Clinical Policy: Skin and Soft Tissue Substitutes for Diabetic Foot Ulcers and Venous Leg Ulcers

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

Description

This policy outlines the medical necessity criteria for skin substitutes for diabetic foot ulcers (DFUs) and venous leg ulcers (VLUs) in the treatment of chronic wounds and is intended for use by Medicare health plans affiliated with Centene Corporation® in Medicare Administrative Contractors (MAC) jurisdictions with an absence of full coverage criteria provided by the Centers for Medicare and Medicaid Services (CMS) and the applicable MAC. These policy criteria are sourced from Local Coverage Determinations (LCDs) Wound Application of Cellular and/or Tissue Based Products (CTPs), Lower Extremities (L36690), Application of Skin Substitute Grafts for Treatment of DFU and VLU of Lower Extremities (L36377), and Application of Bioengineered Skin Substitutes to Lower Extremity Chronic Non-Healing Wounds (L35041), which are supported by peer-reviewed literature and guidelines. Additionally, criteria related to specific products considered medically necessary for DFUs and VLUs is sourced from peer-reviewed scientific literature.[8-78]

Standard treatment of chronic lower extremity ulcers or skin loss primarily includes infection and edema control, mechanical offloading, mechanical compression or limb elevation, debridement of necrotic or infected tissue, and management of concomitant and inciting medical issues (blood glucose control, tobacco use). Maintenance of a therapeutic environment with appropriate dressings to preclude further trauma facilitates development of healthy granulation tissue and encourages re-epithelialization. The fundamental basis for non-healing of a wound is of paramount importance and must be corrected prior to consideration of additional therapy, consistent with the criteria below. A failed response is defined as an ulcer or skin deficit that has failed to respond to documented appropriate wound-care measures, has increased in size or depth, or has not changed in baseline size or depth and has no indication that improvement is likely (such as granulation, epithelialization or progress towards closing).[1,2] Application of evidence-based wound care measures helps to ensure patients receive optimal care and progress towards treatment goals, thus minimizing the risks of treatment strategies of uncertain value.

The U.S. Food and Drug Administration (FDA) does not refer to any product or class of products as “skin substitutes.” However, products commonly described as cellular and/or tissue-based products (CTPs) are regulated by the FDA under one of four categories depending on the origin and composition of the product. The specific skin substitute products classified as medically necessary for the treatment of DFUs and/or VLUs have demonstrated safety and effectiveness and, therefore, benefit the patient by promoting healing and accelerating wound closure.[1,2]

Note: For criteria applicable to non-Medicare plans, please see CP.MP.185 Skin and Soft Tissue Substitutes for Chronic Wounds

Policy/Criteria

I. It is the policy of Medicare health plans affiliated with Centene Corporation® that up to four initial applications of skin and soft tissue substitutes will be considered medically reasonable and necessary for diabetic foot ulcers and venous leg ulcers when all of the following criteria are met:[1-3]

A. Wound is chronic, defined as a wound that does not respond to at least four weeks of standard wound treatment as a component of organized, comprehensive, conservative therapy;
B. Wound characteristics and treatment plan are documented;
C. Standard wound care has failed, evidenced by all the following:
   1. The ulcer or skin deficit has been treated with appropriate wound-care measures, including debridement, standard dressings, compression, off-loading;
   2. Wound area has reduced by <50% in four weeks[7];
D. Documentation of effort to cease nicotine use, including from sources other than cigarettes, but excluding nicotine replacement therapy, for at least four weeks during conservative wound care and prior to planned bioengineered skin replacement therapy, or no nicotine use;
E. 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 U.S. Food and Drug Administration (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 0.6 or toe pressure greater than 30 millimeters of mercury [mmHg]);
F. One of the following:
   1. Diabetic foot ulcer (DFU), and all the following:
      a. Diagnosis of Type 1 or Type 2 Diabetes and medical management for the condition;
      b. Documented conservative wound care for ≥ four weeks;
      c. Wound is without evidence of osteomyelitis or nidus of infection;
      d. One of the following products is requested:
         i. AmnioBand, guardian (Q4151);
         ii. Affinity (Q4159);
         iii. Apligraf (Q4101);
         iv. DermACELL, DermACELL AWM, or DermACELL AWM porous (Q4122);
         v. Derma-Gide (Q4203);
         vi. Dermagraft (Q4106);
         vii. Epicord (Q4187);
         viii. Epifix (Q4186);
         ix. FlexHD or AllopatchHD (Q4128);
         x. Grafix PRIME, GrafixPL PRIME, Stravix and StravixPL (Q4133);
         xi. GraftJacket (Q4107);
         xii. Integra dermal regeneration template or Integra Omniograft dermal regeneration matrix (Q4105);
         xiii. Kerecis Omega 3 (Q4158);
         xiv. Kerecis Omega3 MariGen shield (A2019);
         xv. NuShield (Q4160);
         xvi. Oasis wound matrix (Q4102);

xvii. PriMatrix (Q4110);
xviii. Theraskin (Q4121);

2. Venous leg ulcers (VLU), all of the following:
   a. A chronic, non-infected VLU has failed to respond to documented conservative wound-care measures for ≥ four 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. A venous duplex ultrasound has been completed to assess saphenous vein incompetency/venous reflux and contributory superficial ulcer bed perforators;
   d. One of the following products is requested:
      i. AmnioBand, guardian (Q4151);
      ii. Apligraf (Q4101);
      iii. Dermagraft (Q4106);
      iv. Epifix (Q4186);
      v. Oasis wound matrix (Q4102);

