Molina Clinical Policy
Skin and Soft Tissue Substitutes
Policy No. 357

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DISCLAIMER

This Molina Clinical Policy (MCP) is intended to facilitate the Utilization Management process. Policies are not a supplementation or recommendation for treatment; Providers are solely responsible for the diagnosis, treatment, and clinical recommendations for the Member. It expresses Molina's determination as to whether certain services or supplies are medically necessary, experimental, investigational, or cosmetic for purposes of determining appropriateness of payment. The conclusion that a particular service or supply is medically necessary does not constitute a representation or warranty that this service or supply is covered (e.g., will be paid for by Molina) for a particular Member. The Member's benefit plan determines coverage – each benefit plan defines which services are covered, which are excluded, and which are subject to dollar caps or other limits. Members and their Providers will need to consult the Member's benefit plan to determine if there are any exclusion(s) or other benefit limitations applicable to this service or supply. If there is a discrepancy between this policy and a Member's plan of benefits, the benefits plan will govern. In addition, coverage may be mandated by applicable legal requirements of a State, the Federal government or CMS for Medicare and Medicaid Members. CMS's Coverage Database can be found on the CMS website. The coverage directive(s) and criteria from an existing National Coverage Determination (NCD) or Local Coverage Determination (LCD) will supersede the contents of this MCP and provide the directive for all Medicare members.[1] References included were accurate at the time of policy approval and publication.

OVERVIEW

Normal healthy skin provides a protective barrier for the body, aids in thermoregulation, and provides tactile sensations. Wounds, acute or chronic, are disruptions of the skin's structural and functional integrity and normally transition through distinct phases until the skin's structure and function are restored. Usual care for wounds can involve removing necrotic tissue, applying dressings that maintain a moist wound environment, treating wound infections, and restoring blood flow to the wound site. If these procedures fail to restore the healing process additional therapies, such as the application of skin substitutes to promote wound healing, may be considered (Snyder et al. 2020; Shahrohki 2023).

Skin or soft tissue substitutes are proposed as a treatment to cover open wounds and promote healing by preventing dehydration, reducing risk of infection, and providing a scaffold to support newly generated cells. The three most common uses for skin substitutes are to treat venous leg ulcers, diabetic foot ulcers, and burns. Skin substitutes, also known as bioengineered, tissue-engineered, or artificial skin, are a heterogeneous group of products and can generally be classified into 3 main types: cellular (comprised of living cells), acellular (composed of synthetic materials or tissue from which living cells have been removed), or a combination of cellular and acellular components. Due to the unique characteristics of each skin substitute product, there is no simple, universally accepted classification system that allows for categorization of all the products that are commercially available. Selection of a skin substitute should consider the type of wound, which layers of the skin are to be replaced, and the need for temporary versus permanent placement (Shahrohki 2023).

For this policy, the following definitions will be utilized:

- *Acellular Products*: A product composed of synthetic materials or tissue from which living cells have been removed. These are the most common commercially available skin substitute products.
- *Allografts/Allogenic*: A product derived from a human source other than the patient, such as a cadaver
- *Autograft/Autologous*: A product derived from the patient's own body
- *Bioengineered*: Products synthetic in nature, or composite products derived from processed or cultured cells
- *Human Cells, Tissues, or Cellular or Tissue-based Products (HCT/Ps)*: Products containing or consisting of human cells or tissues that are intended for implantation, transplantation, infusion, or transfer into a human recipient.
- *Xenograft/Xenographic*: A product derived from non-human (e.g., animal tissue) sources

Regulatory Status

Skin substitutes are developed from different materials and therefore are evaluated by different Food and Drug Administration (FDA) pathways. Some products are regulated and sold in the United States through the Premarket Approval (PMA) process, the 510(k) Premarket clearance process, or the Humanitarian Device Exemption (HDE) process. Others are regulated as human cells, tissues, and cellular and tissue-based products (HCT/Ps) derived from human cadaver skin and human placental membranes per the Public Health Service Act 361 and 21 Code of Federal Regulations (CFR) 1270 & 1271. Any list of commercially available skin substitutes should not be considered comprehensive due to the expanding nature of the industry and ongoing FDA approvals, including skin substitute products currently in development or in the clinical trial phase.

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COVERAGE POLICY

Medically Necessary

Use of a skin or soft tissue substitute may be **considered medically necessary** when **ALL** the following indications are met:

1. Member is 18 years or older
2. Documentation of wound characteristics and treatment plan are present prior to skin or soft tissue substitute application
3. The skin or soft tissue substitute product must be FDA approved **OR** meet all applicable regulations and standards established by the American Association of Tissue Banks for procuring and processing human cells, tissues, and cellular or tissue-based products (HCT/Ps)
4. Member is free from all the following absolute contraindications:
    a. Active infection or vasculitis in wound to be treated
    b. Involvement of tendon, muscle, joint capsule, or exposed bone or sinus tracts
    c. Active tobacco smoking
        i. Documentation of Member smoking cessation or in current smoking cessation program required
    d. Hypersensitivity or allergy to any components of the skin substitute (e.g., allergy to avian, bovine, porcine, equine products)
    e. For *Diabetic Foot Ulcers*:
        i. Uncontrolled blood sugar, as evidence by a HgA1c ≥ 12% in the last 90 days
        ii. Active Charcot deformity or major structural abnormalities of the affected foot
5. The wound to be treated meets **ONE** of the following indications:
    a. Breast Reconstruction: Skin substitutes for this indication must be used on wounds resulting from a medically necessary breast reconstruction procedure.
        i. AlloDerm
        ii. AlloMax
        iii. Cortiva
        iv. DermACELL
        v. FlexHD
    b. Burn Wounds: Skin substitutes for this indication must be used on partial or full thickness thermal burns *post wound excision*, when hemostasis has been achieved and sufficient full-thickness allograft is not available.
        i. Artiss
            1. Indicated to adhere to autologous skin grafts to surgically prepared wound beds resulting from burns
        ii. Biobrane
            1. Indicated to be used as a temporary covering of a partial thickness freshly debrided or excised burn wound
        iii. Biobrane-L
            1. Indicated to be used as a temporary covering of a partial thickness freshly debrided or excised burn wound
            2. Must be used as an adjunct to meshed autograft
        iv. Epicel
            1. Indicated to be used for deep dermal or full thickness burns comprising a total body surface area of greater than or equal to 30%
            2. May be used in conjunction with split-thickness autografts or alone in patients for whom split-thickness autografts may not be an option

