

MEDICAL POLICY

POLICY TITLE	AMNIOTIC MEMBRANE AND AMNIOTIC FLUID
POLICY NUMBER	MP 1.159
CLINICAL BENEFIT	☐ MINIMIZE SAFETY RISK OR CONCERN. ☒ MINIMIZE HARMFUL OR INEFFECTIVE INTERVENTIONS. ☐ ASSURE APPROPRIATE LEVEL OF CARE. ☐ ASSURE APPROPRIATE DURATION OF SERVICE FOR INTERVENTIONS. ☒ ASSURE THAT RECOMMENDED MEDICAL PREREQUISITES HAVE BEEN MET. ☐ ASSURE APPROPRIATE SITE OF TREATMENT OR SERVICE.
Effective date:	10/1/2026

POLICY

Treatment of nonhealing diabetic lower-extremity ulcers using the following human amniotic membrane products (i.e., Affinity®, AmnioBand® Membrane, Biovance®, EpiCord®, EpiFix®, Grafix™, NuShield®) may be considered **medically necessary**.

Human amniotic membrane grafts with or without suture may be considered **medically necessary** for the treatment of the following ophthalmic indications:

- Neurotrophic keratitis with ocular surface damage and inflammation that does not respond to conservative therapy;
- Corneal ulcers and melts that do not respond to initial conservative therapy;
- Corneal perforation when there is active inflammation after corneal transplant requiring adjunctive treatment;
- Bullous keratopathy as a palliative measure in patients who are not candidates for curative treatment (e.g., endothelial or penetrating keratoplasty);
- Partial limbal stem cell deficiency with extensive diseased tissue where selective removal alone is not sufficient;
- Moderate or severe Stevens-Johnson syndrome;
- Persistent epithelial defects that do not respond within 2 days to conservative therapy;
- Severe dry eye (DEWS 3 or 4) with ocular surface damage and inflammation that remains symptomatic after Steps 1, 2, and 3 of the dry eye disease management algorithm (see Policy Guidelines); or
- Moderate or severe acute ocular chemical burn.

Human amniotic membrane grafts with suture or glue may be considered **medically necessary** for the treatment of the following ophthalmic indications:

- Corneal perforation when corneal tissue is not immediately available; or
- Pterygium repair when there is insufficient healthy tissue to create a conjunctival autograft.

Human amniotic membrane grafts with or without suture are considered **investigational** for all ophthalmic indications not outlined above. There is insufficient evidence to support a general conclusion concerning the health outcomes or benefits associated with the above procedures.

POLICY GUIDELINES

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Non-healing of diabetic wounds is defined as less than a 20% decrease in wound area with standard wound care for at least 2 weeks, based on the entry criteria for clinical trials (e.g., Zelen et al [2015]).

Tear Film and Ocular Surface Society staged management for dry eye disease (Jones et al, 2017)

Step 1:

- Education regarding the condition, its management, treatment and prognosis
- Modification of local environment
- Education regarding potential dietary modifications (including oral essential fatty acid supplementation)
- Identification and potential modification/elimination of offending systemic and topical medications
- Ocular lubricants of various types (if meibomian gland dysfunction is present, then consider lipid containing supplements)
- Lid hygiene and warm compresses of various types

Step 2:

If above options are inadequate consider:

- Non-preserved ocular lubricants to minimize preservative-induced toxicity
- Tea tree oil treatment for Demodex (if present)
- Tear conservation
- Punctal occlusion
- Moisture chamber spectacles/goggles
- Overnight treatments (such as ointment or moisture chamber devices)
- In-office, physical heating and expression of the meibomian glands
- In-office intense pulsed light therapy for meibomian gland dysfunction
- Prescription drugs to manage dry eye disease
- Topical antibiotic or antibiotic/steroid combination applied to the lid margins for anterior blepharitis (if present)
- Topical corticosteroid (limited duration)
- Topical secretagogues
- Topical non-glucocorticoid immunomodulatory drugs (such as cyclosporine)
- Topical LFA-1 antagonist drugs (such as lifitegrast)
- Oral macrolide or tetracycline antibiotics

Step 3:

If above options are inadequate consider:

- Oral secretagogues
- Autologous/allogeneic serum eye drops
- Therapeutic contact lens options
- Soft bandage lenses
- Rigid scleral lenses

Step 4:

If above options are inadequate consider:

- Topical corticosteroid for longer duration
- Amniotic membrane grafts

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- Surgical punctal occlusion
 - Other surgical approaches (e.g. tarsorrhaphy, salivary gland transplantation)
- Dry eye severity level DEWS 3 to 4
- Discomfort, severity, and frequency - Severe frequent or constant
 - Visual symptoms - chronic and/or constant, limiting to disabling
 - Conjunctival Injection - +/- or +/+
 - Conjunctive Staining - moderate to marked
 - Corneal Staining - marked central or severe punctate erosions
 - Corneal/tear signs - Filamentary keratitis, mucus clumping, increase in tear debris
 - Lid/meibomian glands - Frequent
 - Tear film breakup time - < 5
 - Schirmer score (mm/5 min) - < 5

Cross-References:

MP 2.028 Eye Care

MP 1.158 Bio-Engineered Skin, Soft Tissue Substitutes and Amniotic Membranes

MP 4.033 Diagnosis and Treatment of Dry Eye Syndrome

PRODUCT VARIATIONS

This policy is only applicable to certain programs and products administered by Capital Blue Cross and subject to benefit variations. Please see additional information below.

FEP PPO - Refer to FEP Medical Policy Manual. The FEP Medical Policy manual can be found at:

<https://www.fepblue.org/benefit-plans/medical-policies-and-utilization-management-guidelines/medical-policies>.

DESCRIPTION/BACKGROUND

Human amniotic membrane (HAM) consists of 2 conjoined layers, the amnion, and chorion, and forms the innermost lining of the amniotic sac or 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.

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, anti-fibroblastic, and antimicrobial properties. HAM is considered nonimmunogenic and has not been observed to

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cause a substantial immune response. It is believed that these properties are retained in cryopreserved HAM and HAM products, resulting in a readily available tissue with regenerative potential. In support, 1 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. Additional indications studied in preclinical models include tendonitis, tendon repair, and nerve repair. The availability of HAM opens the possibility of regenerative medicine for an array of conditions.

RATIONALE

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.

Diabetic Lower-Extremity Ulcers

For individuals who have non-healing diabetic lower-extremity ulcers who receive a patch formulation of HAM or placental membrane (i.e., Affinity, AmnioBand Membrane, AmnioExcel, Biovance, EpiCord, EpiFix, Grafix, NuShield), 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 non-healing (<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 (i.e., Affinity, AmnioBand Membrane, Biovance, EpiCord, EpiFix, Grafix, NuShield), 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 an 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 formulation of HAM, the evidence includes 3 RCTs. Relevant outcomes are symptoms, morbid events, functional outcomes, and quality of life. The published evidence on HAM for the treatment of venous leg ulcers includes 2 multicenter RCTs with EpiFix and 1 multicenter RCT with Amnioband. One RCT reported a larger percent wound closure at 4 weeks, but the

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percentage of patients with complete wound closure at 4 weeks did not differ between EpiFix and the standard of care. A second RCT evaluated complete wound closure at 12 weeks after weekly application of EpiFix or standard dressings with compression, but interpretation is limited by methodologic concerns. A third RCT demonstrated significantly greater blinded assessor-confirmed rates of complete wound closure at 12 weeks after weekly or twice-weekly application of AmnioBand Membrane with compression bandaging compared with compression bandaging alone. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

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 that the technology results in an improvement in the net health outcome.

Plantar Fasciitis

For individuals who have plantar fasciitis who receive an injection of amniotic membrane, the evidence includes preliminary studies and a larger (N=145) patient-blinded comparison of micronized injectable-HAM and placebo control. Injection of micronized amniotic membrane resulted in greater improvements in the visual analog score for pain and the Foot Functional Index compared to placebo controls. The primary limitation of the study is that this is an interim report with 12-month results pending. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

Ophthalmic Conditions

Sutured HAM transplant has been used for many years for the treatment of ophthalmic conditions. Many of these conditions are rare, leading to difficulty in conducting RCTs. The rarity, severity, and variability of the ophthalmic condition was taken into consideration in evaluating the evidence.