G. Requested use complies with FDA-approved indications for the specific product;
H. Only one skin substitute will be simultaneously in place per wound episode. Note: product change within the wound episode is allowed, with a total of up to four initially authorized and total applications not to exceed the eight-application limit per wound per 12–16-week episode of care;
I. The graft will 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;
J. The following documentation requirements will be met for each application:
   1. Graphic evidence of ulcer size, depth, and characteristics of the ulcer or photo documentation of the ulcer at baseline and follow-up with measurements of wound including size and depth;
   2. A complete description of the procedure including product used (with identifying package label or National Drug Code (NDC) in the chart) and size of product used;
   3. If multiple sizes of a specific product are available, the size that best fits the wound is utilized, with the least amount of wastage;
   4. If a portion of a product is discarded, documentation includes all the following:
      a. The amount administered and wasted;
      b. The date, time, and amount of product wasted and the reason for the wastage.

      Note:
      - When a portion of a single use package must be discarded, payment will be made for the portion discarded along with the amount applied up to the amount of the product on the package label.
      - All documentation must be maintained in the member/enrollee's medical record and made available upon request.

K. None of the following contraindications:
   1. Inadequate control of underlying conditions or exacerbating factors (e.g., uncontrolled diabetes, active infection, and active Charcot arthropathy of the ulcer extremity, vasculitis or continued tobacco smoking without physician attempt to effect 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 Medicare health plans affiliated with Centene Corporation® that continued treatment beyond the initial four applications and up to a total of eight applications with skin and soft tissue substitutes/cellular and tissue-based products (CTPs) is **medically necessary** for diabetic foot ulcers (DFU) or venous leg ulcers (VLU) when all the following criteria are met:

A. Request is for one of the following:
   1. For DFU, one of the following products is requested:
      a. AmnioBand, guardian (Q4151);
      b. Affinity (Q4159);
      c. Apligraf (Q4101);
      d. DermACELL, DermACELL AWM, or DermACELL AWM porous (Q4122);
      e. Derma-Gide (Q4203);
      f. Dermagraft (Q4106);
      g. Epicord (Q4187);
      h. Epifix (Q4186);
      i. FlexHD or AllopatchHD (Q4128);
      j. Grafix PRIME, GrafixPL PRIME, Stravix and StravixPL (Q4133);
      k. GraftJacket (Q4107);
      l. Integra dermal regeneration template or Integra Omniograft dermal regeneration matrix (Q4105);
      m. Kerecis Omega 3 (Q4158);
      n. Kerecis Omega3 MariGen shield (A2019);
      o. NuShield (Q4160);
      p. Oasis wound matrix (Q4102);
      q. PriMatrix (Q4110);
      r. Theraskin (Q4121);
   2. For VLU, one of the following products is requested:
      a. AmnioBand, guardian (Q4151);
      b. Apligraf (Q4101);
      c. Dermagraft (Q4106);
      d. Epifix (Q4186);
      e. Oasis wound matrix (Q4102);

B. Requested use complies with labeled indications;

C. Documentation includes all the following:
   1. Explanation of why extended time or additional applications (beyond the initial four) are medically necessary for the specific member/enrollee's wound;
   2. That the treatment plan regarding the initial four applications has resulted in wound healing and expectation that the wound will continue to heal with this plan;
   3. Estimated time for extended treatment, number of additional applications anticipated, and plan of care if healing is not achieved as planned;

4. Modifiable risk factors, such as diabetes, venous insufficiency, and neuropathy, are being addressed adequately to improve likelihood of healing;
5. For VLU, appropriate consultation and management for the diagnosis and stabilization of any venous-related disease;
6. Additional documentation from each of the initial four applications, and for all subsequent applications, includes all the following:
   a. A complete description of the procedure including product used (with identifying package label or NDC in the chart) and size of product used;
   b. Graphic evidence of ulcer size, depth, and characteristics of the ulcer or photo documentation of the ulcer at baseline and follow-up with measurements of wound including size and depth;
   c. The skin substitute is 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;
   d. When multiple sizes of a specific product are available, the size that best fits the wound with the least amount of wastage is utilized;

D. Only one skin substitute will be simultaneously in place per wound episode with the first skin substitute graft/CTP application beginning the episode of care. **Note:** Product change within the wound episode is allowed; total applications not to exceed the eight-application limit per wound per 12–16-week episode of care;

E. When a portion of a product was discarded, the medical record clearly demonstrates the amount administered and wasted, in addition to the date, time, amount of product wasted and the reason for the wastage.

Note:

- When a portion of a single use package must be discarded, payment will be made for the portion discarded along with the amount applied up to the amount of the product on the package label.
- All documentation must be maintained in the member/enrollee's medical record and made available upon request.

III. It is the policy of Medicare health plans affiliated with Centene Corporation that skin and soft tissue substitutes for diabetic foot ulcers and venous leg ulcers are **not medically necessary** for the following indications or scenarios:[1-3]

A. Partial thickness loss with the retention of epithelial appendages, as epithelium will repopulate the deficit from the appendages, negating the benefit of overgrafting;

B. Simultaneous use of more than one product for the episode of wound.

C. Repeat or alternative applications of skin substitute grafts when a previous full course of applications was unsuccessful. Unsuccessful treatment is defined as increase in size or depth of an ulcer or no change in baseline size or depth and no sign of improvement or indication that improvement is likely (such as granulation, epithelialization or progress towards closing) for a period of 4 four weeks past start of therapy.