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v. Integra Meshed Bilayer Wound Matrix or Integra Dermal Regeneration Matrix
   1. Indicated ONLY when sufficient autograft is contraindicated or unavailable at time of excision
   2. Indicated for the postexcisional treatment of a full thickness deep partial thickness burn
   3. Indicated for 1 time use

vi. Oasis Wound Matrix
   1. Indicated for second degree burns

vii. OrCel
   1. Indicated for healing donor site wounds in burn patients

viii. Suprathel Wound and Burn Dressing
   1. Indicated for temporary coverage of first or second degree burns

ix. TransCyte
   1. Indicated for temporary wound covering of a surgically excised full-thickness or deep partial-thickness thermal burns until autograft is possible

c. Diabetic Foot Ulcers (DFU): Skin substitutes for this indication must be used on partial or full thickness DFU between 1cm^2 to 25cm^2 with documented adequate circulation that has not responded to at least 6 weeks of conventional wound therapy including debridement, standard dressings, compression, and off-loading. *Skin substitute treatment must be used in conjunction with standard DFU therapy for Member with a Type 1 or Type 2 DM diagnosis.*

i. AlloPatch
   1. Indicated for full thickness DFUs. Initial treatment is up to 5 applications, additional applications may be applied if there is evidence of wound healing and are limited to a maximum of 8 applications in twelve weeks

ii. Amnioband
   1. Indicated for full thickness DFUs. Initial treatment is up to 5 applications, additional applications may be applied if there is evidence of wound healing and are limited to a maximum of 8 applications in twelve weeks

iii. Apligraf
   1. Indicated for full thickness DFUs. Additional applications may be applied after initial application once a week if there is evidence of wound healing and are limited to a maximum of 4 applications in twelve weeks

iv. DermACELL AWM
   1. Indicated for partial or full thickness DFUs with a maximum of 2 applications

v. Dermagraft
   1. Indicated for full thickness DFUs. Initial treatment is up to 5 applications, additional applications may be applied if there is evidence of wound healing and are limited to a maximum of 8 applications in twelve weeks

vi. EpixFix Amniotic Membrane
   1. Indicated for partial or full thickness DFUs. Additional applications may be applied after initial application once a week if there is evidence of wound healing and are limited to a maximum of 4 applications in twelve weeks

vii. Geistlich DermaGide Advance Wound Matrix
   1. Indicated for full thickness DFUs. Initial treatment is up to 5 applications, additional applications may be applied if there is evidence of wound healing and are limited to a maximum of 8 applications in twelve weeks

viii. Grafix
   1. Indicated for full thickness DFUs. Initial treatment is up to 5 applications, additional applications may be applied if there is evidence of wound healing and are limited to a maximum of 8 applications in twelve weeks

ix. GraftJacket NOW
   1. Indicated for partial or full thickness DFUs for only 1 application

x. Integra Dermal Regeneration Matrix
   1. Indicated for partial or full thickness DFUs. Additional applications may be applied after initial application once a week if there is evidence of wound healing and are limited to a maximum of 4 applications in twelve weeks

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xi. Oasis Wound Matrix or Oasis Ultra Tri-Layer Matrix
    1. Indicated for partial or full thickness DFUs. Additional applications may be applied after initial application once a week if there is evidence of wound healing and are limited to a maximum of 4 applications in twelve weeks
xii. PriMatrix
    1. Indicated for partial or full thickness DFUs. Additional applications may be applied after initial application once a week if there is evidence of wound healing and are limited to a maximum of 3 applications in twelve weeks
xiii. TheraSkin
    1. Indicated for partial or full thickness DFUs. Additional applications may be applied after initial application once a week if there is evidence of wound healing and are limited to a maximum of 4 applications in twelve weeks

d. Venous Stasis Ulcers (VSU): Skin substitutes for this indication must be used on VSUs of at least 1 cm^2 with documented adequate circulation unresponsive to at least 4 weeks of conventional wound therapy including debridement, standard dressings, compression, and off-loading. *Skin substitute treatment must be used in conjunction with standard VSU therapy.*
    i. AmnioBand
        1. Indicated for partial or full thickness venous stasis ulcers. Initial treatment is limited to 1 application, additional applications may be applied once a week if there is evidence of wound healing and are limited to a maximum of 12 applications in twelve weeks
    ii. Apligraf
        1. Indicated for partial or full thickness venous stasis ulcers. Initial treatment is limited to 1 application, additional applications may be applied once a week if there is evidence of wound healing and are limited to a maximum of 4 applications in twelve weeks
    iii. EpiFix Amniotic Membrane
        1. Indicated for partial or full thickness venous stasis ulcers. Initial treatment is limited to 1 application, additional applications may be applied once a week if there is evidence of wound healing and are limited to a maximum of 4 applications in twelve weeks
    iv. Grafix
        1. Indicated for partial or full thickness venous stasis ulcers. Initial treatment is limited to 1 application, additional applications may be applied once a week if there is evidence of wound healing and are limited to a maximum of 6 applications in twelve weeks
    v. Oasis Wound Matrix or Oasis Ultra Tri-Layer Matrix
        1. Indicated for partial or full thickness venous stasis ulcers. Initial treatment is limited to 1 application, additional applications may be applied once a week if there is evidence of wound healing and are limited to a maximum of 4 applications in twelve weeks
    vi. PriMatrix
        1. Indicated for partial or full thickness venous stasis ulcers. Initial treatment is limited to 1 application, additional applications may be applied once a week if there is evidence of wound healing and are limited to a maximum of 3 applications in twelve weeks
    vii. TheraSkin
        1. Indicated for partial or full thickness venous stasis ulcers. Initial treatment is limited to 1 application, additional applications may be applied once a week if there is evidence of wound healing and are limited to a maximum of 4 applications in twelve weeks

e. Dystrophic Epidermolysis Bullosa
    i. OrCel
        1. Indicated for use in patients with mitten hand deformities due to recessive dystrophic epidermolysis bullosa (rdeb) as an adjunct to standard autograft procedures for covering wounds and donor sites created after surgical release of hand contractures

Continuation of Therapy

1. Skin or soft tissue substitute use in the treatment of chronic wounds will last no more than 12 weeks
2. Skin substitute applications must comply with FDA guidelines for the specific product and shall not exceed 10

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applications or treatments per 12-week period of care

3. Only one skin or soft tissue substitute may be used per wound at a time. Product change within the wound episode is allowed, not to exceed the application limit per wound per 12-week period of care.

