MEDICAL POLICY – 7.01.149
Amniotic Membrane and Amniotic Fluid

BCBSA Ref. Policy: 7.01.149
Effective Date: May 1, 2018
Last Revised: April 3, 2018
Replaces: N/A

RELATED MEDICAL POLICIES:
2.01.16 Recombinant and Autologous Platelet-Derived Growth Factors as a Treatment of Wound Healing and Other Non-Orthopedic Conditions
8.01.52 Orthopedic Applications of Stem-Cell Therapy (Including Allograft and Bone Substitute Products Used with Autologous Bone Marrow)

Select a hyperlink below to be directed to that section.

POLICY CRITERIA | CODING | RELATED INFORMATION
EVIDENCE REVIEW | REFERENCES | HISTORY

Clicking this icon returns you to the hyperlinks menu above.

Introduction

The amniotic membrane and amniotic fluid are structures that surround the fetus in the uterus (womb). The fluid protects the fetus from injury. The membrane is a thin mesh of protein and contains growth factors, stem cells, and other items crucial to a developing fetus. Processing and then using the amniotic membrane and/or fluid (after delivery), has been proposed to treat a number of conditions in adults. High quality medical studies show that using specific amniotic membrane products may be useful for treating diabetic ulcers in some cases, for specific eye conditions, and for a disorder known as Stevens-Johnson syndrome. This policy describes when these products may be considered medically necessary. Using amniotic membrane for other conditions or using amniotic fluid products is considered unproven (investigational).

Note: The Introduction section is for your general knowledge and is not to be taken as policy coverage criteria. The rest of the policy uses specific words and concepts familiar to medical professionals. It is intended for providers. A provider can be a person, such as a doctor, nurse, psychologist, or dentist. A provider also can be a place where medical care is given, like a hospital, clinic, or lab. This policy informs them about when a service may be covered.

Policy Coverage Criteria
<table>
<thead>
<tr>
<th>Service</th>
<th>Medical Necessity</th>
</tr>
</thead>
</table>
| Treatment of nonhealing diabetic lower-extremity ulcers | Treatment of nonhealing* diabetic lower-extremity ulcers using the following human amniotic membrane products may be considered medically necessary:  
- AmnioBand® Membrane  
- Biovance®  
- Epifix®  
- Grafix™  

*Note: Nonhealing is defined as less than a 20% decrease in wound area with standard wound care for at least 2 weeks. |

<table>
<thead>
<tr>
<th>Service</th>
<th>Investigational</th>
</tr>
</thead>
</table>
| Sutured human amniotic membrane grafts      | Sutured human amniotic membrane grafts may be considered medically necessary for the treatment of the following ophthalmic indications:  
- acute ocular Stevens-Johnson syndrome  
- corneal ulcers and melts  
- neurotrophic keratitis  
- persistent epithelial defects (defined as):  
  - failed to respond to 2 days of any: topical lubricants or antibiotics, therapeutic contact lens, or patching (see Related Information for more details)  
  - pterygium repair  

Sutured human amniotic membrane grafts are considered investigational for the treatment of all other ophthalmic conditions including but not limited to:  
- dry eye syndrome  
- burns  
- corneal perforation  
- bullous keratopathy  
- limbus stem cell deficiency  
- after photorefractive keratectomy  

**Human amniotic membrane without suture**  
Human amniotic membrane without suture (eg, Prokera®, AmbioDisk™) for ophthalmic indications is investigational.
Injection of micronized or particulated human amniotic membrane is considered investigational for all indications including but not limited to treatment of:
- osteoarthritis
- plantar fasciitis

Injection of human amniotic fluid is considered investigational for all indications.

All other human amniotic membrane products and indications not listed above are considered investigational, including but not limited to treatment of lower-extremity ulcers due to venous insufficiency.