Neurotrophic Keratitis with Ocular Surface Damage and Inflammation That Does Not Respond to Conservative Therapy

For individuals who have neurotrophic keratitis with ocular surface damage and inflammation that does not respond to conservative therapy who receive HAM, the evidence includes an RCT. Relevant outcomes are symptoms, morbid events, functional outcomes, and quality of life. An RCT of 30 patients showed no benefit of sutured HAM graft compared to tarsorrhaphy or bandage contact lens. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

Corneal Ulcers and Melts That Do Not Respond to Initial Medical Therapy

For individuals who have corneal ulcers and melts, that do not respond to initial medical therapy who receive HAM, the evidence includes a systematic review of primarily case series and a

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non-randomized comparative study. Relevant outcomes are symptoms, morbid events, functional outcomes, and quality of life. Corneal ulcers and melts are uncommon and variable and additional RCTs are not expected. The systematic review showed healing in 97% of patients with an improvement of vision in 53% of eyes. One retrospective comparative study with 22 patients found more rapid and complete epithelialization and more patients with a clinically significant improvement in visual acuity following early treatment with self-retained amniotic membrane when compared to historical controls. Corneal ulcers and melts are uncommon and variable and RCTs are not expected. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

Corneal Perforation When There is Active Inflammation After Corneal Transplant Requiring Adjunctive Treatment

For individuals who have corneal perforation when there is active inflammation after corneal transplant requiring adjunctive treatment who receive HAM, the evidence is limited. Relevant outcomes are symptoms, morbid events, functional outcomes, and quality of life. No comparative evidence was identified for this indication. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

Bullous Keratopathy as a Palliative Measure in Patients Who are Not Candidates for a Curative Treatment (e.g., Endothelial or Penetrating Keratoplasty)

For individuals who have bullous keratopathy and who are not candidates for curative treatment (e.g., endothelial or penetrating keratoplasty) who receive HAM, the evidence includes an RCT. Relevant outcomes are symptoms, morbid events, functional outcomes, and quality of life. An RCT found no advantage of sutured HAM over the simpler stromal puncture procedure for the treatment of pain from bullous keratopathy. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

Partial Limbal Stem Cell Deficiency with Extensive Diseased Tissue Where Selective Removal Alone is Not Sufficient

For individuals who have partial limbal stem cell deficiency with extensive diseased tissue where selective removal alone is not sufficient who receive HAM, the evidence is limited. Relevant outcomes are symptoms, morbid events, functional outcomes, and quality of life. No comparative trials were identified on HAM for limbal stem cell deficiency. Improvement in visual acuity has been reported for some patients who have received HAM in conjunction with removal of the diseased limbus. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

Moderate or Severe Stevens-Johnson Syndrome

For individuals who have moderate or severe Stevens-Johnson syndrome who receive HAM, the evidence includes an RCT. Relevant outcomes are symptoms, morbid events, functional outcomes, and quality of life. The evidence on HAM for the treatment of Stevens-Johnson syndrome (includes 1 RCT with 25 patients [50 eyes]) found improved symptoms and function with HAM compared to medical therapy alone. Large RCTs are unlikely due to the severity and rarity of the disease. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

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Persistent Epithelial Defects and Ulceration That Do Not Respond to Conservative Therapy

For individuals who have persistent epithelial defects that do not respond to conservative therapy who receive HAM, the evidence is limited. Relevant outcomes are symptoms, morbid events, functional outcomes, and quality of life. No comparative trials were identified on persistent epithelial defects and ulceration. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

Severe Dry Eye with Ocular Surface Damage and Inflammation That Does Not Respond to Conservative Therapy

For individuals who have severe dry eye with ocular surface damage and inflammation that does not respond to conservative therapy, who receive HAM, the evidence includes an RCT and a large case series. Relevant outcomes are symptoms, morbid events, functional outcomes, and quality of life. The evidence on HAM for severe dry eye with ocular surface damage and inflammation includes an RCT with 20 patients and a retrospective series of 84 patients (97 eyes). Placement of self-retained HAM for 2 to 11 days reduced symptoms and restored a smooth corneal surface and corneal nerve density for as long as 3 months. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

Moderate or Severe Acute Ocular Chemical Burns

For individuals who have moderate or severe acute ocular chemical burn who receive HAM, the evidence includes 3 RCTs. Relevant outcomes are symptoms, morbid events, functional outcomes, and quality of life. Evidence includes a total of 197 patients with acute ocular chemical burns who were treated with HAM transplantation plus medical therapy or medical therapy alone. Two of the 3 RCTs did not show a faster rate of epithelial healing, and there was no significant benefit for other outcomes. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

Corneal Perforation When Corneal Tissue is Not Immediately Available

For individuals who have corneal perforation when corneal tissue is not immediately available who receive sutured HAM, the evidence is limited. Relevant outcomes are symptoms, morbid events, functional outcomes, and quality of life. The standard treatment for corneal perforation is corneal transplantation, however, HAM may provide temporary coverage of the severe defect when corneal tissue is not immediately available. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