D. Retreatment of healed ulcers, those showing greater than 75% size reduction and smaller than 0.5 square cm.

E. Re-treatment within one (1) year of any given course of skin substitute treatment for a venous stasis ulcer or (diabetic) neuropathic foot ulcer.

Note:

- It is expected that where multiple sizes of a specific product are available, the size that best fits the wound with the least amount of wastage will be utilized.[4,5]
- Repeat use of surgical preparation services in conjunction with skin substitute

application codes will be considered not reasonable and necessary. It is expected that each wound will require the use of appropriate wound preparation code at least once at initiation of care prior to placement of the skin substitute graft.[1-3]

- The following documentation requirements apply, and all documentation must be maintained in the medical chart and made available upon request:[4,5]
    - Every page of the record must be legible and include appropriate patient identification information (e.g., complete name, dates of service(s)). The documentation must include the legible signature of the physician or non-physician practitioner responsible for and providing the care to the patient.
    - The submitted medical record must support the use of the selected ICD-10-CM code(s). The submitted CPT/HCPCS code must describe the service performed.
    - Medical record documentation must support the medical necessity of the services as directed in this policy.
    - The documentation must support that the service was performed and must be included in the patient's medical record. This information is normally found in the history and physical, office/progress notes, hospital notes, and/or procedure report.
    - The medical record must clearly show that the criteria above have been met as well as the appropriate diagnosis and response to treatment.
    - The documentation must support the need for cellular and/or tissue-based product (CTP) application and the product used.
    - A description of the wound(s) must be documented at baseline (prior to beginning conservative treatment) relative to size, location, stage, duration, and presence of infection, in addition to type of treatment given and response.
    - All information must be updated in the medical record throughout treatment.
    - Wound description must also be documented pre and post treatment with the skin substitute graft being used.
    - If obvious signs of worsening or lack of treatment response is noted, continuing treatment with the skin substitute would not be considered medically reasonable and necessary without documentation of a reasonable rationale for doing so.
    - Documentation of smoking history, and that the patient has received counseling on the effects of smoking on surgical outcomes and treatment for smoking cessation (if applicable) as well as outcome of counselling must be in the medical record.
    - The amount of utilized and wasted skin substitute must be clearly documented in the procedure note with the following minimum information:
        - Date, time and location of ulcer treated;
        - Name of skin substitute and how product supplied;
        - Amount of product unit used;
        - Amount of product unit discarded;
        - Reason for the wastage;
        - Manufacturer's serial/lot/batch or other unit identification number of graft material. When manufacturer does not supply unit identification, record must document such.

Background

Centers for Medicare & Medicaid Services[1-3]

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 major public health problems. 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.

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.

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 various synthetic occlusive dressings, some ulcers fail to heal and may benefit from a skin substitute.

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.

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.

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.

Cellular and/or tissue-based products (CTPs) were developed to address problems with autografts, allografts, and xenografts. These consist of biologic covers for refractory wounds with full thickness skin loss secondary to third degree burns, diabetic neuropathic ulcers and the skin loss of chronic venous stasis or venous hypertension. The production of these biologic CTPs varies by company and product but generally involves the creation of immunologically inert biological products containing protein, hormones or enzymes seeded into a matrix which may provide protein or growth factors intended to stimulate or facilitate healing or promote epithelization. There are currently a broad range of bioengineered products available for soft tissue coverage to affect closure. Sufficient data is available to establish distinct inferiority to human skin autografts and preclude their designation as skin equivalence.

Diabetic Foot Ulcers (DFUs):

