Clinical Policy: Skin Substitutes for Chronic Wounds

Reference Number: CP.MP.185
Date of Last Revision: 10/22
Effective Date: 12/01/22

Coding Implications
Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description

Patients receiving skin replacement surgery with a skin substitute graft should be under the care of a wound care physician or surgeon. It is imperative that systemic disease be monitored/treated to ensure adequate healing of the wound site. This policy addresses the medical necessity criteria for skin substitutes in the treatment of chronic wounds.

***Note:** For skin substitutes for burns, refer to CP.MP.186 Burn Surgery.*

Policy/Criteria

I. It is the policy of health plans affiliated with Centene Corporation® that skin substitutes are **medically necessary** for diabetic foot ulcers, venous stasis ulcers, or venous leg ulcers when all of the following criteria are met:

A. Age ≥ 18 years, or diabetic (Type 1 or Type 2);
B. Wound is chronic, defined as a wound that does not respond to at least 4 weeks of standard wound treatment as a component of organized, comprehensive, conservative therapy;
C. Wound characteristics and treatment plan are documented;
D. Standard wound care has failed, evidenced by all of the following:
   1. The ulcer or skin deficit has been treated with appropriate wound-care measures, including debridement, standard dressings (including silver dressings), compression, off-loading;
   2. Wound has increased in size or depth; or has not changed in baseline size or depth and there is no indication that improvement is likely (such as granulation, epithelialization or progress towards closing);
E. Documentation of effort to cease nicotine use, including from sources other than cigarettes, but excluding nicotine replacement therapy, for at least 4 weeks during conservative wound care and prior to planned bioengineered skin replacement therapy, or no nicotine use;
F. Wound characteristics, all of the following:
   1. Partial- or full-thickness ulcer with a clean, granular base;
   2. No involvement of tendon, muscle, joint capsule, or exposed bone or sinus tracts, unless Integra® is used per FDA guidelines;
   3. No wound infection; wound must be clean and free of necrotic debris or exudate;
   4. Member/enrollee has adequate circulation/oxygenation to support tissue growth/wound healing, as evidenced by physical examination (e.g., Ankle-Brachial Index [ABI] of no less than 0.7 or TCOM pressure greater than 30 millimeters of mercury [mmHg]);
G. For lower extremity chronic wounds (diabetic foot ulcer or venous leg ulcer), one of the following:
   1. Diabetic foot ulcer (DFU), and all of the following:

a. Hgb A1c of ≤ 8 or documentation of improving control;
b. Documented conservative wound care for ≥ 4 weeks;
c. Wound is without evidence of osteomyelitis or nidus of infection;

2. Venous stasis ulcer (VSU) or venous leg ulcers (VLU), all of the following:
   a. A chronic, non-infected ulcer VSU or VLU has failed to respond to documented conservative wound-care measures for ≥ 4 weeks with documented compliance;
   b. Completed assessment includes:
      i. History (prior ulcers, thrombosis risks);
      ii. Physical exam (edema, skin changes);
      iii. ABI (Ankle-Brachial Index) and duplex scan to confirm Clinical-Etiology-Anatomy-Pathophysiology (*CEAP);
   c. If VLU is present, a venous duplex ultrasound has been completed to assess saphenous vein incompetency/venous reflux and contributory superficial ulcer bed perforators;
3. Full thickness skin-loss ulcer is the result of abscess, injury or trauma and has failed to respond to appropriate control of infection, foreign body, tumor resection, or other disease process for ≥ 4 weeks;

H. Requested applications comply with FDA guidelines for the specific product, not to exceed 10 applications or treatments;
I. Only one skin substitute will be simultaneously in place per wound episode. Product change within the wound episode is allowed, not to exceed the 10 application limit per wound per 12 week episode of care;
J. None of the following contraindications:
   1. Inadequate control of underlying conditions or exacerbating factors (e.g., uncontrolled diabetes with Hgb A1c > 8%, or no documented improvement of glucose levels in the last 4 weeks, active infection, and active Charcot arthropathy of the ulcer surface, vasculitis or continued tobacco smoking without physician attempt to affect smoking cessation);
   2. Known hypersensitivity to any component of the specific skin substitute graft (e.g., allergy to avian, bovine, porcine, equine products);
   3. Partial thickness loss with the retention of epithelial appendages (epithelium will repopulate the deficit).