Pterygium Repair When There is Insufficient Healthy Tissue to Create a Conjunctival Autograft

For individuals who have pterygium repair when there is insufficient healthy tissue to create a conjunctival autograft who receive HAM, the evidence includes RCTs and systematic reviews of RCTs. Relevant outcomes are symptoms, morbid events, functional outcomes, and quality of life. Systematic reviews of RCTs have been published that found that conjunctival or limbal autograft is more effective than HAM graft in reducing the rate of pterygium recurrence. The

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evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

DEFINITIONS

N/A

DISCLAIMER

Capital Blue Cross' medical policies are used to determine coverage for specific medical technologies, procedures, equipment, and services. These medical policies do not constitute medical advice and are subject to change as permitted by law or applicable clinical evidence from independent treatment guidelines. Treating providers are solely responsible for medical advice and treatment of members. These policies are not a guarantee of coverage or payment. Payment of claims is subject to a determination regarding the member's benefit program and eligibility on the date of service, and a determination that the services are medically necessary and appropriate. Final processing of a claim is based upon the terms of contract that applies to the members' benefit program, including benefit limitations and exclusions. If a provider or a member has a question concerning this medical policy, please contact Capital Blue Cross' Provider Services or Member Services.

CODING INFORMATION

Note: This list of codes may not be all-inclusive, and codes are subject to change at any time. The identification of a code in this section does not denote coverage as coverage is determined by the terms of member benefit information. In addition, not all covered services are eligible for separate reimbursement.

Covered when medically necessary:

Trade Name	HCPCS Code
Affinity®	Q4159
AmnioBand® Membrane	Q4151
Biovance®	Q4154
Epifix®	Q4186
Epicord®	Q4187
Grafix®	Q4132, Q4133
NuShield®	Q4160

Investigational:

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Trade Name	HCPCS Code
Theracor™	A2049
Carbon Life	Q4207
DermaBind SL Optic™	Q4223
AmchoMatrix	Q4243
Abiomend membrane and abiomend hydromembrane	Q4356
Abiomend xplus membrane and abiomend xplus hydromembrane	Q4355
Acapatch	Q4325
Acesso	Q4311
Acesso ac	Q4312
AlloGen	Q4212
Alloply	Q4323
AlloWrap™	Q4150
Amchoplast	Q4316
Amchoplast fd	Q4360
Amnio burgeon dual-layer membrane	Q4365
Amnio burgeon membrane and hydromembrane	Q4363
Amnio burgeon xplus membrane and xplus hydromembrane	Q4364
AmnioAMP-MP	Q4250
Amnioarmor™	Q4188
Amniocore sl	Q4367
AmnioExcel®	Q4137
Amnio-maxx or Manio-maxx lite	Q4239
Amniotext	Q4245
Amniowound	Q4181
Amnion bio or Axomembrane	Q4211

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Amnioplast 1	Q4334
Amnioplast 2	Q4335
Amniocore™	Q4227
Amniocyte	Q4242
AmnioMatrix®	Q4139
Amnipliy	Q4249
Amniorepair or AltiPly	Q4235
Amniotext patch	Q4247
Amniotx	Q4324
AmnioWrap2™	Q4221
Ardeograft	Q4333
Artacent ac (flowable)	Q4189
Artacent ac (patch)	Q4190
Artacent c	Q4336
Artacent trident	Q4337
Artacent velos	Q4338
Artacent vericlen	Q4339
Artacent® Wound	Q4169
Ascent	Q4213
Axolotl ambien or Axolotl Cryo	Q4215
Axolotl dualgraft	Q4332
Axolotl graft	Q4331
BioDDryFlex®	Q4138
BioDfence™	Q4140
BioNextPATCH	Q4228
BioWound, BioWound Plus™, BioWound XPlus™	Q4217
Caregraft	Q4322
carePATCH	Q4236