- *Affinity*: One randomized controlled trial (RCT) with a sample size of 76 reported wound closure at 16 weeks of 63% in Affinity arm and 38% in standard of care (SOC) arm (n=38).[8]
- *AmnioBand, guardian*: One RCT with a sample size of 60 reported a healing rate at 12 weeks was 90% for the AmnioBand group versus 40% for the Apligraf group.[9] Another RCT with a sample size of 40 reported at 12 weeks 85% of the DFU in the AmnioBand group healed compared with 25% in the SOC group.[10] Additionally, a RCT with a sample size of 80 reported at 12 weeks 85% of the DFUs in the AmnioBand group achieved healing compared with 33% of the DFUs in the SOC group.[11]
- *Apligraf*: One RCT with a sample size of 208 reported wound closure at 12 weeks of 56% for the Apligraf group and 28% for the SOC group,[12] another RCT with a sample size of 72 reported on wound closure at 12 weeks of 55.2% for Apligraf and 34.3% for SOC,[13] and another RCT with a sample size of 82 reported on wound healing at 12 weeks of 51.5% for Apligraf and 26.3% for SOC.[14] One RCT with a sample size of 60 reported on wound closure at 6 weeks of 95% for EpiFix, 45% for Apligraf, and 35% for SOC.[15]
- *DermACELL, awm, porous*: One RCT with a sample size of 168 reported the healing rate at 16 weeks was 67.9% in the DermACELL arm, 48.1% in the SOC arm, 47.8% in the GraftJacket arm.[16,17] Further, a prospective study with a sample size of 61 of large complex wounds treated with DermACELL reported 24.6% closure at 16 weeks.[18]
- *Derma-Gide*: One RCT with a sample size of 40 reported wound closure at 12 weeks of 85% of the Derma-Gide group and 30% of the SOC group (interim analysis).[19] Another RCT with a sample size of 105 reported wound closure at 12 weeks of 83% of the Derma-Gide group and 45% of the SOC group,[20] and there are further retrospective case series and a bench report.[21-23]
- *Dermagraft*: One RCT with a sample size of 314 reported wound closure at 12 weeks of 30% of the Dermagraft group and 18.3% in the SOC group.[24] Another RCT with a sample size of 50 reported on wound closure at 12 weeks with 50% for the Dermagraft and 8% in the SOC group.[25] Additionally, one RCT with a sample size of 23 reported wound closure at 20 weeks with 90.91% in the Theraskin group and 66.67% in the Dermagraft group.[26]
- *Epicord*: One RCT with a sample size of 155 reported wound closure at 12 weeks of 70% for EpiCord and 48% for SOC.[27]
- *Epifix*: One RCT with a sample size of 25 reported wound healing at six weeks in the EpiFix group of 92% and 8% in the SOC group.[28] Another RCT with a sample size of 60 reported on wound closure at 6 weeks of 95% for EpiFix, 45% for Apligraf and 35% for SOC.[29] Further, one RCT with a sample size of 104 reported wound closure at 12 weeks of 73% for Apligraf, 97% for EpiFix and 51% for SOC,[30] and another RCT with a sample size of 110 reported on wound closure at 12 weeks of 70% EpiFix and 50% SOC in the intention-to-treat (ITT) analysis.[31]
- *FlexHD or AllopatchHD*: One RCT with a sample size of 40 reported a wound healing at 12 weeks of 80% for AlloPatch and 20% for SOC;[32] an additional 40 participants enrolled and reported similar results.[33] There is literature also in breast reconstruction, rotator cuff repair, hernia repair, lab research,[34-36] and a retrospective report.[32]
- *Grafix stravix prime pl*: One RCT with a sample size of 97 reported wound closure at 12 weeks was 62% in the Grafix group and 21% in the SOC group.[37] There was also a retrospective report with a sample size of 441.[38]
- *GraftJacket*: One RCT with a sample size of 40 reported on wound healing at 12 weeks

with a 67.4% reduction with GraftJacket and 34% with SOC.[39] Another RCT with a sample size of 28 reported on wound closure at 16 weeks of 85.71% in the GraftJacket arm and 28.57% in SOC, [40] and one RCT with a sample size of 86 reported on mean wound healing time of 12 weeks was 30.4% with GraftJacket and 53.9% with SOC.[41] Additionally, one RCT with a sample size of 168 reported on wound closure at 16 weeks of 67.9% for DermACELL, 47.8% for GraftJacket, and 48.1% for SOC.[42,43] These studies were included in a meta-analysis[44] and GraftJacket in another.[45]

- *Integra or Omniograft dermal regeneration template*: One RCT with a sample size of 307 reported wound closure at 16 weeks of 51% in the Integra group and 32% in the SOC group.[46]
- *Kerecis Omega3/Kerecis omega3, MariGen shield*: One RCT with a sample size of 170 was conducted for healing in the punch biopsy site.[47] One RCT with a sample size of 49 reported wound closure at 12 weeks of 67% for Kerecis and 32% for SOC,[48] and another RCT with a sample size of 102 reported 56.9% wound closure by 12 weeks in the Kerecis group and 31.4% in the SOC group.[49] Further, another RCT with a sample size of 255 reported wound closure by 16 weeks of 44% in Kerecis group and 26% in SOC.[50]
- *NuShield*: One RCT with a sample size of 218 reported on wound closure at 12 weeks with 50% closure for NuShield and 35% for SOC alone.[51] Additional literature is a case report,[52] retrospective report with 50 wounds,[53] and literature in talar dome lesions.
- *Oasis wound matrix*: One RCT with a sample size of 26 reported no difference in closure time for Dermagraft (84.6%) or Oasis Wound Matrix (76.9%).[54] Another RCT with a sample size of 73 reported on wound healing at 12 weeks of 49% for Oasis wound matrix and 28% for Regranex gel.[55]
- *Primatrix*: One RCT with a sample size of 161 reported wound closure at 12 weeks of 59.5% for the PrimMatrix arm and 35.4% for the SOC arm.[56] Further evidence includes a prospective trial with a sample size of 55[57], retrospective[58,59] and lab trials.[60]
- *Theraskin*: One RCT with a sample size of 50 reported on wound healing at 12 weeks was 76% for TheraSkin and 36% for SOC.[61] Another RCT with a sample size of 23 reported wound closure at 20 weeks with 90.91% in the Theraskin group and 66.67% in the Dermagraft group.[62] Further evidence includes a small prospective study with a sample size of 29,[63] retrospective cohort studies,[64,65] and a lab study.[66]

Venous Leg Ulcers (VLUs):

