Clinical Policy: EpiFix Wound Treatment
Reference Number: CP.MP.140
Effective Date: 04/17
Last Review Date: 04/17

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

Description
EpiFix® (MiMedx Group) is dehydrated human amniotic tissue that is used as an allograft material (or tissue graft) to treat nonhealing wounds. It is prepared using a proprietary process by which placental tissues are gently separated, cleaned of viable cells, reassembled, and dehydrated, preserving factors important in healing. EpiFix is processed from human tissue according to the American Association of Tissue Banks (AATB) standards, and is regulated as a human cell, tissue, or cellular or tissue-based product.

Policy/Criteria
I. It is the policy of health plans affiliated with Centene Corporation® that EpiFix is medically necessary for the treatment of chronic foot ulcers when all of following criteria are met:
   A. Age ≥ 18 years;
   B. Type I or Type II diabetes;
   C. Foot ulcer surface area* > 1cm² and < 25cm²;
   D. Ulcer duration of ≥ 4 weeks, unresponsive to standard wound care;
   E. No clinical signs of infection;
   F. Ulcer does not probe to tendon, muscle, capsule or bone;
   G. Serum creatinine < 3.0 mg/dl;
   H. HbA1c < 12%;
   I. Adequate circulation to the affected extremity as demonstrated by dorsum transcutaneous oxygen test (TcPO2) > 30mmHg, or ankle-brachial index (ABI) between 0.7 and 1.2 or triphasic or biphasic Doppler arterial waveforms at the ankle of affected leg.
   *Surface area can be calculated by multiplying width in cm by length in cm.

II. It is the policy of health plans affiliated with Centene Corporation that continued treatment with EpiFix is not medically necessary when the ulcer fails to heal by ≥ 50% within the first 6 weeks of treatment. Treatment beyond 12 weeks is considered not medically necessary regardless of wound status.

III. It is the policy of health plans affiliated with Centene Corporation that treatment with EpiFix for any other types of nonhealing wounds is considered investigational.

Background
Lower extremity ulceration is a common complication for patients with diabetes. Diabetic foot ulcers lead to some form of amputation in 20% of patients and are associated with higher morbidity and mortality. The presence of peripheral vascular disease, neuropathy and poor blood glucose control contribute to the development of lower extremity wounds, their slow rate of healing and their propensity to recur. Evidence-based guidelines for the management of lower extremity diabetic ulcers include moist dressings, debridement, wound offloading, infection
控制和实施高级伤口治疗，如果伤口大小在4周的标准治疗后没有减少40%或更多。

EpiFix被提议用于促进细胞迁移以增强急性伤口的软组织修复，这些伤口自由于坏死组织和感染；部分厚度和全厚度伤口；静脉性、糖尿病性、压力和慢性血管性溃疡；创伤性伤口，包括烧伤；和外科伤口。EpiFix不适用于探触到骨骼或感染的伤口。EpiFix通常由伤口护理专家在门诊设置中订购和使用。

通常用于使用EpiFix的步骤包括：
- 手术清创感染或腐烂组织，直到伤口底部可见且有良好的血流。
- 如有必要，修剪EpiFix膜条产生1毫米（mm）的重叠与伤口边缘。产品可以干燥或湿润后与生理盐水应用。
- 确认EpiFix膜的正确方向，然后将其放在伤口上并用胶带固定。
- 用非粘附性接触层覆盖，然后用湿敷料覆盖。

膜通常在应用后2周内融入伤口床。

整体证据质量评估EpiFix是低的，然而，对于糖尿病患者，尽管有限，研究报告了在伤口大小和伤口比例更高的患者中使用EpiFix与使用标准治疗的患者相比，报告了更大的伤口关闭率和更高的伤口愈合率。文献综述随机临床试验（RCT）的皮肤移植或组织替换治疗足部溃疡的人，表明皮肤移植或替换的完成闭合率显著改善。没有特定类型的皮肤移植或组织替换显示出优于另一种皮肤移植或组织替换对伤口愈合的影响。

一项前瞻性、随机、对照、平行组、多中心临床试验的60名患者报告称，脱水人胚膜（简称EpiFix）优于标准伤口护理（SWC）和生物工程皮肤替代物（Apligraf）在4-6周内完全愈合的伤口。

