BlueCross BlueShield Arizona

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EVIDENCE-BASED CRITERIA	**ORIGINAL EFFECTIVE DATE: 05/21/24**
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AMNIOTIC MEMBRANE AND AMNIOTIC FLUID

Non-Discrimination Statement and Multi-Language Interpreter Services information are located at the end of this document.

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Evidence-Based Criteria must be read in its entirety to determine coverage eligibility, if any.

This Evidence-Based Criteria provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide BCBSAZ complete medical rationale when requesting any exceptions to these guidelines.

The section identified as "Description" defines or describes a service, procedure, medical device or drug and is in no way intended as a statement of medical necessity and/or coverage.

The section identified as "Criteria" defines criteria to determine whether a service, procedure, medical device or drug is considered medically necessary or experimental or investigational.

State or federal mandates, e.g., FEP program, may dictate that any drug, device or biological product approved by the U.S. Food and Drug Administration (FDA) may not be considered experimental or investigational and thus the drug, device or biological product may be assessed only on the basis of medical necessity.

Evidence-Based Criteria are subject to change as new information becomes available.

For purposes of this Evidence-Based Criteria, the terms "experimental" and "investigational" are considered to be interchangeable.

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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.

This review covers products that do not require FDA approval or clearance. The list of products named in this review is not a complete list of all commercially available products.

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 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, antifibroblastic, and antimicrobial properties. HAM is considered nonimmunogenic and has not been observed to 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, one 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.

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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 proteins, carbohydrates, peptides, fats, amino acids, 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.

Tear Film and Ocular Surface Society: Dry Eye Disease Management Algorithm

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

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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
- 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

Criteria:

- Treatment of nonhealing diabetic lower-extremity ulcers with less than 20% decrease in wound area after standard wound care for at least 2 weeks using the following human amniotic membrane products is considered ***medically necessary***:

  1. Affinity®
  2. AmnioBand® Membrane
  3. AmnioExcel®
  4. Biovance®
  5. EpiCord®

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6. EpiFix®

7. Grafix™

- Human amniotic membrane grafts with or without suture for the treatment of the following ophthalmic indications are considered ***medically necessary*** with documentation of **ANY** of the following:

  1. Neurotrophic keratitis with ocular surface damage and inflammation that does not respond to conservative therapy

  2. Corneal ulcers and melts that do not respond to initial conservative therapy

  3. Corneal perforation when there is active inflammation after corneal transplant requiring adjunctive treatment

  4. Bullous keratopathy as a palliative measure in individuals who are not candidates for curative treatment (e.g., endothelial or penetrating keratoplasty)

  5. Partial limbal stem cell deficiency with extensive diseased tissue where selective removal alone is not sufficient

  6. Moderate or severe Stevens-Johnson syndrome

  7. Persistent epithelial defects that do not respond within 2 days to conservative therapy

  8. 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

  9. Moderate or severe acute ocular chemical burn

- Human amniotic membrane grafts with suture or glue for the treatment of the following ophthalmic indications are considered ***medically necessary*** with documentation of **ANY** of the following:

  1. Corneal perforation when corneal tissue is not immediately available

  2. Pterygium repair when there is insufficient healthy tissue to create a conjunctival autograft

- Human amniotic membrane grafts with or without suture for all other ophthalmic indications not previously listed or if above criteria not met are considered ***experimental or investigational*** when any **ONE** or more of the following criteria are met:

  1. Lack of final approval from the appropriate governmental regulatory bodies (e.g., Food and Drug Administration); or
  2. Insufficient scientific evidence to permit conclusions concerning the effect on health outcomes; or

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3. Insufficient evidence to support improvement of the net health outcome; or
4. Insufficient evidence to support improvement of the net health outcome as much as, or more than, established alternatives; or
5. Insufficient evidence to support improvement outside the investigational setting.

- Injection of micronized or particulated human amniotic membrane for all indications is considered ***experimental or investigational*** when any **ONE** or more of the following criteria are met:

  1. Lack of final approval from the appropriate governmental regulatory bodies (e.g., Food and Drug Administration); or
  2. Insufficient scientific evidence to permit conclusions concerning the effect on health outcomes; or
  3. Insufficient evidence to support improvement of the net health outcome; or
  4. Insufficient evidence to support improvement of the net health outcome as much as, or more than, established alternatives; or
  5. Insufficient evidence to support improvement outside the investigational setting.

  These indications include, *but are not limited to:*

  - Osteoarthritis
  - Plantar fasciitis

- Injection of human amniotic fluid for all indications is considered ***experimental or investigational*** when any **ONE** or more of the following criteria are met:

  1. Lack of final approval from the appropriate governmental regulatory bodies (e.g., Food and Drug Administration); or
  2. Insufficient scientific evidence to permit conclusions concerning the effect on health outcomes; or
  3. Insufficient evidence to support improvement of the net health outcome; or
  4. Insufficient evidence to support improvement of the net health outcome as much as, or more than, established alternatives; or
  5. Insufficient evidence to support improvement outside the investigational setting.

- All other human amniotic products not listed above are considered ***experimental or investigational*** when any **ONE** or more of the following criteria are met:

  1. Lack of final approval from the appropriate governmental regulatory bodies (e.g., Food and Drug Administration); or
  2. Insufficient scientific evidence to permit conclusions concerning the effect on health outcomes; or
  3. Insufficient evidence to support improvement of the net health outcome; or
  4. Insufficient evidence to support improvement of the net health outcome as much as, or more than, established alternatives; or
  5. Insufficient evidence to support improvement outside the investigational setting.