- *AmnioBand, guardian*: One randomized controlled trial (RCT) with a sample size of 60 reported healing rates at 12 weeks were 75% in the two AmnioBand groups and 30% in the standard of care (SOC) group.[67]
- *Apligraf*: One RCT with a sample size of 275 reported on wound closure at six months of 63% for Apligraf and 49% for SOC.[68] Another RCT with a sample size of 120 reported on wound closure at 24 weeks of 47% for Apligraf and 19% for SOC,[69] and another RCT with a sample size of 31 reported on wound healing at 12 weeks of 93.3% for Theraskin and 75% for Apligraf.[70]
- *Dermagraft*: One RCT with a sample size of 366 reported on wound closure at 12 weeks of 34% for Dermagraft and 31% for SOC.[71]
- *Epifix*: One RCT with a sample size of 53 reported on wound reduction in four weeks for 62% for EpiFix and 32% for SOC.[72] Another RCT with a sample size of 109 reported wound closure at 16 weeks for VLU was 71% for EpiFix and 44% for SOC.[73] The follow-up report included intention-to-treat (ITT) analysis reported similar results with 50% in the EpiFix group and 31% in SOC.[74]
- *Oasis wound matrix*: One RCT with a sample size of 48 reported wound closure at eight

weeks of 80% for Oasis wound matrix and 65% for SOC.[75] Another RCT with a sample size of 120 reported on wound healing at 12 weeks of 55% in Oasis group and 34% in SOC.[76] Further, a RCT with a sample size of 89 reported on wound closure at 12 weeks with 47.1% for Dermagraft, 73.7% for Oasis, and 57.9% for SOC,[77] and another RCT with a sample size of 84 reported on wound closure at 12 weeks of 71% Oasis and 46% SOC.[78]

The following skin substitutes had either no supportive scientific literature identified or insufficient evidence to support the medical necessity of DFU/VLU indications:

1. Ac5 advanced wound system (ac5)
2. Acesso dl, Acesso tl
3. Activate matrix
4. AlloDerm
5. Allogen, per cc
6. Alloskin, Alloskin ac
7. Allowrap DS or DRY
8. American amnion, American amnion AC, American Amnion, Tri-Layer
9. Amnio bio or axobiomembrane
10. Amnio quad-core
11. Amnio Wound
12. Amnioamp-MP
13. Amnioarmor
14. AmnioBand particulate, 1 mg
15. Amniocore, Amniocore pro, Amniocore pro+
16. Amniocyte plus, per 0.5cc
17. Amnioexcel, Amnioexcel plus or biodexcel
18. Amniomatrix or Biodmatrix, injectable, 1 cc
19. Amnio-maxx or amnio-maxx lite
20. Amniorepair or Altiply
21. Amniotext patch
22. Amniotext, per cc
23. Amnio-tri-core amniotic
24. Amniowrap2
25. Amniply, for topical use only
26. Apis
27. Architect ecm px fx
28. Artacent ac, 1 mg
29. Artacent am
30. Artacent cord
31. Artacent wound
32. Arthroflex
33. Ascent, 0.5 mg
34. Axolotl ambient or axolotl cryo, 0.1mg
35. Axolotl graft or axolotl dualgraft
36. Barrera SL or barrera dl
37. Bellacell HD or Surederm
38. Bio-connekt wound matrix
39. BioDFence dryflex
40. Bionextpatch
41. Biovance, Biovance Tri-Layer or biovance 3L
42. Carepatch
43. Celera dual layer or celera dual membrane
44. Cellesta cord, Cellesta or Cellesta Duo
45. Cellesta flowable amnion per 0.5cc
46. Cocoon membrane
47. Cogenex amniotic membrane
48. Cogenex flowable amnion, per 0.5cc
49. Coll-e-derm
50. Complete aa, Complete aca, Complete sl, Complete ft
51. Corecyte, for topical use only, per 0.5cc
52. Coretext or protext, per cc
53. Corplex
54. Corplex P, per cc
55. Cryo-cord
56. Cygnus
57. Cygnus dual
58. Cygnus, matrix
59. Cymetra, injectable, 1 cc
60. Cytal (formerly Matristem)
61. Dermabind dl, Dermabind ch, Dermabind sl
62. DermaBind tl or Amniobind
63. Dermacyte amniotic membrane allograft
64. Dermapure
65. Dermavest, plurivest
66. Derm-maxx

67. Emerge matrix
68. Enverse
69. Epieffect
70. EpiFix injectable, 1 mg
71. Esano a, Esano aaa, Esano ac, Esano aca
72. Excellagen, 0.1cc
73. EZ-derm
74. Floweramnioflo, 0.1 cc
75. Floweramniopatch
76. Flowerderm
77. Fluid flow or fluid gf, 1 cc
78. Gammagraft
79. Genesis amniotic membrane
80. Grafix core, grafixpl core
81. Grafix plus
82. GraftJacket Xpress, injectable, 1 cc
83. Helicoll
84. Hmatrix
85. Hyalomatrix
86. Impax, Impax dual layer membrane, Impax dual later amniotic graft
87. Innovaburn or Innovamatrix xl
88. Innovamatrix ac, Innovamatrix fs
89. Innovamatrix pd 1mg
90. Integra bilayer dermal matrix wound dressing
91. Integra flowable wound matrix, injectable, 1 cc
92. Integra Meshed Bilayer Wound Matrix
93. Interfyl, 1 mg
94. Keramatrix or Kerasorb
95. Keroxx (2.5G/CC), 1 cc
96. Lamellas xt, Lamellas
97. Matriderm
98. Matrion
99. Matristem micromatrix, 1 mg, MAtristem wound matrix, Matristem burn matrix
100. Mediskin
101. Membrane graft or membrane wrap
102. Membrane wrap-hydro
103. Memoderm, Dermaspan, Tranzgraft, or Integuply
104. Mgl-complete
105. Microlyte, Matrix
106. Miro3d
107. Miroderm
108. Mirragen adv wnd matrix
109. MyOwnSkin
110. Neomatrix
111. Neopatch or Therion
112. Neostim tl, Neostim membrane, Neostim dl
113. Neox 100 or clarix 100
114. Neox cord 1K, Neox Cord rt, or Clarix cord 1K
115. Neox Flo or Clarix Flo, 1 mg
116. Novachor
117. Novafix, Novafix dl
118. Novosorb Synpath Dermal Matrix
119. Nudyn dl or nudyn dl mesh, Nudyn sl or nudyn slw
120. Oasis burn matrix
121. Oasis Tri-Layer Matrix
122. Omeza collagen matrix, per 100 mg
123. Orion
124. Palingen or Promarx, 0.36 mg per 0.25cc
125. Palingen, palingen xplus, or Promarx
126. Permeaderm b, Permeaderm c
127. Phoenix wound matrix
128. Polycyte, for topical use only, per 0.5cc
129. Porcine implant, Permacol
130. Procenta, per 200 mg
131. Progenamatrix
132. PuraPly, PuraPly xt
133. PuraPly, am
134. Rebound matrix
135. Reguard, for topical use
136. Relese
137. Repriza
138. Resolve matrix
139. Restorigin
140. Restorigin, 1 cc
141. Restrata
142. Revita
143. Revitalon
144. Revoshield + amniotic barrier, per sq cm
145. Sanopellis
146. Signature apatch
147. Skin te
148. Strattice TM
149. Supra sdrm
150. Suprathel