NOT Medically Necessary

The following indications and/or skin or soft tissue substitutes are considered **experimental, investigational, or unproven** due to insufficient evidence in the peer-reviewed medical literature to establish long-term safety, efficacy, and effect on net health outcomes:

1. Skin substitutes are **not medically necessary** for **ANY** of the following indications:
   a. Any indications other than those noted in the clinical criteria section above
   b. Decubitus ulcer treatment
   c. Continued treatment when the ulcer fails to heal by ≥ 50% within the first 6 weeks of treatment
   d. Treatment beyond 12 weeks regardless of wound status
   e. Continued skin substitute use after treatment failure, defined as the repeat or alternative application course (of up to 12 weeks) of skin substitute grafts within one year of any given course of skin substitute treatment for a venous stasis ulcer or diabetic foot ulcer
   f. Retreatment of healed ulcers (those showing greater than 75% size reduction and smaller than $1cm^2$)

2. All other skin or soft tissue substitutes products not included in the clinical criteria section above are considered **experimental, investigational, and unproven** due to insufficient evidence in the peer reviewed medical literature and include, but are not limited to**, ALL the following:

Acesso DL or Acesso TL
Actigraft
Activate Matrix
Affinity Human Amniotic Allograft
AlloGen
AlloSkin or AlloSkin RT
AltiPly
AmniCore Pro
AmniCore Pro+
Amnio Quad-Core
Amnio Tri-Core Amniotic
Amnio Wound
Amnio Wrap2
AmnioAMP-MP
AmnioArmor
AmnioBand
AmnioBind or DermaBind TL
AmnioCore
AmnioCyte Plus
AMNIOEXCEL products (AMNIOEXCEL Amniotic Allograft Membrane)
AmnioHeal Plus
AMNIOMATRIX
Amnio-Maxx or Amnio-Maxx
AMNIOREPAIR
AmnioText or AmnioText patch
Amnio Wound
AMNIPLY
Artacent products (Artacent Flex, Artacent Wound)
Arthroflex
Ascent
AxoBioMembrane
Axolotl Ambient or Axolotl Cryo
Axolotl Graft or Axolotl DualGraft
Barrera SL or Barrera DL
InteguPly
Interfyl
Kerecis Omega3
Keroxx (including Keroxx Flowable Wound Matrix)
Marigen Omega3
Matrion
MatriStem (MatriStem Burn Matrix, MatriStem Micromatrix, and MatriStem Wound Matrix)
Mediskin
Memoderm
Microlyte Matrix
MIRODERM Biologic Wound Matrix
Mirragen Advanced Wound Matrix
MyOwn Skin
NeoMatriX
NeoPatch
NeoStim Membrane, NeoStim TL
Membrane, NeoStimDL
NEOX
NEOX FLO
Novachor
Novafix
Novafix DL
NovoSorb SynPath
NuDYN
NuShield
Omeza Collagen Matrix
ORION
PalinGen (PalinGen Membrane, PalinGen XPlus Membrane, PalinGen XPlus Hydromembrane, PalinGen Flow, PalinGen SportFlow, ProMatrX ACF)
Phoenix Wound Matrix
Polycyte
PriMatrix
Procenta

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BellaCell HD
bio-ConneKt
BioDfence or BioDFence DryFlex
BioNextPATCH
carePATCH
Cellesta products (Cellesta Amniotic Membrane, Cellesta Flowable Amnion)
Clarix Regenerative Matrix
Cogenex Amniotic Membrane or Cogenex Flowable Amnion
Coll-e-Derm
Conexa
Corecyte
Coretext or Protext
CorMatrix
Corplex or Corplex P
CoreText
Cryo-Cord
Cymetra
Cygnus products (Cygnus MATRIX, Cygnus MAX, and Cygnus SOLO)
Cytal products (Cytal Wound Matrix, MatriStem Wound Matrix, Multilayer Wound Matrix)
Dermacyte Amniotic Membrane Allograft
Dermacyte Amniotic Wound Care Liquid
Derma-Gide
Derm-Maxx
EpiCord products (EpiCord Dehydrated Human Umbilical Cord Allograft)
E-Z Derm
GammaGraft
Genesis Amniotic Membrane
Helicoll
hMatrix
Human Health Factor 10 Amniotic Patch
Hyalomatrix
InnovaBurn
InnovaMatrix products (InnovaMatrix XL, InnovaMatrix AC, InnovaMatrix FS, InnovaMatrix PD)
ProText
PuraPly products (PuraPly Antimicrobial Wound Matrix, PuraPly AM, PuraPly AM XT, PuraPly XT)
REGUaRD
Relese
Repriza
Restorigin Amnion Patch or AFT
Restrata or Restrata Minimatrix
Revita
SkinTE
STRATTICE
Stravix or StravixPL
Supra SDRM
Suprathel
Surederm
Surfactor
surgiGRAFT
SurgiMend
Talymed
TenSIX
TheraGenesis
TheraSkin
Therion
TissueMend
Transcyte (except for indication specified in this policy)
TruSkin
Unite Biomatrix
Vendaje
Vim
WoundEx or WoundEx Flow
WoundFix products (WoundFix Membrane, WoundFix Plus Membrane, WoundFix XPlus Membrane)
WoundPlus Membrane or E-graft
XCelliStem
XCellerate
XCM BIOLOGIC Tissue Matrix
XWRAP/XWRAP ECM
Zenith Amniotic Membrane

** Any other skin substitute not specified in this policy as medically necessary (according to criteria section) are considered experimental, investigational, and/or unproven.

DOCUMENTATION REQUIREMENTS. Molina Healthcare reserves the right to require that additional documentation be made available as part of its coverage determination; quality improvement; and fraud; waste and abuse prevention processes. Documentation required may include, but is not limited to, patient records, test results and credentials of the provider ordering or performing a drug or service. Molina Healthcare may deny reimbursement or take additional appropriate action if the documentation provided does not support the initial determination that the drugs or services were medically necessary, not investigational or experimental, and otherwise within the scope of benefits afforded to the member, and/or the documentation demonstrates a pattern of billing or other practice that is inappropriate or excessive.

SUMMARY OF MEDICAL EVIDENCE

Benefits for other conditions other than those listed in the coverage criteria using skin substitutes for wound healing have not been clearly demonstrated in robust clinical studies published in the peer reviewed medical literature. Evidence directly comparing different skin substitute products or types is extremely limited and insufficient to inform whether any one product or product type is superior to other products. Safety data were generally limited but do not suggest skin substitutes are associated with serious harms or greater safety risks than standard wound care alone.

Breast Reconstruction
The use of acellular dermal matrices (ADMs) has been widely used in post-mastectomy breast reconstruction since the early 2000's, despite it being an off-label use. There are currently no FDA approved ADMs specifically indicated

for use in breast reconstruction. In March 2021, the FDA issued a safety brief that communicated concern that certain ADMs used in breast reconstruction had higher complications rates when used in implant-based breast reconstruction than in patients who underwent the procedure without the use of ADMs. The FDA highlighted the need for high quality large RCTs to establish the safety and efficacy of ADMs in breast reconstruction and recommended that each patient be counseled on the potential risks and benefits prior to surgery.

Arnaout et al. (2021) conducted a RCT comparing Alloderm-RTU to DermACELL in immediate subpectoral implant-based breast reconstruction. The primary outcome of the study was the duration of postoperative drain placement, as a surrogate endpoint for the extent of seroma formation, with secondary outcomes including episodes of seroma aspiration following drain removal, removal of the implant, unplanned revisional surgery/return to the operating room, wound infection requiring antibiotics, wound dehiscence or need for debridement, capsular contracture, and red breast syndrome. A total of 62 patients were randomized 1:1; however, only 59 patients were included in final analysis for a spread of Alloderm-RTU (n=38 breasts) and DermACELL (n=40 breasts). The mean duration of drain placement was 10.8 days (standard deviation, SD, 5.5) with Alloderm-RTU and 9.2 days (SD 4.5) with DermACELL. Complications within the first 6 months post op were wound infections requiring antibiotics occurred in 3 breasts (7.9%) with Alloderm-RTU and 1 (2.5%) with DermACELL (p = 0.35), unplanned reoperation due to complications was necessary for 6 breasts (15.8%) with Alloderm-RTU and 3 breasts (7.5%) with DermACELL (p = 0.30), and a minor complication (seroma requiring aspiration, red breast syndrome, wound dehiscence, wound infection, hematoma, skin necrosis, and capsular contracture) rate of 36.8% in Alloderm-RTU group and 32.5% in the DermACELL group. The authors concluded that there were minimal differences between the two products and that further studies into a cost analysis of each should be explored.