### Coding

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Q4131</td>
<td>EpiFix or Epicord, per sq cm</td>
</tr>
<tr>
<td>Q4132</td>
<td>Grafix Core, per sq cm</td>
</tr>
<tr>
<td>Q4133</td>
<td>Grafix Prime, per sq cm</td>
</tr>
<tr>
<td>Q4137</td>
<td>AmnioExcel or BioDExCel, per sq cm</td>
</tr>
<tr>
<td>Q4139</td>
<td>AmnioMatrix or BioDMatrix, injectable, 1 cc.</td>
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<tr>
<td>Q4145</td>
<td>EpiFix, injectable, 1 mg</td>
</tr>
<tr>
<td>Q4148</td>
<td>Neox 1k, per sq cm</td>
</tr>
<tr>
<td>Q4151</td>
<td>AmnioBand or Guardian, per sq cm</td>
</tr>
<tr>
<td>Q4154</td>
<td>Biovance, per sq cm</td>
</tr>
<tr>
<td>Q4155</td>
<td>NeoxFlo or ClarixFlo, 1 mg</td>
</tr>
<tr>
<td>Q4156</td>
<td>Neox 100, per sq cm</td>
</tr>
<tr>
<td>Q4162</td>
<td>AmnioPro Flow, BioSkin Flow, BioRenew Flow, WoundEx Flow, Amniogen-A, Amniogen-C, 0.5 cc</td>
</tr>
<tr>
<td>Q4163</td>
<td>AmnioPro, BioSkin, BioRenew, WoundEx, Amniogen-45, Amniogen-200, per sq cm</td>
</tr>
</tbody>
</table>
Definition of Terms

**Persistent epithelial defect:** A defect that failed to close completely after 5 days of conservative treatment or has failed to demonstrate a decrease in size after 2 days of conservative treatment.

**Conservative treatment:** The use of topical lubricants and/or topical antibiotics and/or therapeutic contact lens and/or patching. Failure of multiple modalities should not be required prior to moving to human amniotic membrane grafts. An amniotic membrane graft requires less effort on the part of the patient to adhere to a treatment regimen and has a significant advantage in regarding treatments requiring multiple drops per day.

Evidence Review

Description

Several commercially available forms of human amniotic membrane (HAM) and amniotic fluid can be administered by patches, topical application, or injection. Amniotic membrane and amniotic fluid are being evaluated for the treatment of a variety of conditions, including chronic full-thickness diabetic lower extremity ulcers, venous ulcers, knee osteoarthritis, plantar fasciitis, and ophthalmic conditions.
Background

Human Amniotic Membrane

Human amniotic membrane (HAM) consists of 2 conjoined layers (the amnion and chorion) and forms the innermost lining of the amniotic sac and placenta. When prepared for use as an allograft, the membrane is harvested immediately after birth, cleaned, sterilized, and either cryopreserved or dehydrated. Many products available using amnion, chorion, amniotic fluid, and umbilical cord are being studied for the treatment of a variety of conditions, including chronic full-thickness diabetic lower-extremity ulcers, venous ulcers, knee osteoarthritis, plantar fasciitis, and ophthalmic conditions. The products are formulated either as patches, which can be applied as wound covers, or as suspensions or particulates, or connective tissue extractions, which can be injected or applied topically (see Table 1).

Fresh amniotic membrane contains collagen, fibronectin, and hyaluronic acid, along with a combination of growth factors, cytokines, and anti-inflammatory proteins such as interleukin-1 receptor antagonist. There is evidence that the tissue has anti-inflammatory, antifibroblastic, and antimicrobial properties. HAM is considered to be non-immunogenic and has not been observed to cause substantial immune response. It is believed that these properties are retained in cryopreserved HAM (C-HAM) and dehydrated HAM (D-HAM) products, resulting in a readily available tissue with regenerative potential. In support, one D-HAM product has been shown to elute growth factors into saline and stimulate the migration of mesenchymal stem cells both in vitro and in vivo.

