCT/ review paper	Insufficient evidence
MyOwnSkin	No literature found	
Neomatrix	No literature found	
Neopatch or Therion	No literature found	
Neostim tl, Neostim membrane, Neostim dl	No literature found	
Neox 100 or clarix 100	No literature found	
Neox cord 1K, Neox Cord rt, or Clarix cord 1K	Prospective trial (n=32) basic science report, case series and small retrospective reports	Insufficient evidence
Neox Flo or Clarix Flo, 1 mg	Case series	Insufficient evidence
Novachor	No literature found	
Novafix, Novafix dl	No literature found	
Novosorb Synpath Dermal Matrix	Book chapter (bench studies) (review article)	Insufficient evidence

Nudyn dl or nudyn dl mesh, Nudyn sl or nudyn slw	No literature found	
Oasis burn matrix	No literature found	
Oasis Tri-Layer Matrix	RCT (n=82) reported on wound closure at 12 weeks with 54% for Oasis Tri-layer and 32% for SOC.	Insufficient evidence for DFU/VLU
Omeza collagen matrix, per 100 mg	Bench papers	Insufficient evidence lacks clinical studies
Orion	No literature found	
Palingen or Promarx, 0.36 mg per 0.25cc	Literature in plantar fasciitis	Insufficient evidence for DFU/VLU
Palingen, palingen xplus, or Promarx	Literature in plantar fasciitis	Insufficient evidence for DFU/VLU
Permeaderm b, Permeaderm c	No literature found	
Phoenix wound matrix	Case series	Insufficient evidence
Polycyte, for topical use only, per 0.5cc	No literature found	
Porcine implant, Permacol	Evidence in hernia repair	Insufficient evidence for DFU/VLU
Procenta, per 200 mg	No literature found	
Progenamatrix	Case series	Insufficient evidence
PuraPly, PuraPly xt	Prospective, noninterventional study (n=307)	Insufficient evidence

PuraPly, am	Prospective, noninterventional study (n=307), case series	Insufficient evidence
Rebound matrix	No literature found	
Reguard, for topical use	No literature found	
Relese	No literature found	
Repriza	Literature in plastic surgery	Insufficient evidence for DFU/VLU
Resolve matrix	No literature found	
Restorigin	No literature found	
Restorigin, 1 cc	No literature found	
Restrata	RCT (n=46) with complete wound closure over 12 weeks in 56% (25/46) in the treatment group vs. 29% (21/46) in the SOC group. Retrospective review 82 wounds	1. High risk of bias due to blinding and outcome measures.[151] 2. Insufficient evidence due to low certainty[149]
Revita	No literature found	
Revitalon	No literature found	
Revoshield + amniotic barrier, per sq cm	No literature found	
Sanopellis	No literature found	
Signature apatch	No literature found	
Skin te	No literature found	
Strattice TM	Evidence in abdominal wall closure/hernia repair	Insufficient evidence for DFU/VLU

Supra sdrm	One RCT	Insufficient evidence for DFU/VLU
Suprathel	No literature found	
Surfactor or Nudyn, per 0.5cc	No literature found	
Surgicord	No literature found	
Surgigraft, Surgraft tl, Surgraft ft, Surgraft xt, Surgigraft-dual	No literature found	
SurgiMend Collagen Matrix, per 0.5 sq cm	Evidence in breast surgery	Insufficient evidence for DFU/VLU
Surgraft	No literature found	
Symphony	No literature found	
Tag	No literature found	
Talymed	One RCT, one case report, literature on use in bone wound healing and lab research.	Insufficient evidence
Tensix	Case reports	Insufficient evidence
Theragenesis	Retrospective report, case series, animal studies, evidence in trauma, burn, necrotizing fasciitis and other conditions but not specific to DFU/VLU.	Insufficient evidence for DFU/VLU
Transcyte	Literature in burns	Insufficient evidence for DFU/VLU
Truskin	No literature found	

Unite biomatrix	Abstract and case report.	Insufficient evidence
Via Matrix	No literature found	
Vendaje, Vendaje ac	No literature found	
VIM	No literature found	
Woundex flow, Bioskin flow, 0.5 cc	No literature found	
Woundex, BioSkin	Retrospective study (n=20).	Insufficient evidence
Woundfix, Biowound, Woundfix plus, biowound plus, Woundfix xplus or biowound xplus	No literature found	
Woundplus membrane or e-graft	No literature found	
Xcell amnio matrix	No literature found	
Xcellerate	No literature found	
Xcellistem, 1 mg	No literature found	
XCM biologic tissue matrix	Literature for chest wall defects	Insufficient evidence for DFU/VLU
Xwrap	No literature found	
Zenith amniotic membrane	No literature found	

Change Log

Document Version	Major or Minor Revision?	Date	Name	Comments
1.0	New	12/15/2024	Stefanie Caswell	New