Note: Treatment of any chronic skin wound will typically last no more than 12 weeks.

II. It is the policy of health plans affiliated with Centene Corporation that skin substitutes are **not medically necessary** for the following indications or scenarios:
A. All indications not noted in **Policy/criteria I**;
B. Decubitus (pressure) ulcer treatment;
C. Continued skin substitute use after treatment failure, which is 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;
D. Retreatment of healed ulcers (those showing greater than 75% size reduction and smaller than 1 square cm).

Background

According to the Centers for Medicare & Medicaid Services (CMS), chronic wounds of the lower extremities, including venous stasis ulcers (VSU), venous leg ulcers (VLU), diabetic foot ulcers (DFU) and pressure sores, are a major public health problem. While lower extremity ulcers have numerous causes, such as burns, trauma, mixed venous-arterial disease, immobility and vasculitis, nutritional or other neuropathy, over 90% of the lesions in the United States are related to venous stasis disease and diabetic neuropathy.[1] These wounds frequently require detailed interventions to start the healing process again; furthermore, patients experience significant functional loss, wound recurrence, and increased morbidity.[6]

Standard care for lower extremity wounds and ulcers includes infection control, management of edema, mechanical offloading of the affected limb, mechanical compression, limb elevation, debridement of necrotic tissue, management of systemic disease and counseling on the risk of continued tobacco use. Additionally, maintenance of a therapeutic wound environment with appropriate dressings can facilitate development of healthy granulation tissue and re-epithelialization. Dressings are essential to wound management because the appropriate dressing not only maintains the moisture balance within the wound, but the dressing also controls exudate, which protects the wound from additional trauma.[1,2]

A wound that has not healed within one to three months may be considered a chronic wound and can be a challenge to treat effectively. Even with advancements in standard wound care and synthetic occlusive dressings, some ulcers fail to heal and may benefit from a skin substitute.[1,2] Skin substitutes promote wound healing by replacing extracellular matrix.[7] Skin substitutes are categorized based on the composition of epidermal, dermal, and composite skin present.[7] They are heterogeneous and can be largely separated into two primary categories: cellular (comprised of living cells); or acellular (composed of synthetic materials or tissue from which living cells have been removed).[8,9] The categories are further split based on composition and source of material, including xenograft, acellular allograft, cellular allograft, autograft and synthetic skin substitute choices.[7]

For VLU, an evaluation for the presence of saphenous vein reflux is essential prior to consideration of skin substitutes. If there is significant saphenous vein incompetency and reflux (valve closure time defined as > 500 milliseconds), or if ulcer bed veins are identified as contributory on ultrasound, a referral to a vascular surgeon or interventional radiologist is required. Endovascular laser or radiofrequency ablation can enhance rates of healing compared to other treatments for significant saphenous vein reflux. Without significant reflux, sclerotherapy may also be more beneficial.[3]

According to a 2016 Cochrane review, the overall therapeutic outcome of skin grafts and tissue replacements used with standard wound care demonstrated an increase in the healing rate of foot ulcers and slightly fewer amputations in patients with diabetes compared with standard wound care alone.[10] The Wound Healing Society updated their guidelines in 2016, indicating that cellular and acellular skin equivalents positively affect healing in diabetic ulcers by “releasing therapeutic amounts of growth factors, cytokines, and other proteins that stimulate the wound bed.”[11]

There are currently a wide variety of bioengineered products available for soft tissue coverage to affect closure.[6]