Use of a HAM graft, which is fixated by sutures, is an established treatment for disorders of the corneal surface, including neurotrophic keratitis, corneal ulcers and melts, following pterygium repair, Stevens-Johnson syndrome, and persistent epithelial defects. Amniotic membrane products that are inserted like a contact lens have more recently been investigated for the treatment of corneal and ocular surface disorders. Amniotic membrane patches are also being evaluated for the treatment of various other conditions, including skin wounds, burns, leg ulcers, and prevention of tissue adhesion in surgical procedures (see Related Medical Policies). Additional indications studied in pre-clinical models include tendonitis, tendon repair, and nerve repair. The availability of HAM opens the possibility of regenerative medicine for an array of conditions.
Amniotic Fluid

Amniotic fluid surrounds the fetus during pregnancy and provides protection and nourishment. In the second half of gestation, most of the fluid is a result of micturition and secretion from the respiratory tract and gastrointestinal tract of the fetus, along with urea. The fluid contains carbohydrates, proteins and peptides, amino acids, fats, enzymes, hormones, pigments, and fetal cells. Use of human and bovine amniotic fluid for orthopedic conditions was first reported in 1927. Amniotic fluid has been compared with synovial fluid, containing hyaluronan, lubricant, cholesterol, and cytokines. Injection of amniotic fluid or amniotic fluid–derived cells is currently being evaluated for the treatment of osteoarthritis and plantar fasciitis.

Amniotic membrane and amniotic fluid are also being investigated as sources of pluripotent stem cells. Pluripotent stem cells can be cultured and are capable of differentiation toward any cell type. The use of stem cells in orthopedic applications is addressed in a separate policy (see Related Medical Policies).

Table 1. Amniotic Membrane and Amniotic Fluid Preparations: Preparation and Components

<table>
<thead>
<tr>
<th>Product (Supplier)</th>
<th>Preparation</th>
<th>Components</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Cryopreserved, Dehydrated, or Extracted</td>
<td>Amnion</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patch</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Affinity™ (NuTech Medical)</td>
<td>C</td>
<td></td>
</tr>
<tr>
<td>AlloWrap™ (AlloSource)</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td>AmbioDisk® (IOP Ophthalmics)</td>
<td>D</td>
<td></td>
</tr>
<tr>
<td>AmbioDry5® (IOP Ophthalmics)</td>
<td>D</td>
<td></td>
</tr>
<tr>
<td>AmnioBand® Membrane (MTF Wound Care)</td>
<td>D</td>
<td></td>
</tr>
<tr>
<td>AmnioClear™ (Liventa Bioscience)</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td>AmnioExcel® (Derma Sciences)</td>
<td>D</td>
<td></td>
</tr>
<tr>
<td>AmnioFix® (MiMedx)</td>
<td>D</td>
<td></td>
</tr>
<tr>
<td>AmnioGraft® (BioTissue)</td>
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<tr>
<td>Artacent® Wound (Tides Medical)</td>
<td>D</td>
<td></td>
</tr>
<tr>
<td>Product (Supplier)</td>
<td>Preparation</td>
<td>Components</td>
</tr>
<tr>
<td>-------------------</td>
<td>-------------</td>
<td>------------</td>
</tr>
<tr>
<td></td>
<td>Cryopreserved, Dehydrated, or Extracted</td>
<td>Amnion</td>
</tr>
<tr>
<td>BioDDryFlex® (BioD)</td>
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<td>X</td>
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<tr>
<td>BiDfence™ (BioD)</td>
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<td>X</td>
</tr>
<tr>
<td>BioSkin (thin - 45 microns, HRT)*</td>
<td>D</td>
<td>X</td>
</tr>
<tr>
<td>BioSkin (thick - 200 microns, HRT)*</td>
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<tr>
<td>Biovance® (Alliqua Biomedical)</td>
<td>D</td>
<td>X</td>
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<tr>
<td>Clarix® (Amniox Medical)</td>
<td>C</td>
<td>X</td>
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<tr>
<td>Cygnus (Vivex Biomedical)</td>
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<tr>
<td>Cygnus Max (Vivex Biomedical)</td>
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<tr>
<td>EpiCord™ (MiMedx)</td>
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<tr>
<td>EpiFix® (MiMedx)</td>
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</tr>
<tr>
<td>Dermavest™ (Aedicell)*</td>
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<td></td>
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<tr>
<td>Grafix® (Osiris)</td>
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<td>Guardian/AmnioBand® (MTF Wound Care)</td>
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<td>Neox® 100 (Amniox Medical)</td>
<td>C</td>
<td></td>
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<tr>
<td>Neox® Cord (Amniox Medical)</td>
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<tr>
<td>Neox® Wound Allograft (Amniox Medical)</td>
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<td>NuShield™ (NuTech Medical)</td>
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<td>PalinGen® Membrane (Ammio ReGen Solutions)</td>
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<td>Plurivest™ (Aedicell)*</td>
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<td>Prokera® (Bio-Tissue)</td>
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<td>Revitalon™ (Medline Industries)</td>
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<td>WoundEx® (45 microns, Skye Biologics)*</td>
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</tr>
<tr>
<td>WoundEx® (200 microns, Skye Biologics)*</td>
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</tbody>
</table>