Wu et al. (2013) conducted an open label prospective case series on the dimensional changes and stretching of ADMs in tissue expander implant-based breast reconstruction. The primary outcome of the study was to measure the construct size on post op day 1 and post op month 3 to assess stretching. Thirty-one patients were included in the study and resulted in a mean perimeter increase from 38 (6) cm on postoperative day 1-42 (7) cm at month 3 (+11%; P=0.002), and a surface area increased from 73 (22) to 88 (28) cm2 (+21%; range, 4-35%; P=0.002). The secondary outcome of the study was patient satisfaction, which was comparable to those who did not receive an ADM in their reconstruction. Safety outcomes revealed complications in the ADM group were late seroma, red breast syndrome and urinary tract infection versus cellulitis, expander explantation, delayed wound healing and skin necrosis in those that did not receive an ADM. The authors concluded that the use of ADMs was a viable treatment modality with moderate stretching and comparable patient satisfaction in implant-based breast reconstruction.

McCarthy et al. (2012) conducted a double blind RCT on the use of ADMs in two stage implant-based breast reconstruction. Following their mastectomy 70 patients were randomized 1:1 into the ADM group (n= 36) versus the tissue expander (TE) group (n=34). The primary outcome evaluated was patient pain report, which was evaluated pre-operatively and five times post-operatively using the Visual Analog Scale (VAS) and the BREAST-Q© Physical Well-Being: Chest and Upper Body Scale. The results revealed there were no differences in patient pain via both VAS scores and immediate post-op narcotic use between the two groups at any time point in the assessments. Similarly, there were no differences in physical well-being in the immediate post-operative period, during the expansion phase, or prior to the exchange period (p= 0.52, p=0.77, p=0.82, respectively) via the BREAST-Q scale. In congruence with the lack of differentiation between the two groups, both cohorts had similar complication rates. The authors concluded that the use of ADMs neither hinders nor enhances post – operative outcomes in implant-based breast reconstruction.

Burn Wounds

The evidence suggests that bioengineered skin substitutes for deep dermal burns appears to improve the long-term functional and cosmetic outcomes and increase quality of life. Less pain, shorter wound healing time, and shorter hospital stays were observed with skin substitutes when compared to silver sulphadiazine dressings in another review of lower quality studies (Wasiak et al. 2013). FDA-approved skin substitutes have varying levels of medical evidence based on the product and the condition being treated. FDA approved skin substitutes for the treatment of burns by the 510(k) process are based only on evidence consisting of small unblinded studies of poor quality. For full or partial thickness burns with greater than 30% BSA involvement, the FDA has set up a process to allow the use of skin substitutes for patients who have sustained extensive tissue loss which necessitates a life-saving intervention.

Gardien et al. (2023) conducted a prospective, open label intrapatient randomized controlled trial. The study aimed to evaluate the short- and long-term safety and efficacy of an acellular dermal substitute. The study compared NovoMatrix

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(Matricel GmbH), a dermal collagen/elastin-based scaffold with split-thickness skin graft (STSG) alone. Twenty-five patients aged ≥18 years with full-thickness wounds that required skin grafting were included. Outcomes measured included elasticity, overall scar assessment, color, and patient scar preference. The dermal matrix group exhibited a significantly higher elasticity ration compared to the standard treatment group at 12 months follow-up. Evaluation utilizing the Patient and Observer Scar Assessment Scale (POSAS) at 3 months, 12 months, and 6 years revealed notable advantages in the dermal matrix-treated area, particularly in the observer scale's "pliability" and "relief," as well as in the patient scale's "pain" ($p = 0.076$, $p = 0.080$, and $p = 0.059$, respectively). However, there was no significant difference observed in erythema or melanin index between treatment groups. At the 6-year follow-up most patients had no preference (47%) or preferred the dermal matrix area (40%) in the overall scar assessment. The Novomaix skin substitute was found to be a safe treatment option for full-thickness wounds, with long-term evaluation suggesting comparable final scar quality between the treatments.

Wardhana and Valeria (2022) conducted a systematic review and analyzed the effectiveness of skin substitutes in the treatment of acute burns. Thirteen articles were included in the review and six types of skin substitutes were evaluated including Biobrane, TransCyte, Integra, Glyaderm, Suprathel, and Apligraft. Burns ranged from superficial to full-thickness depth with TBSA from 2-97%. Across four studies Biobrane showed significantly shortened wound healing time and reduced pain scores compared to treatment with silver sulfadiazine. Two studies reported a shorter length of hospitalization and a decreased frequency of dressing changes compared to the silver sulfadiazine group. When compared to modern dressings (e.g., Duoderm and Duoderm + Intrasite + Acticoat) Biobrane demonstrated comparable outcomes in wound healing time, pain, dressing change frequency and Vancouver Scar Scale (VSS) scores. Transcyte was significantly more effective in decreasing wound healing time, pain alleviation, reducing dressing change frequency, and managing scar formation compared to silver sulfadiazine. Integra presented better scar outcomes compared to allograft based on the Hamilton burn-scar scoring system. Suprathel was compared to split-thickness skin grafts (STSG) for full thickness burns. VSS parameters including pigmentation, pliability, and height had similar results between the two groups. On the patient and observer scar assessment scale (POSAS) elasticity, relief, and pliability were significantly superior in the Suprathel group compared to the STSG group. Apligraf when combined with autograft produced superior results in scar evaluation compared to the STSG group. All skin substitutes included in the review demonstrated, at minimum, non-inferior to superior performance when compared to conventional treatment modalities in treating various burn wounds.

Blome-Eberwein et al. (2021) conducted a feasibility study on the complications and outcomes of using the absorbable synthetic membrane Suprathel in the treatment of second-degree burns. Two hundred and twenty-nine burn patients were treated with Suprathel after the wound bed was appropriately excised or debrided and hemostasis was achieved. The average total body surface area was 8.9% (1%-60%) with an average time to healing of 13.7 days for ≥ 90% epithelialization with 11.9 days for pediatric patients versus 14.7 days for adults. One hundred percent of the wounds treated with Suprathel healed without grafting. Throughout the treatment period, the average pain level was 1.9 on a 10-point scale and average length of stay was 6.9 days. Complications included 27 patients developed hypertrophic scarring in some areas (11.7%), infection rate of 3.8% (8/229), and failure or progression to full thickness in part of the wounds was 5.2% (12/229). The authors concluded that Suprathel is a simple and effective alternative solution to healing burn wounds.