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Cellesta/Cellesta duo	Q4184
Cellesta Cord	Q4214
Cellesta flowable	Q4185
Choripty	Q4359
Clarix®	Q4156
Clarix® Flo	Q4155
Cogenex flowable amnion	Q4230
Cogenex amniotic membrane	Q4229
Corecyte	Q4240
Corplex	Q4232
Corplex P	Q4231
Corplex p or theracor p or allacor p	A2035
Coretext or Protext	Q4246
Cryo-cord	Q4237
Cygnus	Q4170
Cygnus disk	Q4362
Dermabind fm	Q4313
Dermacyte	Q4248
Dermacyte ac matrix amniotic membrane allograft	Q4343
Dermavest™ or Plurivest	Q4153
Derm-maxx	Q4238
Dual layer amnio burgeon x-membrane	Q4366
Duoamnion	Q4327
E-graft	Q4318
Enclose tl matrix	Q4351
Epifix Injectable	Q4145
Epixpress	Q4361
Floweramnioflo	Q4177

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Floweramniopatch	Q4178
Fluid flow or Fluid GF	Q4206
Genesis	Q4198
Interfyl®	Q4171
Mantle dl matrix	Q4349
Matrion	Q4201
Matrix hd allograft dermis	Q4345
Most	Q4328
Neopatch or Therion	Q4176
Neox® Cord	Q4148
Neox® Flo	Q4155
Neox® Wound	Q4156
Restorigin	Q4191
Novafix®	Q4208
Novafix DL	Q4254
Overlay sl matrix	Q4352
Palingen dual-layer membrane	Q4354
PalinGen® Membrane	Q4173
PalinGen® SportFlow	Q4174
Palisade dm matrix	Q4350
Pellograft	Q4320
Plurivest™	Q4153
Polycyte	Q4241
Procenta	Q4244
Rampart dl matrix	Q4347
Reeva ft	Q4314
Regenelink amniotic membrane allograft	Q4315
Reguard	Q4255
Renograft	Q4321

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Restorigin	Q4191
Restorigin Injectable	Q4192
Revita	Q4180
Revitalon™	Q4157
Sanograft	Q4319
Sentry sl matrix	Q4348
Shelter dm matrix	Q4346
Simpligraft	Q4340
Simplimax	Q4341
Singlay	Q4329
Surgenex, Surfactor, and Nudyn	Q4233
Surgicord	Q4218
SurgiGRAFT™	Q4183
Theramend	Q4342
Total	Q4330
Tri-membrane wrap	Q4344
Vitograft	Q4317
WoundEx®	Q4163
WoundEx® Flow	Q4162
Woundfix, Woundfix Plus, Wounfix XPlus (see BioWound above)	Q4217
Woundplus	Q4326
Xceed tl matrix	Q4353
Xcellerate	Q4234
Xwrap	Q4204
Xwrap dual	Q4358
Choripty	Q4359
Amchoplast fd	Q4360
Epixpress	Q4361

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Cygnus disk	Q4362
Amnio burgeon membrane and hydromembrane	Q4363
Amnio burgeon xplus membrane and xplus hydromembrane	Q4364
Amnio burgeon dual-layer	Q4365
Dual layer amnio burgeon x-membrane	Q4366
Amniocore	Q4367
SUMMIT AC	Q4398
SUMMIT FX	Q4399
POLYGON3 MEMBRANE	Q4400
ABSOLV3 MEMBRANE	Q4401
XWRAP 2.0	Q4402
XWRAP DUAL PLUS	Q4403
XWRAP HYDRO PLUS	Q4404
XWRAP FENESTRA PLUS	Q4405
XWRAP FENESTRA	Q4406
XWRAP TRIBUS	Q4407
XWRAP HYDRO	Q4408
AMNIOMATRIXF3X	Q4409
AMCHOMATRIXDL	Q4410
AMNIOMATRIXF4X	Q4411
CHORIOFIX	Q4412
CYGNUS SOLO	Q4413
SIMPLICHOR	Q4414
ALEXIGUARD SL-T	Q4415
ALEXIGUARD TL-T	Q4416
ALEXIGUARD DL-T	Q4417
NUFORM	Q4420

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Dermabind dl, dl+, dlX	Q4427
Dermabind sl,sl+,slX	Q4428
Dermabind ch n, Dermabind ch x	Q4229
Preteck	Q4438
Instagraft	Q4439