在100名患有慢性下肢糖尿病性溃疡的患者中，每周应用Apligraf（n = 33）、EpiFix（n = 32）或标准伤口护理（SWC）（n = 35）与胶原-藻酸盐敷料作为对照。Apligraf、EpiFix和SWC的完全闭合率分别为73%（24/33）、97%（31/32）和51%（18/35）（调整后P = 0.00019）。EpiFix组的伤口愈合率显著高于SWC组。平均愈合时间是47.9天（Apligraf）、23.6天（EpiFix组）和57.4天（SWC组）。

A prospective, randomized, controlled, parallel group, multi-center clinical trial of 60 patients reported that dehydrated human amnion/chorion membrane (i.e., EpiFix) is superior to standard wound care (SWC) and bioengineered skin substitutes (i.e., Apligraf) in achieving complete wound closure within 4–6 weeks. Rates and time to closure at a longer time interval and factors influencing outcomes remained unassessed; therefore, the study was continued in order to achieve at least 100 patients. With the larger cohort, the authors compared clinical outcomes at 12 weeks in 100 patients with chronic lower extremity diabetic ulcers treated with weekly applications of Apligraf (n = 33), EpiFix (n = 32) or standard wound care (SWC) (n = 35) with collagen-alginate dressing as controls. The proportion of wounds achieving complete closure within the 12-week study period were 73% (24/33), 97% (31/32), and 51% (18/35) for Apligraf, EpiFix and SWC, respectively (adjusted P = 0.00019). Subjects treated with EpiFix had a very significant higher probability of their wounds healing compared to SWC alone. Mean time-to-heal within 12 weeks was 47.9 days with Apligraf, 23.6 days with EpiFix group and 57.4 days with the SWC alone group.
The evidence to assess the effectiveness and safety of EpiFix for the treatment of other types of nonhealing wounds, including venous leg ulcers is very limited. A multicenter, randomized, controlled study of 84 patients evaluating the safety and efficacy of one or two applications of dehydrated human amnion/chorion membrane allograft and multilayer compression therapy vs. multilayer compression therapy alone in the treatment of venous leg ulcers reported at 4 weeks, 62% in the allograft group and 32% in the control group showed a greater than 40% wound closure. After 4 weeks, wounds treated with allograft had reduced in size a mean of 48.1% compared with 19.0% for controls. Venous leg ulcers treated with allograft had a significant improvement in healing at 4 weeks compared with multilayer compression therapy alone.5

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 2016, 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 considered medically necessary per policy criteria when billed with Q4131

<table>
<thead>
<tr>
<th>CPT® Codes</th>
<th>Description</th>
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<tr>
<td>15275</td>
<td>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</td>
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<tr>
<td>15276</td>
<td>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)</td>
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HCPCS codes considered medically necessary per policy criteria

<table>
<thead>
<tr>
<th>HCPCS Codes</th>
<th>Description</th>
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<tr>
<td>Q4131</td>
<td>EpiFix or Epicord, per sq cm</td>
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ICD-10-CM diagnosis codes that support medical necessity

<table>
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<tr>
<th>ICD-10-CM Code</th>
<th>Description</th>
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<tbody>
<tr>
<td>E08.621</td>
<td>Diabetes mellitus due to underlying condition with foot ulcer</td>
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<tr>
<td>E09.621</td>
<td>Drug or chemical induced diabetes mellitus with foot ulcer</td>
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<tr>
<td>E10.621</td>
<td>Type 1 diabetes mellitus with foot ulcer</td>
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<tr>
<td>E11.621</td>
<td>Type 2 diabetes mellitus with foot ulcer</td>
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<tr>
<td>E13.621</td>
<td>Other specified diabetes mellitus with foot ulcer</td>
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CPT codes NOT medically necessary when billed with Q4131
Clinical Policy
EpiFix Wound Treatment

<table>
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<tr>
<td>15277</td>
<td>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</td>
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<tr>
<td>15278</td>
<td>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)</td>
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Reviews, Revisions, and Approvals

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<th>Date</th>
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<tr>
<td>Policy developed</td>
<td>04/17</td>
<td>04/17</td>
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References


**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.

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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. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

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**Note: For Medicaid members**, 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**, 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](http://www.cms.gov) for additional information.

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