Hundeshagen et al. (2018) conducted a prospective RCTs comparing Suprathel versus Mepilex Ag in treating burn wounds. The outcomes assessed were re-epithelialization, wound pain, discomfort during dressing changes, and treatment cost, as well as a Patient and Observer Scar Assessment Scale was performed at 1 month post burn. A total of 62 patients were enrolled with 30 in the Mepilex Ag group and 32 in the Suprathel group. Mean TBSA burned was 5.9 ± 5.8% (range, 1–29%) in the Mepilex Ag group and 5.5 ± 4.6% (range, 1–20%) in the Suprathel group. Subjective patient findings in favor of Suprathel were significantly lower pain ratings in those treated with Suprathel during the first 5 days after burn injury ($P < 0.05$) with ratings converging at a common lower level after this time, and patients rated the overall appearance of their healed wound better after treatment with Suprathel (S: 2; Confidence Interval, 1.4–3.5; M: 4.5; Confidence Interval, 3.8–6.2; $P = 0.002$). Subjective findings that did not show significant differences between groups were patient ratings for pain, itch, color, stiffness, thickness, and irregularity at the 1-month assessment. Objective findings were the median time to complete re-epithelialization was 12 days in both groups ($P = 0.75$) with 20% (6/30) of patients having a re-epithelialization time greater than 21 days in the Mepilex Ag group versus 7% (2/30) in the Suprathel group ($P = 0.25$). At the 1-month assessment observer scores of the healed wound at this time did not show significant differences for vascularity, pigmentation, thickness, relief, pliability, surface, or overall appearance. Observer score for pliability (M: 5; S: 2; $P = 0.08$) and patient score for irregularity (M: 3.5; S: 2; $P = 0.075$) approached

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significance. The adverse events consisted of infection, of which 2 infections (8%) were confirmed in the Suprathel group versus none observed in the Mepilex Ag group (P = 0.5). The cost per square centimeter of Mepilex Ag was $0.08, and on average, each patient required 2 dressing changes. Suprathel cost $0.56 per square centimeter and was applied once per patient, resulting in direct product costs of $0.16/cm2 per patient for Mepilex Ag and $0.56/cm2 per patient for Suprathel. The authors concluded that both dressings were viable treatments for burn wounds.

Lower Limb Ulcers
The evidence suggests that skin substitutes appear to heal more chronic foot ulcers than standard wound care alone and may prevent amputation in patients with diabetes. Using skin substitutes may result in a lower incidence of wound infection and does not appear to present unique or serious safety concerns. Evidence suggests that more patients with chronic venous leg ulcers that do not heal with standard care alone experience complete healing when a bilayer human skin equivalent or allograft is used in addition to standard care.

Alvaro-Afonso et al. (2020) conducted a systematic review of the recent advances in dermo epidermal skin substitutes for the treatment of diabetic foot ulcers (DFUs). A total of 28 RCTs were reviewed to analyze rates of complete wound closure and time to healing for 17 commonly available dermal skin substitutes. The healing rates after 12 weeks and time to complete closure in DFUs were heterogeneous among the 28 RCTs, with the best 12-week healing rates accomplished with dermal cellular substitutes (Epifix, 100% and Amnioband, 85%). The authors concluded that skin substitutes used in conjunction with standard care appear to improve the healing rates of DFUs compared to standard wound care alone. The authors stated more homogenous studies are needed to confirm these findings, with studies considering wound size and comorbidities.

Lantis et al. (2021) conducted a randomized controlled trial evaluating the safety and efficacy of using a fetal bovine acellular dermal matrix (FBADM) in conjunction with standard of care (SOC) to treat DFUs were evaluated. The study included 226 patients, with 110 assigned to the FBADM group and 116 to the SOC group. Eligible patients had confirmed type 1 or 2 diabetes, a hemoglobin A1c ≤ 12%, a foot ulcer lasting at least 2 weeks, an ulcer area between 1–12 cm2 post-debridement, and adequate vascular perfusion. Exclusion criteria included active infection, exposed tendon or bone, or wound reduction ≥ 30% during the 2-week run-in period. Outcome measures included time to closure, weekly closure rate, percentage area reduction at 12 weeks, incidence of closure and ulcer duration, and recurrence. A significantly higher proportion of wounds treated with FBADM (45.6%) achieved complete closure compared to SOC alone (27.9%) (p = 0.008). Median closure time was 43 days for FBADM versus 57 days for SOC. At 12 weeks, FBADM treatment resulted in a 2.2 times greater likelihood of complete closure compared to SOC. No adverse events related to the product or procedure were noted. Limitations included the inability to blind investigators or subjects, a short follow-up of four weeks, and potential patient selection bias favoring healthier individuals with DFUs. Overall, the study suggests FBADM, combined with SOC, as a reasonable therapy for treatment of DFUs.

Bianchi et al. (2019) conducted an analysis to assess if intention-to-treat (ITT) and per-protocol (PP) both demonstrate superiority of EpiFix over standard moist dressings as a treatment for venous leg ulcers (VLU). The data analyzed was collected from the RCT conducted by Bianchi et al. (2018) that compared VLU treatment with EpiFix versus standard wound care. One hundred and twenty-eight patients were 1:1 randomized between the two groups, 64 to the EpiFix group and 64 to the standard care group with a primary outcome of the incidence of healing at 12 weeks. The healing rate of the ITT group was 50% for EpiFix and 31% for standard wound care. The healing rate of the PP group was 60% for EpiFix and 35% for standard wound care. Within both ITT and PP analyses, these differences were statistically significant; P = 0.0473, ITT and P = 0.0128, PP. The authors concluded that the Kaplan-Meier plot of time to heal within 12 weeks for the ITT and PP populations demonstrated a superior wound-healing trajectory for EpiFix compared to standard wound care alone.

Farivar et al. (2019) conducted a study to evaluate the efficacy of cryopreserved placental tissue wound matrix (Grafix) in the management of chronic venous leg ulcers. Twenty-one patients were included in the study for a total of 30 VLUs, all of which were men. The patients were enrolled only after failing 12 weeks of standard wound therapy, and therefore served as their own control. The average area of the VLUs before Grafix initiation was 12.2 cm^2 (SD, ±14.6 cm2; range, 3.3-12.3 cm^2), and after Grafix treatment there was a mean reduction in wound surface area by 79% (SD, ±27.3%; P < .001 compared with standard therapy) after a mean treatment time of 10.9 weeks. Eighty percent of VLUs were reduced in size by half compared with 25% with standard therapy (P < .001), and complete wound healing was achieved in 53% (16/30) of VLUs refractory to standard therapy. The results led the authors to conclude that adjunct therapy with a skin substitute, such as Grafix, provides superior wound healing than standard therapy alone; however,

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larger RCTs are needed to confirm these findings.