REFERENCES

1. Parolini O, Soncini M, Evangelista M, et al. Amniotic membrane and amniotic fluid-derived cells: potential tools for regenerative medicine?. *Regen Med*. Mar 2009; 4(2): 275-91. PMID 19317646
2. Koob TJ, Rennert R, Zabek N, et al. Biological properties of dehydrated human amnion/chorion composite graft: implications for chronic wound healing. *Int Wound J*. Oct 2013; 10(5): 493-500. PMID 23902526
3. Shimberg M, Wadsworth K. The use of amniotic-fluid concentrate in orthopaedic conditions. *J Bone Joint Surg*. 1938;20(1):167-177.
4. U.S. Food and Drug Administration. Public Safety Notification on Amniotic Fluid Eyedrops. October 17, 2024. <https://www.fda.gov/vaccines-blood-biologics/safety-availability-biologics/public-safety-notification-amniotic-fluid-eyedrops>.
5. U.S. Food and Drug Administration. Warning Letters. 2025. <https://www.fda.gov/inspections-compliance-enforcement-and-criminal-investigations/compliance-actions-and-activities/warning-letters>.
6. U.S. Food and Drug Administration. Warning Letter: Integra LifeSciences Corporation. December 19,2024. <https://www.fda.gov/inspections-compliance-enforcement-and-criminal-investigations/warning-letters/integra-lifesciences-corporation-698850-12192024>.
7. U.S. Food and Drug Administration. Regulatory Considerations for Human Cells, Tissues, and Cellular and Tissue-Based Products: Minimal Manipulation and Homologous Use Guidance for Industry and Food and Drug Administration Staff. 2017 <https://www.regulations.gov/document?D=FDA-2017-D-6146-0003>
8. Food and Drug Administration. 510(k) Summary: ProKera™ Bio-Tissue Inc. (K032104). 2003; https://www.accessdata.fda.gov/cdrh_docs/pdf3/K032104.pdf.
9. Cazzell SM, Caporusso J, Vayser D, et al. Dehydrated Amnion Chorion Membrane versus standard of care for diabetic foot ulcers: a randomised controlled trial. *J Wound Care*. Jul 01 2024; 33(Sup7): S4-S14. PMID 38973638
10. Serena TE, Yaakov R, Moore S, et al. A randomized controlled clinical trial of a hypothermically stored amniotic membrane for use in diabetic foot ulcers. *J Comp Eff Res*. Jan 2020; 9(1): 23-34. PMID 31691579
11. Ananian CE, Dhillon YS, Van Gils CC, et al. A multicenter, randomized, single-blind trial comparing the efficacy of viable cryopreserved placental membrane to human fibroblast-derived dermal substitute for the treatment of chronic diabetic foot ulcers. *Wound Repair Regen*. May 2018; 26(3): 274-283. PMID 30098272

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12. Tettelbach W, Cazzell S, Sigal F, et al. A multicentre prospective randomised controlled comparative parallel study of dehydrated human umbilical cord (EpiCord) allograft for the treatment of diabetic foot ulcers. *Int Wound J.* Feb 2019; 16(1): 122-130. PMID 30246926
13. DiDomenico LA, Orgill DP, Galiano RD, et al. Use of an aseptically processed, dehydrated human amnion and chorion membrane improves likelihood and rate of healing in chronic diabetic foot ulcers: A prospective, randomised, multi-centre clinical trial in 80 patients. *Int Wound J.* Dec 2018; 15(6): 950-957. PMID 30019528
14. Snyder RJ, Shimozaki K, Tallis A, et al. A Prospective, Randomized, Multicenter, Controlled Evaluation of the Use of Dehydrated Amniotic Membrane Allograft Compared to Standard of Care for the Closure of Chronic Diabetic Foot Ulcer. *Wounds.* Mar 2016; 28(3): 70-7. PMID 26978860
15. Zelen CM, Gould L, 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.* Dec 2015; 12(6): 724-32. PMID 25424146
16. Zelen CM, Serena TE, Gould L, et al. Treatment of chronic diabetic lower extremity ulcers with advanced therapies: a prospective, randomised, controlled, multi-centre comparative study examining clinical efficacy and cost. *Int Wound J.* Apr 2016; 13(2): 272-82. PMID 26695998
17. Tettelbach W, Cazzell S, Reyzelman AM, et al. A confirmatory study on the efficacy of dehydrated human amnion/chorion membrane dHACM allograft in the management of diabetic foot ulcers: A prospective, multicentre, randomised, controlled study of 110 patients from 14 wound clinics. *Int Wound J.* Feb 2019; 16(1): 19-29. PMID 30136445
18. Lavery LA, Fulmer J, Shebetka KA, et al. The efficacy and safety of Grafix® for the treatment of chronic diabetic foot ulcers: results of a multi-centre, controlled, randomised, blinded, clinical trial. *Int Wound J.* Oct 2014; 11(5): 554-60. PMID 25048468
19. Smiell JM, Treadwell T, Hahn HD, et al. Real-world Experience With a Decellularized Dehydrated Human Amniotic Membrane Allograft. *Wounds.* Jun 2015; 27(6): 158-69. PMID 26061491
20. Frykberg RG, Gibbons GW, Walters JL, et al. A prospective, multicentre, open-label, single-arm clinical trial for treatment of chronic complex diabetic foot wounds with exposed tendon and/or bone: positive clinical outcomes of viable cryopreserved human placental membrane. *Int Wound J.* Jun 2017; 14(3): 569-577. PMID 27489115
21. Serena TE, Carter MJ, Le LT, et al. A multicenter, randomized, controlled clinical trial evaluating the use of dehydrated human amnion/chorion membrane allografts and multilayer compression therapy vs. multilayer compression therapy alone in the treatment of venous leg ulcers. *Wound Repair Regen.* 2014; 22(6): 688-93. PMID 25224019
22. Bianchi C, Cazzell S, Vayser D, et al. A multicentre randomised controlled trial evaluating the efficacy of dehydrated human amnion/chorion membrane (EpiFix®) allograft for the treatment of venous leg ulcers. *Int Wound J.* Feb 2018; 15(1): 114-122. PMID 29024419
23. Bianchi C, Tettelbach W, Istwan N, et al. Variations in study outcomes relative to intention-to-treat and per-protocol data analysis techniques in the evaluation of efficacy for treatment of venous leg ulcers with dehydrated human amnion/chorion membrane allograft. *Int Wound J.* Jun 2019; 16(3): 761-767. PMID 30864259