**Suspension, particulate, or extraction**

| AmnioBand® Particulate (MTF Wound Care) | D | X | X | | |
## Product (Supplier) | Preparation | Components | Amnion | Chorion | Amniotic Fluid | Umbilical Cord
--- | --- | --- | --- | --- | --- | ---
AmnioMatrix® (Derma Sciences) | D | X | X | X | X | X
AmnioVisc™ (Lattice Biologics) | NS | X | X | X | X
BioSkin® Flow (HRT) | E | X | X | X | X | X
Clarix® Flo (Amnio Medical) | C | X | X
Interfyl™ (Alliqua Biomedical) | NS | X | X
Neox® Flo (Amnio Medical) | C | X
OrthoFlo™ (MiMedx) | D | X
PalinGen® Flow (Amnio ReGen Solutions) | C | X | X
PalinGen® SportFlow (Amnio ReGen Solutions) | C | X | X
ProMatrX™ ACF (Amnio ReGen Solutions) | C | X | X
ReNu™ (NuTech Medical) | D | X | X
WoundEx® Flow (Skye Biologics) | E | X | X | X | X

C: cryopreserved; D: dehydrated; E: extracted connective tissue; HRT: Human Regenerative Technologies; MTF: Musculoskeletal Transplant Foundation; NS: not specified.

* Processed by HRT and marketed under different tradenames.

AmnioClip (FORTECH GmbH) is a ring designed to hold the amniotic membrane in the eye without sutures or glue fixation. A mounting device is used to secure the amniotic membrane within the AmnioClip. The AmnioClip currently has CE approval in Europe.

### Summary of Evidence

**Diabetic Lower-Extremity Ulcers**

For individuals who have nonhealing diabetic lower-extremity ulcers who receive a patch or flowable formulation of HAM (i.e., AmnioBand Membrane, Biovance, Epifix, Grafix), the evidence includes randomized controlled trials (RCTs). Relevant outcomes are symptoms, morbid events, functional outcomes, and quality of life. The RCTs evaluating amniotic and placental membrane
products for the treatment of nonhealing (<20% healing with ≥2 weeks of standard care) diabetic lower-extremity ulcers have compared HAM with standard care or with an established advanced wound care product. These trials used wound closure as the primary outcome measure, and some used power analysis, blinded assessment of wound healing, and intention-to-treat analysis. For the HAM products that have been sufficiently evaluated (ie, AmnioBand Membrane, Biovance, Epifix, Grafix), results have shown improved outcomes compared with standard care, and outcomes that are at least as good as an established advanced wound care product. Improved health outcomes in the RCTs are supported by multicenter registries. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

**Lower-Extremity Ulcers due to Venous Insufficiency**

For individuals who have lower-extremity ulcers due to venous insufficiency who receive a patch or flowable formulation of HAM, the evidence includes 2 RCTs. Relevant outcomes are symptoms, morbid events, functional outcomes, and quality of life. The evidence on HAM for the treatment of lower-extremity venous ulcers includes 2 multicenter RCTs with EpiFix. One RCT reported larger percent wound closure at 4 weeks, but the percentage of patients with complete wound closure did not differ between EpiFix and standard of care. A second multicenter RCT reported a significant difference in complete healing at 12 weeks, but the interpretation is limited by methodologic concerns. Well-designed and well-conducted RCTs that compare HAM with the standard of care for venous insufficiency ulcers are needed. The evidence is insufficient to determine the effects of the technology on health outcomes.