Harding et al. (2013) conducted a RCT to analyze venous leg ulcer healing when treated with Dermagraft vs compression therapy alone (control group). Three hundred and sixty-six patients were included, 186 in the Dermagraft group vs 180 in the control group. The primary outcome was the proportion of patients with completely healed study ulcers by 12 weeks. In the Dermagraft group 64 (34%) of 186 patients experienced healing by week 12 compared with 56 (31%) of 180 patients in the control group (P = 0·235). For ulcers ≤ 12 months duration, 49 (52%) of 94 patients in the Dermagraft group versus 36 (37%) of 97 patients in the control group healed at 12 weeks (P = 0·029). For ulcers ≤ 10 cm^2, complete healing at week 12 was observed in 55 (47%) of 117 patients in the Dermagraft group compared with 47 (39%) of 120 patients in the control group (P = 0·223). Adverse event rates did not markedly differ between the two groups. The authors concluded that as the efficacy of Dermagraft appeared to improve younger ulcers, the suggestion is made that Dermagraft should be utilized early in wound care; however, more studies are needed.

Marston et al. (2003) conducted a RCT that demonstrated Dermagraft treatment for diabetic foot ulcers of greater than six weeks duration showed a 30% rate of healing in comparison to 18% healing when standard wound care was utilized alone. In a meta-analysis reviewing the use of acellular regenerative tissue matrix treatment for diabetic foot ulcers, complete wound healing was seen in 43% of patients compared to 30% with continued conservative treatment.

National and Specialty Organizations

The **International Society for Burn Injury (ISBI)** (2016) published the *ISBI Practice Guidelines for Burn Care*. The aim was to provide guidance for those with burns to improve care overall. The ISBI also defined the most effective and efficient methods of evaluation and management of burn injuries. In relation to skin substitutes the document recommended that following excision or debridement, a deep burn wound should be covered with autograft skin or an appropriate skin substitute.

The **Wound Healing Society (WHS)** published *WHS Guidelines Update: Diabetic Foot Ulcer Treatment Guidelines* (Lavery et al. 2020) that offered support for use of skin substitutes by assigning a Level 1 recommendation of the evidence that cellular and acellular skin equivalents improve DFU healing.

The **Society For Vascular Surgery (SVS)**, **American Podiatric Medical Association (APMA)**, and the **Society For Vascular Medicine (SVM)** jointly published *The Management of Diabetic Foot: A Clinical Practice Guideline by the Society for Vascular Surgery* (Hingorani et al. 2016). The guideline offers recommendations regarding prevention, examination for peripheral neuropathy, education for patients and their families, and strategies for glycemic control to reduce DFUs manifestation and complications. The guideline also offers recommendations on the treatment of DFUs, including the use of biologics (platelet-derived growth factor (PDGF)], living cellular therapy, extracellular matrix products, amniotic membrane products) to aid in the healing of chronic DFUs that have not shown improvement with conventional therapy after at least 4 weeks.

The **Agency for Healthcare Research and Quality (AHRQ)** published a Technology Assessment Program Technical Brief on *Skin Substitutes for Treating Chronic Wounds* (Snyder et al. 2020) in which different skin substitute products commercially available in the United States used to treat chronic wounds are described and examined in order to classify them. In addition, the brief identified and assessed RCTs and suggested best practices for future studies on skin substitutes. Ultimately the authors concluded “Studies rarely reported clinical outcomes, such as amputation, wound recurrence at least 2 weeks after treatment ended, or patient-related outcomes, such as return to function, pain, exudate, and odor. The lack of studies examining the efficacy of most skin substitute products and the need for better-designed and reported studies providing more clinically relevant data in this field are this Technical Brief’s clearest implications.”

The **International Work Group on Diabetic Foot (IWGDF)** published *Guidelines on Interventions to Enhance Healing of Foot Ulcers in People with Diabetes* (Chen et al. 2023) in which the recommendation was made to consider the use of placental derived products in DFUs that have not improved with standard therapy, the products are recommended to be used as an adjunct therapy to conventional wound management.

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CODING & BILLING INFORMATION

CPT (Current Procedural Terminology) Codes

Code	Description
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 for primary procedure)
15273	Application of skin substitute graft to trunk, arms, legs, total wound surface area greater than or equal to 100 sq cm; first 100 sq cm wound surface area, or 1% of body area of infants and children
15274	Application of skin substitute graft to trunk, arms, legs, total wound surface area greater than or equal to 100 sq cm; each additional 100 sq cm wound surface area, or part thereof, or each additional 1% of body area of infants and children, or part thereof (List separately in addition to code for primary procedure)
15275	Application of skin substitute graft to face, scalp, eyelids, mouth, neck, ears, orbits, genitalia, hands, feet, and/or multiple digits, total wound surface area up to 100 sq cm; first 25 sq cm or less wound surface area
15276	Application of skin substitute graft to face, scalp, eyelids, mouth, neck, ears, orbits, genitalia, hands, feet, and/or multiple digits, total wound surface area up to 100 sq cm; each additional 25 sq cm wound surface area, or part thereof (List separately in addition to code for primary procedure)
15277	Application of skin substitute graft to face, scalp, eyelids, mouth, neck, ears, orbits, genitalia, hands, feet, and/or multiple digits, total wound surface area greater than or equal to 100 sq cm; first 100 sq cm wound surface area, or 1% of body area of infants and children
15278	Application of skin substitute graft to face, scalp, eyelids, mouth, neck, ears, orbits, genitalia, hands, feet, and/or multiple digits, total wound surface area greater than or equal to 100 sq cm; each additional 100 sq cm wound surface area, or part thereof, or each additional 1% of body area of infants and children, or part thereof (List separately in addition to code for primary procedure)

HCPCS (Healthcare Common Procedure Coding System) Codes

Code	Description
C5271	Application of low-cost 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
C5272	Application of low-cost 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 for primary procedure)
C5273	Application of low-cost skin substitute graft to trunk, arms, legs, total wound surface area greater than or equal to 100 sq cm; first 100 sq cm wound surface area, or 1% of body area of infants and children
C5274	Application of low-cost 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)
C5275	Application of low-cost 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
C5276	Application of low-cost 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)
C5277	Application of low-cost skin substitute graft to face, scalp, eyelids, mouth, neck, ears, orbits, genitalia, hands, feet, and/or multiple digits, total wound surface area greater than or equal to 100 sq cm; first 100 sq cm wound surface area, or 1% of body area of infants and children
C5278	Application of low cost skin substitute graft to face, scalp, eyelids, mouth, neck, ears, orbits, genitalia, hands, feet, and/or multiple digits, total wound surface area greater than or equal to 100 sq cm; each