151. Surfactor or Nudyn, per 0.5cc
152. Surgicord
153. Surgigraft, Surgraft tl, Surgraft ft, Surgraft xt, Surgigraft-dual
154. SurgiMend Collagen Matrix, per 0.5 sq cm
155. Surgraft
156. Symphony
157. Tag
158. Talymed
159. Tensix
160. Theragenesis
161. Transcyte
162. Truskin
163. Unite biomatrix
164. Via Matrix
165. Vendaje, Vendaje ac
166. VIM
167. Woundex flow, Bioskin flow, 0.5 cc
168. Woundex, BioSkin
169. Woundfix, Biowound, Woundfix plus, biowound plus, Woundfix xplus or biowound xplus
170. Woundplus membrane or e-graft
171. Xcell amnio matrix
172. Xcellerate
173. Xcellistem, 1 mg
174. XCM biologic tissue matrix
175. Xwrap
176. Zenith amniotic membrane

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 2024, 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.

Table 1 - CPT Codes that support medical necessity criteria

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 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)

CPT Codes	Description
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)

Table 2 - HCPCS codes that support medical necessity criteria for diabetic foot ulcers (DFUs)

HCPCS Codes	Description
A2019	Kerecis Omega3 MariGen Shield, per sq cm
Q4101	Apligraf, per sq cm
Q4102	Oasis wound matrix, 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 sq cm
Q4110	PriMatrix, per sq cm
Q4121	TheraSkin, per sq cm
Q4122	DermACELL, DermACELL AWM or DermACELL AWM Porous, per sq cm
Q4128	FlexHD, or AllopatchHD, per sq cm
Q4133	Grafix PRIME, GrafixPL PRIME, Stravix and StravixPL, per sq cm
Q4151	AmnioBand or Guardian, per sq cm
Q4158	Kerecis Omega3, per sq cm
Q4159	Affinity, per sq cm
Q4160	NuShield, per sq cm
Q4186	Epifix, per sq cm
Q4187	Epicord, per sq cm
Q4203	Derma-Gide, per sq cm

Table 3 – HCPCS codes that support medical necessity criteria for venous leg ulcers (VLUs)

HCPCS Codes	Description
Q4101	Apligraf, per sq cm
Q4102	Oasis wound matrix, per sq cm
Q4106	Dermagraft, per sq cm
Q4151	AmnioBand or Guardian, per sq cm
Q4186	Epifix, per sq cm

Table 4 - HCPCS codes that do not support medical necessity criteria

HCPCS Codes	Description
A2001	InnovaMatrix AC, per sq cm
A2002	Mirragen Advanced Wound Matrix, per sq cm
A2004	XCelliStem, 1 mg
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
A2012	Suprathel, per sq cm
A2013	Innovamatrix FS, per sq cm
A2014	Omeza Collagen Matrix, per 100 mg
A2015	Phoenix Wound Matrix, per sq cm
A2016	PermeaDerm B, per sq cm
A2017	PermeaDerm Glove, each
A2018	PermeaDerm C, per sq cm
A2020	AC5 Advanced Wound System (AC5)
A2021	NeoMatriX, per sq cm
A2022	InnovaBurn or InnovaMatrix XL, per sq cm
A2023	InnovaMatrix PD, 1 mg
A2024	Resolve Matrix or XenoPatch, per sq cm
A2025	Miro3D, per cu cm
A2027	MatriDerm, per sq cm
A4175	Miroderm, per sq cm
C9358	Dermal substitute, native, nondenatured collagen, fetal bovine origin (SurgiMend Collagen Matrix), per 0.5 sq cm
C9360	Dermal substitute, native, nondenatured collagen, neonatal bovine origin (SurgiMend Collagen Matrix), per 0.5 sq cm
C9363	Skin substitute (Integra Meshed Bilayer Wound Matrix), per sq cm
C9364	Porcine implant, Permacol, per sq cm
Q4103	Oasis burn matrix, per sq cm
Q4104	Integra bilayer matrix wound dressing (BMWD), per sq cm
Q4108	Integra matrix, per sq cm
Q4111	GammaGraft, per sq cm
Q4112	Cymetra, injectable, 1 cc
Q4113	GRAFTJACKET XPRESS, injectable, 1 cc
Q4114	Integra flowable wound matrix, injectable, 1 cc
Q4115	AlloSkin, per sq cm
Q4116	AlloDerm, per sq cm
Q4117	HYALOMATRIX, per sq cm
Q4118	MatriStem micromatrix, 1 mg
Q4123	AlloSkin RT, per sq cm
Q4124	OASIS ultra tri-layer wound matrix, per sq cm
Q4125	ArthroFlex, per sq cm