**Osteoarthritis**

For individuals who have knee osteoarthritis who receive an injection of suspension or particulate formulation of HAM or amniotic fluid, the evidence includes a feasibility study. Relevant outcomes are symptoms, functional outcomes, quality of life, and treatment-related morbidity. The pilot study assessed the feasibility of a larger RCT evaluating HAM injection. Additional trials, which will have a larger sample size and longer follow-up, are needed to permit conclusions on the effect of this treatment. The evidence is insufficient to determine the effects of the technology on health outcomes.
**Plantar Fasciitis**

For individuals who have plantar fasciitis who receive an injection of suspension or particulate formulation of human amniotic membrane or amniotic fluid, the evidence includes 2 small RCTs. Relevant outcomes are symptoms, functional outcomes, quality of life, and treatment-related morbidity. Research on HAM injections for plantar fasciitis is at an early stage. Evidence includes a small (N=23) double-blind comparison with corticosteroid and a patient-blinded (N=45) comparison of 2 different doses of dehydrated HAM with saline. Additional controlled trials with larger sample sizes and longer follow-up are needed to permit conclusions on the effect of HAM and amniotic fluid injections on plantar fasciitis pain. The evidence is insufficient to determine the effects of the technology on health outcomes.

**Ophthalmic Conditions**

For individuals who have neurotrophic keratitis, corneal ulcers and melts, pterygium repair, Stevens-Johnson syndrome, or persistent epithelial defects who receive sutured HAM graft, the evidence includes several RCTs and a technology assessment. Relevant outcomes are symptoms, morbid events, functional outcomes, and quality of life. The most widely studied condition with a technology assessment of RCT evidence is the use of HAM following pterygium repair. The technology assessment concluded, based on 4 RCTs, that conjunctival or limbal autograft was more effective than HAM. An RCT evaluating HAM for refractory neurotrophic corneal ulcers found that outcomes following HAM graft were similar to conventional therapy. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have ophthalmic disorders other than neurotrophic keratitis, corneal ulcers and melts, pterygium repair, Stevens-Johnson syndrome, or persistent epithelial defects who receive sutured HAM graft, the evidence includes a systemic review article and RCTs. Relevant outcomes are symptoms, morbid events, functional outcomes, and quality of life. A 2012 Cochrane review found a single RCT on HAM graft for acute ocular burns. The trial suggested a benefit in the healing rate for ocular burns, but it was considered at high or uncertain risk of bias due to unequal baseline scores and the lack of masking of the treatment condition. A trial assessing HAM for the treatment of bullous keratopathy reported no difference in clinical outcomes between HAM and stromal puncture. RCTs are needed to evaluate the benefit of HAM for these indications. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have ophthalmic conditions who receive HAM without suture, the evidence includes an RCT (N=20), a within-subject comparative study, and case series. Relevant outcomes include symptoms, morbid events, functional outcomes, and quality of life. A 2012 Cochrane review found a single RCT on HAM graft for acute ocular burns. The trial suggested a benefit in the healing rate for ocular burns, but it was considered at high or uncertain risk of bias due to unequal baseline scores and the lack of masking of the treatment condition. A trial assessing HAM for the treatment of bullous keratopathy reported no difference in clinical outcomes between HAM and stromal puncture. RCTs are needed to evaluate the benefit of HAM for these indications. The evidence is insufficient to determine the effects of the technology on health outcomes.
are symptoms, morbid events, functional outcomes, and quality of life. Traditionally, amniotic membrane has been sutured onto the eye for a variety of severe ocular surface disorders. The Prokera device is novel because it has a ring around the cryopreserved HAM allograft that permits it to be inserted under topical anesthesia, similar to insertion of a contact lens, allowing for more widespread use. Use of Prokera has been reported for refractory dry eye syndrome, ulcerative keratitis, neurotrophic keratitis, recurrent epithelial erosion, high-risk corneal grafts, acute chemical and thermal burns, acute Stevens-Johnson syndrome, necrotizing scleritis, and limbal stem cell deficiency. Current evidence on its use is limited. While the small RCT and case series reported generally positive effects, the prospective comparative trial found no benefit of HAM compared to a bandage contact lens for healing a wound after photorefractive keratectomy. RCTs are needed to determine whether sutureless HAM improves healing for the various ophthalmic disorders. The evidence is insufficient to determine the effects of the technology on health outcomes.