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24. Serena TE, Orgill DP, Armstrong DG, et al. A Multicenter, Randomized, Controlled, Clinical Trial Evaluating Dehydrated Human Amniotic Membrane in the Treatment of Venous Leg Ulcers. *Plast Reconstr Surg*. Nov 01 2022; 150(5): 1128-1136. PMID 36067479
25. Vines JB, Aliprantis AO, Gomoll AH, et al. Cryopreserved Amniotic Suspension for the Treatment of Knee Osteoarthritis. *J Knee Surg*. Aug 2016; 29(6): 443-50. PMID 26683979
26. Pill SG, Ahearn B, Tokish JM, et al. Amniotic Tissue Injections Are an Effective Alternative to Corticosteroid Injections for Pain Relief and Function in Patients With Severe Knee Osteoarthritis: A Double-Blind, Randomized, Prospective Study. *J Am Acad Orthop Surg Glob Res Rev*. Jan 01 2025; 9(1). PMID 39813395
27. Tsikopoulos K, Vasiliadis HS, Mavridis D. Injection therapies for plantar fasciopathy ('plantar fasciitis'): a systematic review and network meta-analysis of 22 randomised controlled trials. *Br J Sports Med*. Nov 2016; 50(22): 1367-1375. PMID 27143138
28. Zelen CM, Poka A, Andrews J. Prospective, randomized, blinded, comparative study of injectable micronized dehydrated amniotic/chorionic membrane allograft for plantar fasciitis--a feasibility study. *Foot Ankle Int*. Oct 2013; 34(10): 1332-9. PMID 23945520
29. Cazzell S, Stewart J, Agnew PS, et al. Randomized Controlled Trial of Micronized Dehydrated Human Amnion/Chorion Membrane (dHACM) Injection Compared to Placebo for the Treatment of Plantar Fasciitis. *Foot Ankle Int*. Oct 2018; 39(10): 1151-1161. PMID 30058377
30. Suri K, Kosker M, Raber IM, et al. Sutureless amniotic membrane ProKera for ocular surface disorders: short-term results. *Eye Contact Lens*. Sep 2013; 39(5): 341-7. PMID 23945524
31. Liu J, Li L, Li X. Effectiveness of Cryopreserved Amniotic Membrane Transplantation in Corneal Ulceration: A Meta-Analysis. *Cornea*. Apr 2019; 38(4): 454-462. PMID 30702468
32. Yin HY, Cheng AMS, Tighe S, et al. Self-retained cryopreserved amniotic membrane for treating severe corneal ulcers: a comparative, retrospective control study. *Sci Rep*. Oct 12 2020; 10(1): 17008. PMID 33046729
33. Paris Fdos S, Gonçalves ED, Campos MS, et al. Amniotic membrane transplantation versus anterior stromal puncture in bullous keratopathy: a comparative study. *Br J Ophthalmol*. Aug 2013; 97(8): 980-4. PMID 23723410
34. Kheirkhah A, Casas V, Raju VK, et al. Sutureless amniotic membrane transplantation for partial limbal stem cell deficiency. *Am J Ophthalmol*. May 2008; 145(5): 787-94. PMID 18329626
35. Pachigolla G, Prasher P, Di Pasquale MA, et al. Evaluation of the role of ProKera in the management of ocular surface and orbital disorders. *Eye Contact Lens*. Jul 2009; 35(4): 172-5. PMID 19474753
36. Sharma N, Thenarasun SA, Kaur M, et al. Adjuvant Role of Amniotic Membrane Transplantation in Acute Ocular Stevens-Johnson Syndrome: A Randomized Control Trial. *Ophthalmology*. Mar 2016; 123(3): 484-91. PMID 26686968
37. Bouchard CS, John T. Amniotic membrane transplantation in the management of severe ocular surface disease: indications and outcomes. *Ocul Surf*. Jul 2004; 2(3): 201-11. PMID 17216092
38. John T, Tighe S, Sheha H, et al. Corneal Nerve Regeneration after Self-Retained Cryopreserved Amniotic Membrane in Dry Eye Disease. *J Ophthalmol*. 2017; 2017: 6404918. PMID 28894606