HCPCS Codes	Description
Q4126	MemoDerm, DermaSpan, TranZgraft or IntéguPly, per sq cm
Q4127	Talymed, per sq cm
Q4130	Strattice TM, per sq cm
Q4132	Grafix Core and GrafixPL Core, per sq cm
Q4134	HMatrix, per sq cm
Q4136	EZ Derm, per sq cm
Q4137	AmnioExcel, AmnioExcel Plus or BioDExcel, per sq cm
Q4138	BioDFence DryFlex, per sq cm
Q4139	AmnioMatrix or BioDMatrix, injectable, 1 cc
Q4140	BioDFence, per sq cm
Q4141	AlloSkin AC, per sq cm
Q4142	XCM biologic tissue matrix, per sq cm
Q4143	Repriza, per sq cm
Q4145	EpiFix, injectable, 1 mg
Q4146	TENSIX, per sq cm
Q4147	Architect, Architect PX, or Architect FX, extracellular matrix, per sq cm
Q4148	Neox Cord 1K, Neox Cord RT, or Clarix Cord 1K, per sq cm
Q4149	Excellagen, 0.1 cc
Q4150	AlloWrap DS or dry, per sq cm
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
Q4161	bio-ConneKt wound matrix, per sq cm
Q4162	WoundEx Flow, BioSkin Flow, 0.5 cc
Q4163	WoundEx, BioSkin, per sq cm
Q4164	Helicoll, per sq cm
Q4166	Cytal, per sq cm
Q4167	Truskin, per sq cm
Q4168	AmnioBand, 1 mg
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
Q4176	NeoPatch or Therion, per sq cm
Q4177	FlowerAmnioFlo, 0.1 cc
Q4178	FlowerAmnioPatch, per sq cm
Q4179	FlowerDerm, per sq cm
Q4180	Revita, per sq cm
Q4181	Amnio Wound, per sq cm
Q4182	Transcyte, per sq cm
Q4183	Surgigraft, per sq cm
Q4184	Cellesta or Cellesta Duo, per sq cm

HCPCS Codes	Description
Q4185	Cellesta Flowable Amnion (25 mg per cc); per 0.5 cc
Q4188	AmnioArmor, per sq cm
Q4189	Artacent AC, 1 mg
Q4190	Artacent AC, per sq cm
Q4191	Restorigin, per sq cm
Q4192	Restorigin, 1 cc
Q4193	Coll-e-Derm, per sq cm
Q4194	Novachor, per sq cm
Q4195	PuraPly, per sq cm
Q4196	PuraPly AM, per sq cm
Q4197	PuraPly XT, per sq cm
Q4198	Genesis Amniotic Membrane, per sq cm
Q4199	Cygnus matrix, per sq cm
Q4200	SkinTE, per sq cm
Q4201	Matrion, per sq cm
Q4202	Keroxx (2.5 g/cc), 1 cc
Q4204	XWRAP, per sq cm
Q4205	Membrane Graft or Membrane Wrap, per sq cm
Q4206	Fluid Flow or Fluid GF, 1 cc
Q4208	Novafix, per sq cm
Q4209	SurGraft, per sq cm
Q4210	Axolotl Graft or Axolotl DualGraft, per sq cm
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	Amnio Wrap2, per sq cm
Q4222	ProgenaMatrix, per sq cm
Q4224	Human Health Factor 10 Amniotic Patch (HHF10-P), per sq cm
Q4225	AmnioBind or DermaBind TL, per sq cm
Q4226	MyOwn Skin, includes harvesting and preparation procedures, per sq cm
Q4227	AmnioCore TM, 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

HCPCS Codes	Description
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
Q4251	Vim, per sq cm
Q4252	Vendaje, per sq cm
Q4253	Zenith Amniotic Membrane, 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
Q4259	Celera Dual Layer or Celera Dual Membrane, per sq cm
Q4260	Signature Apatch, per sq cm
Q4261	TAG, 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 sq cm
Q4266	NeoStim Membrane, per sq cm
Q4267	NeoStim DL, per sq cm
Q4268	SurGraft FT, per sq cm
Q4269	SurGraft XT, per sq cm
Q4270	Complete SL, per sq cm
Q4271	Complete FT, per sq cm
Q4272	Esano A, per sq cm
Q4273	Esano AAA, per sq cm
Q4274	Esano AC, per sq cm
Q4275	Esano ACA, per sq cm
Q4276	ORION, per sq cm
Q4278	EPIEFFECT, per sq cm
Q4279	Vendaje AC, per sq cm
Q4280	Xcell Amnio Matrix, per sq cm
Q4281	Barrera SL or Barrera DL, per sq cm
Q4282	Cygnus Dual, per sq cm
Q4283	Biovance Tri-Layer or Biovance 3L, per sq cm

