Prior Authorization Review Panel

CHC-MCO Policy Submission

A separate copy of this form must accompany each policy submitted for review.
Policies submitted without this form will not be considered for review.

Plan: PA Health & Wellness	**Submission Date: 03/1/2021**
Policy Number: PA.CP.MP.140	**Effective Date: 06/01/18** **Revision Date: 02/2021**
Policy Name: EpiFix Wound Treatment	

Type of Submission – Check all that apply:

- ☐ **New Policy**
- ☐ **Revised Policy***
- ✓ **Retiring Policy –** *This option indicates the retirement of an active policy. If there is no indicated replacement, then "NONE" will be listed as the New/Replacement Policy.*
- ☐ **Annual Review – No Revisions**
- ☐ **Statewide PDL** - *Select this box when submitting policies for Statewide PDL implementation and when submitting policies for drug classes included on the Statewide PDL.*

***All revisions to the policy must be highlighted using track changes throughout the document. Please provide any clarifying information for the policy below:**

This policy is being retired.

Name of Authorized Individual (Please type or print):	**Signature of Authorized Individual:**
Carla Huitt, MD MPH	Carla J Huitt MD MPH

Clinical Policy: EpiFix Wound Treatment

Reference Number: PA.CP.MP.140
Effective Date: 03/18
Last Review Date: ~~10/2019~~2/18/2021

Coding Implications
Revision Log

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 Pa Health & Wellness 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* > $1cm^2$ and < $25cm^2$;
- 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 PA Health & Wellness 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 PA Health & Wellness 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

control and implementation of advanced wound therapies if the ulcer does not decrease in size by 40% or more after 4 weeks of standard therapy. [1]

EpiFix is proposed to promote cellular migration to enhance soft tissue repair in acute and chronic wounds free of necrotic tissue and infection; partial- and full-thickness wounds; venous, diabetic, pressure, and chronic vascular ulcers; trauma wounds, including burns; and surgical wounds. EpiFix is not indicated for wounds that probe to bone or are infected. EpiFix is typically ordered and applied by wound care specialists in an outpatient setting.

The general steps involved in using EpiFix include:

- Surgical debridement of infected or decaying tissue until the wound base is visible and has good blood flow.
- If necessary, trimming of the EpiFix membrane to produce a 1-millimeter (mm) overlap with the wound margin. The product may be applied either dry or moistened with saline.
- Confirmation of the correct orientation of the EpiFix membrane, which is then placed over the wound and secured with adhesive strips.
- Application of a nonadherent contact layer followed by a moist dressing.

The membrane typically incorporates into the wound bed within 2 weeks of application.

The overall quality of evidence evaluating EpiFix is low, however, among diabetic patients with chronic foot ulcers, studies although limited, reported a greater reduction in mean wound size and higher proportion of wound healing among patients treated with EpiFix compared with those treated with standard care.[2] A systematic review of randomized clinical trials (RCTs) of skin grafts or tissue replacements for treating foot ulcers in people with diabetes, concluded the incidence of completed closure of diabetic foot ulcers was significantly improved for the skin grafts or substitutes compared with standard care. No specific type of skin graft or tissue replacement showed a superior effect on ulcer healing over another type of skin graft or tissue replacement.[3]

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.[4] 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.[1]

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EpiFix Wound Treatment

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]

Clinical Guidelines from the Society for Vascular Surgery and the American Venous Forum on the management of venous leg ulcers note that numerous tissue constructs are available for use in chronic wounds that employ either human tissue (amniotic membrane, cryopreserved skin) or animal tissue (bladder, fetal bovine skin, others) in an effort to accelerate VLU closure. Currently, they suggest the use of a porcine small intestinal submucosa tissue construct in addition to compression therapy for the treatment of venous leg ulcers that have failed to show signs of healing after standard therapy for 4 to 6 weeks.[12]

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 2018, 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

CPT® Codes	Description
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)

HCPCS codes considered medically necessary per policy criteria

HCPCS Codes	Description
Q4186	EpiFix or Epicord, per sq cm

ICD-10-CM diagnosis codes that support medical necessity

CLINICAL POLICY

EpiFix Wound Treatment

ICD-10-CM Code	Description
E08.621	Diabetes mellitus due to underlying condition with foot ulcer
E09.621	Drug or chemical induced diabetes mellitus with foot ulcer
E10.621	Type 1 diabetes mellitus with foot ulcer
E11.621	Type 2 diabetes mellitus with foot ulcer
E13.621	Other specified diabetes mellitus with foot ulcer

CPT codes NOT medically necessary when billed with Q4131

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)

Reviews, Revisions, and Approvals	Date	Approval Date
Policy developed	04/18	06/18
Revised I.I TcPO2 ≥ 30mmHg. Replaced deleted code Q4131 with new code Q4186. References reviewed and updated. Specialist review. Updated policy is posted to Sharepoint but is not live yet on AEM; pending effective date coordination with the Health Plans.	10/19	3/20/2020
The policy is being retired	2/2021	

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4. Zelen CM, Gould Ll, Serena TE, et al. A prospective, randomised, controlled, multi-centre comparative effectiveness study of healing using dehydrated human amnion/chorion membrane allograft, bioengineered skin substitute or standard of care for treatment of chronic lower extremity diabetic ulcers. Int Wound J. 2015 Dec;12(6):724-32

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7. Zelen CM, Serena TE, Denoziere G, Fetterolf DE. A prospective randomized comparative parallel study of amniotic membrane wound graft in the management of diabetic foot ulcers. Int Wound J. 2013 Jun 7.
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12. O'Donnell TF Jr, Passman MA, Marston WA, etc. Management of venous leg ulcers: Clinical practice guidelines of the Society for Vascular Surgery and the American Venous Forum. J Vasc Surg. 2014 Aug;60(2 Suppl):3S-59S.2014;60:3S-59S