**Ongoing and Unpublished Clinical Trials**

Some currently unpublished trials that might influence this review are listed in Table 2.

### Table 2. Summary of Key Trials

<table>
<thead>
<tr>
<th>NCT No.</th>
<th>Trial Name</th>
<th>Planned Enrollment</th>
<th>Completion Date</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Ongoing</strong></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>NCT02318511</td>
<td>An Investigation of ReNu™ Knee Injection: Monitoring the Response of Knee Function and Pain in Patients With Osteoarthritis</td>
<td>200</td>
<td>Mar 2018</td>
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<tr>
<td>NCT02609594</td>
<td>A Multi-center Randomized Controlled Clinical Trial Evaluating Two Application Regimens of Amnioband Dehydrated Human Amniotic Membrane and Standard of Care vs. Standard of Care Alone in the Treatment of Venous Leg Ulcers</td>
<td>240</td>
<td>Nov 2018</td>
</tr>
<tr>
<td>NCT02880592</td>
<td>A Multi-center, Randomized Controlled Clinical Trial Evaluating the Effect of Fresh Amniotic Membrane in the Treatment of Diabetic Foot Ulcers</td>
<td>100</td>
<td>Nov 2018</td>
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<tr>
<td>NCT02427191</td>
<td>A Prospective, Single-Blinded, Randomized Controlled Trial of the Micronized dHACM Injection as Compared to the Saline Placebo Injection in the Treatment of Plantar</td>
<td>146</td>
<td>Dec 2018</td>
</tr>
</tbody>
</table>
Clinical Input From Physician Specialty Societies and Academic Medical Centers

While the various physician specialty societies and academic medical centers may collaborate with and make recommendations during this process, through the provision of appropriate reviewers, input received does not represent an endorsement or position statement by the physician specialty societies or academic medical centers, unless otherwise noted.

2017 Input

In response to requests, clinical input on use of human amniotic membrane for ophthalmic disorders was received from 1 specialty society while this policy was under review in 2017.

Based on the evidence and independent clinical input, the clinical input supports that the following indications provide a clinically meaningful improvement in the net health outcome and are consistent with generally accepted medical practice:

- Use of sutured human amniotic membrane (also described as amniotic membrane graft [AMG]) for individuals with:
- Neurotrophic keratitis
- Corneal ulcers and melts
- Following pterygium repair
- Stevens-Johnson syndrome, and
- Persistent epithelial defects.

Based on the evidence and independent clinical input, the clinical input does not support whether the following indications provide a clinically meaningful improvement in the net health outcome or are consistent with generally accepted medical practice:

- Use of sutured AMG for individuals with
- Corneal perforation
- Bullous keratopathy
- Limbus stem cell deficiency, and
- Severe dry eye.

Based on the evidence and independent clinical input, the clinical input does not support whether the following indication provides a clinically meaningful improvement in the net health outcome or is consistent with generally accepted medical practice:

- Use of sutureless AMG (eg, Prokera) instead of sutured AMG.

**Practice Guidelines and Position Statements**

No guidelines or statements were identified.