HCPCS Codes	Description
Q4284	DermaBind SL, per sq cm
Q4285	NuDYN DL or NuDYN DL MESH, per sq cm
Q4286	NuDYN SL or NuDYN SLW, per sq cm
Q4287	DermaBind DL, per sq cm
Q4288	DermaBind CH, per sq cm
Q4289	RevoShield+ Amniotic Barrier, per sq cm
Q4290	Membrane Wrap-Hydro(TM), per sq cm
Q4291	Lamellas XT, per sq cm
Q4292	Lamellas, per sq cm
Q4293	Acesso DL, per sq cm
Q4294	Amnio Quad-Core, per sq cm
Q4295	Amnio Tri-Core Amniotic, per sq cm
Q4296	Rebound Matrix, per sq cm
Q4297	Emerge Matrix, per sq cm
Q4298	AmniCore Pro, per sq cm
Q4299	AmniCore Pro+, per sq cm
Q4300	Acesso TL, per sq cm
Q4301	Activate Matrix, per sq cm
Q4302	Complete ACA, per sq cm
Q4303	Complete AA, per sq cm
Q4304	GRAFIX PLUS, per sq cm
Q4305	American Amnion AC Tri-Layer, per sq cm
Q4306	American Amnion AC, per sq cm
Q4307	American Amnion, per sq cm
Q4308	Sanopellis, per sq cm
Q4309	VIA Matrix, per sq cm

Reviews, Revisions, and Approvals	Revision Date	Approval Date
Policy developed.	03/24	
Annual review. Update to background with no impact on criteria. Updated verbiage in criteria II.A. for clarity. Removed prior criteria II.B. Updated verbiage in now criteria II.B. for clarity. Removed previous criteria II.D. Updated verbiage in now criteria II.C. and D. Removed previous criteria II.G. through I. Updated verbiage in now criteria II.E. for clarity. Added note to new criteria I.G. to see Table 2, HCPCS codes that support medical necessity criteria… Added not regarding documentation requirements under criteria II. Moved HCPCS codes A2009 and Q4304 from table of HCPCS codes that *do not* support medical necessity to HCPCS codes that *do* support medical necessity. References reviewed and updated. Reviewed by external specialist.	04/25	04/25
Annual review. Updated Description with no clinical significance. Added I.F.1.d. concerning list of requested products for DFUs. Added I.F.2.d. concerning list of requested products for VLUs. Updated wording in I.G., II.C., and Note under II.E. with no clinical significance. Updated wording in Background and added "Skin Substitute Product Evidence Assessment" section regarding skin substitute products for treatment of DFUs and	08/25	

Reviews, Revisions, and Approvals	Revision Date	Approval Date
VLUs and skin substitute products considered not medically necessary. Coding tables reviewed. Replaced original Table 2 ("HCPCS codes that support medical necessity criteria") with new Table 2 ("HCPCS codes that support medical necessity criteria for diabetic foot ulcers [DFUs]") and added Table 3 ("HCPCS codes that support medical necessity criteria for venous leg ulcers [VLUs]"). Original Table 3 updated to Table 4. Added the following HCPCS codes to Table 4: A2001, A2002, A2004, A2005, A2008, A2009, A2020, A2021, A2022, A2023, A2024, A2025, A2027, A4175, C9364, Q4103, Q4104, Q4108, Q4111, Q4115, Q4116, Q4117, Q4118, Q4123, Q4124, Q4126, Q4127, Q4132, Q4134, Q4136, Q4137, Q4140, Q4141, Q4142, Q4146, Q4147, Q4148, Q4150, Q4152, Q4153, Q4154, Q4156, Q4157, Q4161, Q4163, Q4166, Q4169, Q4170, Q4173, Q4176, Q4178, Q4180, Q4188, Q4195, Q4196, Q4197, Q4201, Q4213, Q4215, Q4232, Q4236, Q4253, Q4254, Q4262, Q4267, Q4268, Q4269, Q4270, Q4271, Q4272, Q7273, Q4274, Q4275, Q4276, Q4278, Q4280, Q4281, Q4282, Q4283, Q4284, Q4285, Q4286, Q4304, Q4305, Q4306, Q4307, Q4308, Q4309. References reviewed and updated.		
Description updated. Added "up to four initial applications of" to policy statement I. Added medically necessary product types for DFU in I.F.1.d. and for VLU in I.F.2.d. In I.G., removed that applications should not exceed 10 and the note regarding coding tables. In I.H., noted that up to four applications are initially approved, up to a total of eight. Added requirements in I.I and I.J. Added section II and moved section II. non-medically necessary criteria under section III. Updated background with evidence for specific product types. Updated coding tables to reflect medically necessary product types for DFU and VLU, and those considered not medically necessary for either. References updated.	10/25	10/25
Title changed to "Skin and Soft Tissue Substitutes for Diabetic Foot Ulcers and Venous Leg Ulcers." Specified that policy statements I. and III. apply to DFU and VLU. Removed full-thickness skin loss ulcers as an indication in I.F.3.	11/25	11/25
In the policy description, noted the policy intention is "for use by Medicare health plans affiliated with Centene Corporation® in Medicare Administrative Contractor (MAC) jurisdictions with an absence of full coverage criteria provided by the Centers for Medicare and Medicaid Services (CMS) and the applicable MAC."	12/25	

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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 regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

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.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members/enrollees and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers,

member/enrollees and their representatives agree to be bound by such terms and conditions by providing services to members/enrollees and/or submitting claims for payment for such services.

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.