Autologous skin grafts, also referred to as autografts, are permanent covers that use skin from different parts of the individual's body. These grafts consist of the epidermis and a dermal component of variable thickness. A split-thickness skin graft (STSG) includes the entire epidermis and a portion of the dermis. A full thickness skin graft (FTSG) includes all layers of the skin. Although autografts are the optimal choice for full thickness wound coverage, areas for skin harvesting may be limited, particularly in cases of large burns or venous stasis ulceration. Harvesting procedures are painful, disfiguring and require additional wound care.[2,4]

Allografts, which use skin from another human (e.g., cadaver), and Xenografts, which use skin from another species (e.g., porcine or bovine), may also be employed as temporary skin replacements. However, they must later be replaced by an autograft or the ingrowth of the patient's own skin.[2,4]

Bioengineered Skin and Cultured Epidermal Autografts (CEA) are autografts derived from the patient's own skin cells grown or cultured from very small amounts of skin or hair follicle. Production time is prolonged. One such product is grown on a layer of irradiated mouse cells, displaying some components of a xenograft. Widespread usage has not been available due to limited availability or access to the technology.[2,4]

Coding Implications

This clinical policy references Current Procedural Terminology (CPT®). CPT® is a registered trademark of the American Medical Association. All CPT codes and descriptions are copyrighted 2021, American Medical Association. All rights reserved. CPT codes and CPT descriptions are from the current manuals and those included herein are not intended to be all-inclusive and are included for informational purposes only. Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

CPT® Codes	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

CPT® Codes	Description
	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®* Codes	Description
A2001	InnovaMatrix AC, per sq cm
A2002	Mirragen Advanced Wound Matrix, per sq cm
A2003	bio-ConneKt 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
Q4100	Skin substitute, nos
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
Q4105	Integra dermal regeneration template (DRT) or Integra Omnigraft dermal regeneration matrix, per sq cm
Q4106	Dermagraft, per sq cm
Q4107	Graftjacket, per square centimeter
Q4108	Integra matrix, per sq cm
Q4110	Primatrix, per square centimeter

HCPCS®* Codes	Description
Q4111	Gammagraft, per sq cm
Q4115	Alloskin, per sq cm
Q4117	Hyalomatrix, per sq cm
Q4118	Matristem micromatrix, 1mg
Q4121	TheraSkin, per sq cm
Q4122	DermACELL, DermACELL AWM or DermACELL AWM Porous, per sq cmr
Q4123	AlloSkin RT, per sq cm
Q4124	Oasis ultra tri-layer wound matrix, per sq cm
Q4126	MemoDerm, DermaSpan, TranZgraft or IntեguPly, per sq cm
Q4127	Talymed, per sq cm
Q4128	FlexHD, or AllopatchHD, per sq cm
Q4132	Grafix Core and GrafixPL Core, per sq cm
Q4133	Grafix PRIME, GrafixPL PRIME, Stravix and StravixPL, 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 square centimeter
Q4140	BioDFence, per square centimeter
Q4141	Alloskin AC, per square centimeter
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
Q4151	AmnioBand or Guardian, per sq cm
Q4152	DermaPure, per sq cm
Q4153	Dermavest and Plurivest, per sq cm
Q4154	Biovance, per sq cm
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
Q4163	Woundex, bioskin, per sq cm
Q4164	Helicoll, per square cm
Q4165	Keramatrix or Kerasorb, per sq cm
Q4166	Cytal, per square centimeter
Q4169	Artacent wound, per sq cm
Q4170	Cygnus, per sq cm
Q4173	Palingen or Palingen Xplus, per sq cm
Q4175	Miroderm, per sq cm
Q4176	Neopatch or therion, per square centimeter
Q4178	FlowerAmnioPatch, per sq cm
Q4180	Revita, per sq cm