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	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)
C9250	Human plasma fibrin sealant, vapor-heated, solvent-detergent (Artiss), 2ml
Q4101	Apligraf per square centimeter
Q4102	Oasis wound matrix, per sq cm
Q4103	Oasis burn matrix, per sq cm
Q4104	Integra bilayer matrix wound dressing (BMWD), per sq cm
Q4105	Integra dermal regeneration template (DRT) or Integra Omnigraft dermal regeneration matrix, per sq cm
Q4106	Dermagraft per square centimeter
Q4107	GRAFTJACKET, per sq cm
Q4108	Integra matrix, per square centimeter
Q4121	TheraSkin, per sq cm
Q4122	DermACELL, DermACELL AWM or DermACELL AWM Porous, per sq cm~~F~~
Q4124	OASIS ultra tri-layer wound matrix, per sq cm
Q4132	Grafix core and grafixpl core, per square centimeter
Q4133	Grafix PRIME, GrafixPL PRIME, Stravix and StravixPL, per sq cm
Q4151	AmnioBand or Guardian, per sq cm
Q4168	AmnioBand, 1 mg
Q4182	Transcyte per square centimeter
Q4186	Epifix, per square centimeter
A2012	Suprathel, per sq cm
A4100	Skin substitute, FDA-cleared as a device, not otherwise specified
Q4100	Skin substitute, not otherwise specified [use for others not specified]
Q4110	Primatrix, per square centimeter
Q4111	Gammagraft, per sq cm
Q4112	Cymetra, injectable, 1cc
Q4113	Graftjacket xpress, injectable, 1cc
Q4114	Integra flowable wound matrix, injectable, 1cc
Q4115	Alloskin, per sq cm
Q4116	Alloderm, per square centimeter
Q4117	Hyalomatrix, per sq cm
Q4118	Matristem micromatrix, 1mg
Q4123	AlloSkin RT, per sq cm
Q4125	Arthroflex, per square centimeter
Q4126	MemoDerm, DermaSpan, TranZgraft or IntéguPly, per sq cm
Q4127	Talymed, per sq cm
Q4128	FlexHD, or AllopatchHD, per sq cm
Q4130	Strattice tm, per square centimeter
Q4134	Hmatrix, per sq cm
Q4135	Mediskin, per sq cm
Q4136	E-Z Derm, per sq cm
Q4137	Amnioexcel, amnioexcel plus or biodexcel, per square centimeter
Q4138	Biodfense dryflex, per square centimeter
Q4139	Amniomatrix or biodmatrix, injectable, 1 cc
Q4140	BioDFence, per square centimeter
Q4141	Alloskin AC, per square centimeter
Q4142	Xcm biologic tissue matrix, per square centimeter
Q4143	Repriza, per square centimeter
Q4145	Epifix, injectable, 1 mg
Q4146	Tensix, per square centimeter
Q4147	Architect, Architect PX, or Architect FX, extracellular matrix, per square centimeter
Q4148	Neox Cord 1K, Neox Cord RT, or Clarix Cord 1K, per square centimeter
Q4149	Excellagen, 0.1 cc

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Q4150	Allowrap DS or dry, per square centimeter
Q4152	DermaPure, per sq cm
Q4153	Dermavest and Plurivest, per sq cm
Q4154	Biovance, per sq cm
Q4155	Neox Flo or Clarix Flo 1 mg
Q4156	Neox 100 or Clarix 100, per sq cm
Q4157	Revitalon, per sq cm
Q4158	Kerecis Omega3, per sq cm
Q4159	Affinity, per sq cm
Q4160	Nushield, per square centimeter
Q4161	bio-ConneKt wound matrix, per sq cm
Q4162	Woundex flow, bioskin flow, 0.5cc
Q4163	Woundex, bioskin, per sq cm
Q4164	Helicoll, per square cm
Q4165	Keramatrix or Kerasorb, per sq cm
Q4166	Cytal, per square centimeter
Q4167	Truskin, per square centimeter
Q4169	Artacent wound, per sq cm
Q4170	Cygnus, per sq cm
Q4171	Interfyl, 1 mg
Q4173	Palingen or Palingen Xplus, per sq cm
Q4174	Palingen or promatrx, 0.36 mg per 0.25 cc
Q4175	Miroderm, per sq cm
Q4176	Neopatch or Therion, per square centimeter
Q4177	Floweramnioflo, 0.1 cc
Q4178	FlowerAmnioPatch, per sq cm
Q4179	Flowerderm, per square centimeter
Q4180	Revita, per square centimeter
Q4181	Amnio wound, per square centimeter
Q4183	Surgigraft, per sq cm
Q4184	Cellesta or Cellesta Duo, per sq cm
Q4185	Cellesta flowable amnion (25 mg per cc); per 0.5 cc
Q4187	Epicord, per square centimeter
Q4188	AmnioArmor, per sq cm
Q4189	Artacent ac, 1 mg
Q4190	Artacent AC, per sq cm
Q4191	Restorigin, per square centimeter
Q4192	Restorigin, 1 cc
Q4193	Coll-e-derm, per square centimeter
Q4194	Novachor, per square centimeter
Q4195	PuraPly, per square cm
Q4196	PuraPly AM, per square cm
Q4197	Puraply XT, per square cm
Q4198	Genesis amniotic membrane, per square centimeter
Q4200	SkinTE, per sq cm
Q4201	Matrion, per square centimeter
Q4202	Keroxx (2.5g/cc), 1cc
Q4203	Derma-Gide, per sq cm
Q4204	Xwrap, per square centimeter
Q4205	Membrane graft or membrane wrap, per square centimeter
Q4206	Fluid flow or fluid gf, 1 cc
Q4208	Novafix, per sq cm
Q4209	SurGraft, per sq cm