**Medicare National Coverage**

There is no national coverage determination. In the absence of an national coverage determination, coverage decisions are left to the discretion of local Medicare carriers.
Regulatory Status

The U.S. Food and Drug Administration regulates human cells and tissues intended for implantation, transplantation, or infusion through the Center for Biologics Evaluation and Research, under Code of Federal Regulation (CFR) title 21, parts 1270 and 1271. Human amniotic membrane products and amniotic fluid products are included in these regulations.

In 2003, Prokera™ was cleared for marketing by FDA through the 510(k) process for the ophthalmic conformer that incorporates amniotic membrane (K032104). FDA determined that this device was substantially equivalent to the Symblepharon Ring. The Prokera™ device is intended “for use in eyes in which the ocular surface cells have been damaged, or underlying stroma is inflamed and scarred.”

References


History

<table>
<thead>
<tr>
<th>Date</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>07/14/15</td>
<td>New Policy. Policy created with literature review through February 5, 2015; considered investigational.</td>
</tr>
<tr>
<td>05/01/16</td>
<td>Annual Review, approved April 12, 2016. Policy updated with literature review through December 14, 2015; reference 4 added. Policy statements unchanged.</td>
</tr>
<tr>
<td>02/17/17</td>
<td>Coding update. Added HCPCS codes Q4137, Q4151, Q4162, Q4163, and new code Q4168 (effective 01/01/17).</td>
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<tr>
<td>04/01/17</td>
<td>Annual review, approved March 14, 2017. Amniotic membrane products and information were moved to this policy from 7.01.113. Treatment of nonhealing diabetic lower-extremity ulcers using the following (AmnioBand® Membrane, Biovance®, Epifix®, Grafix™) human amniotic membrane products may be considered medically necessary. All other human amniotic membrane products and indications not listed above are considered investigational. Added the word human to other policy statements for clarification.</td>
</tr>
<tr>
<td>06/20/17</td>
<td>Coding update, added HCPCS codes Q4137, Q4151, Q4162, Q4163, and Q4168 back to policy as they were inadvertently left off of the policy when previous update was made on April 1, 2017. Also added HCPCS codes Q4148 and Q4156.</td>
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<tr>
<td>08/01/17</td>
<td>Interim Review, approved July 18, 2017. Policy moved into new format. Policy updated with literature review through April 27, 2017; references 7 and 21-28 added. Clinical input reviewed. Sutured amniotic membrane grafts considered medically necessary for neurotrophic keratitis, corneal ulcers and melts, following pterygium repair, Stevens-Johnson syndrome, and persistent epithelial defects. Ophthalmic products added and discontinued product names removed from Table 1. Added HCPCS codes Q4131-Q4133, Q4145, and Q4154.</td>
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<tr>
<td>05/01/18</td>
<td>Annual Review, approved April 3, 2018. Policy updated with literature review through December 2017; references 10, 12, 17, 24, and 29 added. Specific indications added to the investigational policy statements.</td>
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</tbody>
</table>
Disclaimer: This medical policy is a guide in evaluating the medical necessity of a particular service or treatment. The Company adopts policies after careful review of published peer-reviewed scientific literature, national guidelines and local standards of practice. Since medical technology is constantly changing, the Company reserves the right to review and update policies as appropriate. Member contracts differ in their benefits. Always consult the member benefit booklet or contact a member service representative to determine coverage for a specific medical service or supply. CPT codes, descriptions and materials are copyrighted by the American Medical Association (AMA). ©2018 Premera All Rights Reserved.

Scope: Medical policies are systematically developed guidelines that serve as a resource for Company staff when determining coverage for specific medical procedures, drugs or devices. Coverage for medical services is subject to the limits and conditions of the member benefit plan. Members and their providers should consult the member benefit booklet or contact a customer service representative to determine whether there are any benefit limitations applicable to this service or supply. This medical policy does not apply to Medicare Advantage.
Discrimination is Against the Law

LifeWise Health Plan of Washington complies with applicable Federal civil rights laws and does not discriminate on the basis of race, color, national origin, age, disability, or sex. LifeWise does not exclude people or treat them differently because of race, color, national origin, age, disability or sex.