HCPCS®* Codes	Description
Q4184	Cellesta or Cellesta Duo, per sq cm
Q4186	Epifix, per square centimeter
Q4187	Epicord, per square centimeter
Q4188	AmnioArmor, per sq cm
Q4195	PuraPly, per square cm
Q4196	PuraPly AM , per square cm
Q4197	Puraply XT, per square cm
Q4199	Cygnus matrix, per sq cm
Q4201	Matrion, per sq cm
Q4203	Derma-Gide, per sq cm
Q4232	Corplex, 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
Q4254	Novafix DL, per sq cm

Reviews, Revisions, and Approvals	Revision Date	Approval Date
Policy adapted from WellCare's HS433 Skin Substitutes policy. Removed description information about identification of MD managing chronic conditions. Removed requirement for MD review of all requests. Rearranged some not medically necessary indications into the contraindications section. In I.D, changed requirement for no nicotine use for at least 4 weeks to documentation of effort to cease nicotine use, or no nicotine use for at least 4 weeks. In the diabetic foot ulcer criteria, removed requirement of neuropathy. In I.I.1, changed contraindication of "active Charcot arthropathy of the ulcer extremity" to "active Charcot arthropathy of the ulcer surface." In DFU section, removed documentation of assessment of physical activity, nutrition, physical exam, check of prosthetics, and history of diabetes management, including comorbidities. Changed requirement of HbA1c ≤7% to ≤8%, or with documented improvement of blood glucose in last 4 weeks. Changed HbA1c contraindication to >8% or with no document improvement of blood glucose in last 4 weeks. Reworded some extraneous language with no clinical significance. Removed criteria stating that switching products during an episode of wound care is not allowed. Removed not medically necessary language about repeated billing of surgical preparation services. Revised name of the policy to Skin Substitutes for Chronic Wounds.	04/20	04/20
Added criteria of age ≥ 18 years, or type 1 diabetic. Added to the requirement for documentation of effort to cease nicotine use that this does not include nicotine replacement therapy. Added to section II that all indications not noted in section I are not medically necessary. Added	05/20	06/20

Reviews, Revisions, and Approvals	Revision Date	Approval Date
CPT codes: 15271-15278; updated list of HCPCS codes of current products available, although not inclusive or guarantee of coverage.		
References reviewed and updated. All instances of "member" changed to "member/enrollee." HCPCS codes removed as they are not included in Medicare Article A56696: Q4150, Q4183, Q4190, Q4208-Q4226. Q4210, Q4217, Q4219, and Q4220 removed. New codes added (from Article A56696): Q4176, Q4237, Q4238, and Q4239.	04/21	04/21
Annual review completed. References reviewed and updated. Changed "Review Date" in the header to "Date of Last Revision" and "Date" in the revision log header to "Revision Date." Added "type 2 diabetes" to I.A. Reworded some extraneous language with no clinical significance. Added to I.F.2. "unless Integra® is used per FDA guidelines". Removed I.J.3. "Concurrent treatment with hyperbaric oxygen therapy". Background section updated with no additional impact to criteria. Added the following HCPCS codes: A2001-A2010, Q4199, Q4201, Q4232 and Q4254. Removed Q4119, Q4174. Added reference CMS A56696. Specialist reviewed.	04/22	04/22
Updated description for code Q4128.	10/22	

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Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. “Health Plan” means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan’s affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or

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This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care and are solely responsible for the medical advice and treatment of members/enrollees. This clinical policy is not intended to recommend treatment for members/enrollees. Members/enrollees should consult with their treating physician in connection with diagnosis and treatment decisions.

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Note: For Medicaid members/enrollees, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

Note: For Medicare members/enrollees, to ensure consistency with the Medicare National Coverage Determinations (NCD) and Local Coverage Determinations (LCD), all applicable NCDs, LCDs, and Medicare Coverage Articles should be reviewed prior to applying the criteria set forth in this clinical policy. Refer to the CMS website at http://www.cms.gov for additional information.