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Q4211	Amnion Bio or AxoBioMembrane, per sq cm
Q4212	Allogen, per cc
Q4213	Ascent, 0.5 mg
Q4214	Cellesta Cord, per sq cm
Q4215	Axolotl ambient or axolotl cryo, 0.1 mg
Q4216	Artacent Cord, per sq cm
Q4217	WoundFix, BioWound, WoundFix Plus, BioWound Plus, WoundFix Xplus or BioWound Xplus, per sq cm
Q4218	SurgiCORD, per sq cm
Q4219	SurgiGRAFT-DUAL, per sq cm
Q4220	BellaCell HD or Surederm, per sq cm
Q4221	Amniowrap2, per square centimeter
Q4222	ProgenaMatrix, per sq cm
Q4224	Human Health Factor 10 Amniotic Patch (HHF10-P), per sq cm
Q4225	Amniobind or derma tl, per sq cm
Q4226	MyOwn Skin, includes harvesting and preparation procedures, per sq cm
Q4227	AmnioCoreTM, per sq cm
Q4229	Cogenex Amniotic Membrane, per sq cm
Q4230	Cogenex Flowable Amnion, per 0.5 cc
Q4231	Corplex P, per cc
Q4232	Corplex, per sq cm
Q4233	SurFactor or NuDyn, per 0.5 cc
Q4234	XCellerate, per sq cm
Q4235	AMNIOREPAIR or AltiPly, per sq cm
Q4236	carePATCH, per sq cm
Q4237	Cryo-Cord, per sq cm
Q4238	Derm-Maxx, per sq cm
Q4239	Amnio-Maxx or Amnio-Maxx Lite, per sq cm
Q4240	CoreCyte, for topical use only, per 0.5 cc
Q4241	PolyCyte, for topical use only, per 0.5 cc
Q4242	AmnioCyte Plus, per 0.5 cc
Q4244	Procenta, per 200 mg
Q4245	AmnioText, per cc
Q4246	CoreText or ProText, per cc
Q4247	Amniotext patch, per sq cm
Q4248	Dermacyte Amniotic Membrane Allograft, per sq cm
Q4249	AMNIPLY, for topical use only, per sq cm
Q4250	AmnioAmp-MP, per sq cm
Q4254	Novafix DL, per sq cm
Q4255	REGUaRD, for topical use only, per sq cm
Q4256	MLG-Complete, per sq cm
Q4257	Relese, per sq cm
Q4258	Enverse, per sq cm
Q4262	Dual Layer Impax Membrane, per sq cm
Q4263	SurGraft TL, per sq cm
Q4264	Cocoon Membrane, per sq cm
Q4265	Neostim TL, Per Square Centimeter
Q4266	Neostim Membrane, Per Square Centimeter
Q4267	Neostim DL, Per Square Centimeter
Q4268	Surgraft FT, Per Square Centimeter
Q4269	Surgraft XT, Per Square Centimeter
Q4270	Complete SL, Per Square Centimeter
Q4271	Complete FT, Per Square Centimeter
Q4279	Vendaje ac, per square centimeter

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Q4287	Dermabind dl, per square centimeter
Q4288	Dermabind ch, per square centimeter
Q4289	Revoshield + amniotic barrier, per square centimeter
Q4290	Membrane wrap-hydro, per square centimeter
Q4291	Lamellas xt, per square centimeter
Q4292	Lamellas, per square centimeter
Q4293	Acesso dl, per square centimeter
Q4294	Amnio quad-core, per square centimeter
Q4295	Amnio tri-core amniotic, per square centimeter
Q4296	Rebound matrix, per square centimeter
Q4297	Emerge matrix, per square centimeter
Q4298	Amnicore pro, per square centimeter
Q4299	Amnicore pro+, per square centimeter
Q4300	Acesso tl, per square centimeter
Q4301	Activate matrix, per square centimeter
Q4302	Complete aca, per square centimeter
Q4303	Complete aa, per square centimeter
Q4304	Grafix plus, per square centimeter
Q4311	Acesso, per square centimeter
Q4312	Acesso ac, per square centimeter
Q4313	Dermabind fm, per square centimeter
Q4314	Reeva ft, per square centimeter
Q4315	Regenelink amniotic membrane allograft, per square centimeter
Q4316	Amchoplast, per square centimeter
Q4317	Vitograft, per square centimeter
Q4318	E-graft, per square centimeter
Q4319	Sanograft, per square centimeter
Q4320	Pellograft, per square centimeter
Q4321	Renograft, per square centimeter
Q4326	Woundplus, per square centimeter
Q4327	Duoamnion, per square centimeter
Q4328	Most, per square centimeter
Q4329	Singlay, per square centimeter
Q4330	Total, per square centimeter
Q4331	Axolotl graft, per square centimeter
Q4332	Axolotl dualgraft, per square centimeter
Q4333	Ardeograft, per square centimeter
Q4334	Amnioplast 1, per square centimeter [effective 10/01/2024]
Q4335	Amnioplast 2, per square centimeter [effective 10/01/2024]
Q4336	Artacent c, per square centimeter [effective 10/01/2024]
Q4337	Artacent trident, per square centimeter [effective 10/01/2024]
Q4338	Artacent velos, per square centimeter [effective 10/01/2024]
Q4339	Artacent vericlen, per square centimeter [effective 10/01/2024]
Q4340	Simpligraft, per square centimeter [effective 10/01/2024]
Q4341	Simplimax, per square centimeter [effective 10/01/2024]
Q4342	Theramend, per square centimeter [effective 10/01/2024]
Q4343	Dermacyte ac matrix amniotic membrane allograft, per square centimeter [effective 10/01/2024]
Q4344	Tri-membrane wrap, per square centimeter [effective 10/01/2024]
Q4345	Matrix hd allograft dermis, per square centimeter [effective 10/01/2024]
Q4322	Caregraft, per square centimeter
Q4323	Alloply, per square centimeter
Q4324	Amniotx, per square centimeter
Q4325	Acapatch, per square centimeter

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A2001	Innovamatrix AC Per Sq Cm
A2002	Mirragen Advanced Wound Matrix Per Sq Cm
A2004	Xcellistem Per Sq Cm
A2005	Microlyte Matrix Per Sq Cm
A2006	Novosorb Synpath Dermal Matrix Per Sq Cm
A2007	Restrata Per Sq Cm
A2008	Theragenesis Per Sq Cm
A2009	Symphony Per Sq Cm
A2010	Apis Per Sq Cm
A2011	Supra SDRM, per sq cm
A2013	Innovamatrix FS, per sq cm
A2019	Kerecis Omega3 Marigen Shield, Per Square Centimeter
A2020	Ac5 Advanced Wound System (Ac5)
A2021	Neomatrix, Per Square Centimeter

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APPROVAL HISTORY

08/14/2024	Policy reviewed. Added coverage criteria indications for the use of skin substitutes in breast reconstruction and in the treatment of dystrophic epidermolysis bullosa. Added specific skin substitutes to already covered indications. IRO Peer Reviewed on July 31, 2024, by a practicing physician board certified in Plastic Surgery.
04/10/2024	Policy reviewed. No changes to coverage criteria. Updated Summary of Medical Evidence and References.
12/13/2023	Coding and Billing section updated.
04/13/2023	Policy reviewed. Criteria consolidated. Criteria specific to line of business removed. Coverage in case of acute burn updated. Coverage of EpiFix sheet form clarified. Coding updated. AMR Peer Review. Policy reviewed on April 4, 2023, by a practicing, board-certified physician in Wound Care.
02/09/2022	Policy reviewed, included Actigraft as non-covered.
12/08/2021	Policy reviewed; no changes to criteria; added HCPCS code Q4155 and removed Q4131; added national / specialty items from ASPS, ISBI, WHS SVS/APMA/SVM and updated references.
02/08/2021	Policy reviewed, clinical criteria updated with additional and comprehensive wound specific recommendations for burns, diabetic foot ulcers and venous leg ulcers. Coding updated with all products available. Contraindications and limitations updated; guidelines and references sections revised, condensed, and updated. AMR Peer Review. Policy reviewed on January 13, 2021, by an Advanced Medical Reviews (AMR) practicing, board-certified physician in Plastic Surgery.
04/23/2020	New policy. AMR Peer Review. Policy reviewed on January 3, 2020, by an Advanced Medical Reviews (AMR) practicing, board-certified physician in Plastic Surgery.

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