LifeWise:
• Provides free aids and services to people with disabilities to communicate effectively with us, such as:
  • Qualified sign language interpreters
  • Written information in other formats (large print, audio, accessible electronic formats, other formats)
• Provides free language services to people whose primary language is not English, such as:
  • Qualified interpreters
  • Information written in other languages

If you need these services, contact the Civil Rights Coordinator.

If you believe that LifeWise has failed to provide these services or discriminated in another way on the basis of race, color, national origin, age, disability, or sex, you can file a grievance with:
Civil Rights Coordinator - Complaints and Appeals
PO Box 91102, Seattle, WA 98111
Toll free 855-332-6396, Fax 425-918-5592. TTY 800-842-5357
Email AppealsDepartmentInquiries@LifeWiseHealth.com

You can file a grievance in person or by mail, fax, or email. If you need help filing a grievance, the Civil Rights Coordinator is available to help you.

You can also file a civil rights complaint with the U.S. Department of Health and Human Services, Office for Civil Rights, electronically through the Office for Civil Rights Complaint Portal, available at https://ocrportal.hhs.gov/ocr/office/file/index.html, or by mail or phone at:
U.S. Department of Health and Human Services
200 Independence Avenue SW. Room 509F, HHH Building
Washington, D.C. 20201. 1-800-368-1019, 800-537-7697 (TDD)
Complaint forms are available at

Getting Help in Other Languages

This Notice has Important Information. This notice may have important information about your application or coverage through LifeWise Health Plan of Washington. There may be key dates in this notice. You may need to take action by certain deadlines to keep your health coverage or help with costs. You have the right to get this information and help in your language at no cost. Call 800-592-6804 (TTY: 800-842-5357).

Arabic (Arabic):
لا يمكن للمواطنين الذين لديهم موانع تواصلية يُحوزون خدماتنا للمساعدة في تعليمهم اللغة العربية أو الإنجليزية أو أي غيرها من اللغات على الموقع الإلكتروني، أو قد تكون متوفرة خدماتهم بشكل ممول من الحكومة الاتحادية أو من قسمنا الخاص بالمساعدة. لذا، يمكن للمواطنين الذين لديهم موانع تواصلية الحصول على مساعدات خاصة، بحيث يتم تضمينهم في حزمة مساعدات خاصة للمواطنين الذين لديهم موانع تواصلية.

中文 (Chinese):

Italiano (Italian):
Este aviso contiene información importante. Es posible que este aviso contenga información importante acerca de su solicitud o cobertura a través de LifeWise Health Plan of Washington. Es posible que haya fechas clave en este aviso. Es posible que deba tomar alguna medida antes de determinadas fechas para mantener su cobertura médica o ayuda con los costos. Usted tiene derecho a recibir esta información y ayuda en su idioma sin costo alguno. Llame al 800-592-6804 (TTY: 800-842-5357).


ไทย (Thai): สิทธิ์ของคุณในการรับข้อมูลและข้อเสนอแนะที่มีความสำคัญในการขอและการรับการช่วยเหลือของคุณ


Русский (Russian): Настоящее уведомление содержит важную информацию. Это уведомление может содержать важную информацию о вашем заявлении или страховом покрытии через LifeWise Health Plan of Washington. В настоящем уведомлении могут быть указаны ключевые даты. Вам, возможно, потребуется принять меры к определенным предельным срокам для сохранения страхового покрытия или помощи с расходами. Вы имеете право на бесплатное получение этой информации и помощь на вашем языке. Звоните по телефону 800-592-6804 (TTY: 800-842-5357).

Español (Spanish): Este aviso contiene información importante. Es posible que este aviso contenga información importante acerca de su solicitud o cobertura a través de LifeWise Health Plan of Washington. Es posible que haya fechas clave en este aviso. Es posible que deba tomar alguna medida antes de determinadas fechas para mantener su cobertura médica o ayuda con los costos. Usted tiene derecho a recibir esta información y ayuda en su idioma sin costo alguno. Llame al 800-592-6804 (TTY: 800-842-5357).