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39. McDonald MB, Sheha H, Tighe S, et al. Treatment outcomes in the DRy Eye Amniotic Membrane (DREAM) study. *Clin Ophthalmol.* 2018; 12: 677-681. PMID 29670328
40. Tandon R, Gupta N, Kalaivani M, et al. Amniotic membrane transplantation as an adjunct to medical therapy in acute ocular burns. *Br J Ophthalmol.* Feb 2011; 95(2): 199-204. PMID 20675729
41. Eslani M, Baradaran-Rafii A, Cheung AY, et al. Amniotic Membrane Transplantation in Acute Severe Ocular Chemical Injury: A Randomized Clinical Trial. *Am J Ophthalmol.* Mar 2019; 199: 209-215. PMID 30419194
42. Tamhane A, Vajpayee RB, Biswas NR, et al. Evaluation of amniotic membrane transplantation as an adjunct to medical therapy as compared with medical therapy alone in acute ocular burns. *Ophthalmology.* Nov 2005; 112(11): 1963-9. PMID 16198422
43. Kaufman SC, Jacobs DS, Lee WB, et al. Options and adjuvants in surgery for pterygium: a report by the American Academy of Ophthalmology. *Ophthalmology.* Jan 2013; 120(1): 201-8. PMID 23062647
44. Clearfield E, Muthappan V, Wang X, et al. Conjunctival autograft for pterygium. *Cochrane Database Syst Rev.* Feb 11 2016; 2(2): CD011349. PMID 26867004
45. Toman J, Michael GM, Wisco OJ, et al. Mohs Defect Repair with Dehydrated Human Amnion/Chorion Membrane. *Facial Plast Surg Aesthet Med.* 2022; 24(1): 48-53. PMID 34714143
46. Hingorani A, LaMuraglia GM, Henke P, et al. The management of diabetic foot: A clinical practice guideline by the Society for Vascular Surgery in collaboration with the American Podiatric Medical Association and the Society for Vascular Medicine. *J Vasc Surg.* Feb 2016; 63(2 Suppl): 3S-21S. PMID 26804367
47. Lavery LA, Davis KE, Berriman SJ, et al. WHS guidelines update: Diabetic foot ulcer treatment guidelines. *Wound Repair Regen.* 2016; 24(1): 112-26. PMID 2666343048. Blue Cross Blue Shield Association Medical Policy Reference Manual. 7.01.149 - Amniotic Membrane and Amniotic Fluid. April 2025.

POLICY HISTORY

MP 1.159	10/24/2023 New Policy Created. Criteria taken from MP 4.042
	07/09/2024 Consensus Review. No changes to policy statement. References reviewed and updated.
	04/17/2025 Major review. Title updated to "Amniotic Membrane and Amniotic Fluid". Other indications added to policy aside from ocular indications. Coding updated to match policy statements.
	12/12/2025 Administrative update. Added codes Q4398-Q4417, Q4420.
	3/12/2026 Administrative update. Added codes Q4427-Q4429, Q4438, Q4439. Effective 4/1/2026.
	09/01/2026 Administrative Update. Added new codes A2049, Q4207, Q4223, and Q4243. Effective Date: 10/01/2026.

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