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Other human amniotic products include those derived from the following, *but are not limited to:*

- Products derived from amnion
- Products derived from chorion
- Products derived from amniotic fluid
- Products derived from umbilical cord
- Products derived from Wharton's jelly

➢ All other human amniotic products for all other indications not listed above are considered ***experimental or investigational*** when any **ONE** or more of the following criteria are met:

1. Lack of final approval from the appropriate governmental regulatory bodies (e.g., Food and Drug Administration); or
2. Insufficient scientific evidence to permit conclusions concerning the effect on health outcomes; or
3. Insufficient evidence to support improvement of the net health outcome; or
4. Insufficient evidence to support improvement of the net health outcome as much as, or more than, established alternatives; or
5. Insufficient evidence to support improvement outside the investigational setting.

These indications include, *but are not limited to:*

- Treatment of lower extremity ulcers due to venous insufficiency with less than 30% decrease in wound area after standard wound care for at least 2 weeks
- Repair following Mohs micrographic surgery

These human amniotic products include, *but are not limited to*:

- AlloGen
- AlloWrap™
- AmnioAMP-MP
- Amnioarmor™
- Amnio-maxx or Manio-maxx lite
- Amniotext
- Amniowound
- Amnion bio or Axomembrane
- Amniocore™
- Amniocyte
- AmnioMatrix®
- Amniply
- Amniorepair or AltiPly
- Amniotext patch
- AmnioWrap2™
- Articent ac (flowable)
- Artacent ac (patch)

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- Artacent® Wound
- Artacent® Cord
- Ascent
- Axolotl ambien or Axolotl Cryo
- BioDDryFlex®
- BioDfence™
- BioNextPATCH
- BioWound
- BioWound Plus™
- BioWound XPlus™
- carePATCH
- Cellesta/Cellesta duo
- Cellesta Cord
- Cellesta flowable
- Clarix®
- Clarix® Flo
- Cogenex flowable amnion
- Cogenex amniotic membrane
- Corecyte
- Corplex
- Corplex P
- Coretext or Protext
- Cryo-cord
- Cygnus
- Dermacyte
- Dermavest™ or Plurivest
- Derm-maxx
- Epifix Injectable
- Floweramnioflo
- Floweramniopatch
- Fluid flow or Fluid GF
- Genesis
- Guardian/AmnioBand®
- Interfyl®
- Matrion
- Neopatch or Therion
- Neox® Cord
- Neox® Flo
- Neox® Wound
- Novachor
- Novafix®
- Novafix DL
- NuShield
- PalinGen® Membrane

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- PalinGen® SportFlow
- Plurivest™
- Polycyte
- Procenta
- Reguard
- Restorigin
- Restorigin Injectable
- Revita
- Revitalon™
- Surgenex, Surfactor, and Nudyn
- Surgicord
- SurgiGRAFT™
- WoundEx®
- WoundEx® Flow
- Woundfix
- Woundfix Plus
- Wounfix XPlus
- Xcellerate
- Xwrap

Resources:

Literature reviewed 05/21/24. We do not include marketing materials, poster boards and non-published literature in our review.

Resources prior to 05/21/24 may be requested from the BCBSAZ Medical Policy and Technology Research Department.

1. 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 and regeneration :official publication of the Wound Healing Society [and] the European Tissue Repair Society*. May 2018;26(3):274-283. doi:10.1111/wrr.12645

2. Bianchi C, Cazzell S, Vayser D, Reyzelman AM, Dosluoglu H, Tovmassian G. A multicentre randomised controlled trial evaluating the efficacy of dehydrated human amnion/chorion membrane (EpiFix(®)) allograft for the treatment of venous leg ulcers. *International wound journal*. Feb 2018;15(1):114-122. doi:10.1111/iwj.12843

3. 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. *International wound journal*. Jun 2019;16(3):761-767. doi:10.1111/iwj.13094

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4. Bouchard CS, John T. Amniotic membrane transplantation in the management of severe ocular surface disease: indications and outcomes. *The ocular surface*. Jul 2004;2(3):201-11. doi:10.1016/s1542-0124(12)70062-9

5. 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 international*. Oct 2018;39(10):1151-1161. doi:10.1177/1071100718788549

6. Clearfield E, Muthappan V, Wang X, Kuo IC. Conjunctival autograft for pterygium. *Cochrane Database Syst Rev*. Feb 11 2016;2(2):Cd011349. doi:10.1002/14651858.CD011349.pub2

7. 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. *International wound journal*. Dec 2018;15(6):950-957. doi:10.1111/iwj.12954

8. 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. doi:10.1016/j.ajo.2018.11.001

9. Frykberg RG, Gibbons GW, Walters JL, Wukich DK, Milstein FC. 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. *International wound journal*. Jun 2017;14(3):569-577. doi:10.1111/iwj.12649

10. 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. doi:10.1016/j.jvs.2015.10.003

11. 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. doi:10.1155/2017/6404918

12. Kaufman SC, Jacobs DS, Lee WB, Deng SX, Rosenblatt MI, Shtein RM. Options and adjuvants in surgery for pterygium: a report by the American Academy of Ophthalmology. *Ophthalmology*. Jan 2013;120(1):201-8. doi:10.1016/j.ophtha.2012.06.066

13. Kheirkhah A, Casas V, Raju VK, Tseng SC. Sutureless amniotic membrane transplantation for partial limbal stem cell deficiency. *Am J Ophthalmol*. May 2008;145(5):787-94. doi:10.1016/j.ajo.2008.01.009

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14. Koob TJ, Rennert R, Zabek N, et al. Biological properties of dehydrated human amnion/chorion composite graft: implications for chronic wound healing. *International wound journal*. Oct 2013;10(5):493-500. doi:10.1111/iwj.12140

15. Lavery LA, Davis KE, Berriman SJ, et al. WHS guidelines update: Diabetic foot ulcer treatment guidelines. *Wound repair and regeneration : official publication of the Wound Healing Society [and] the European Tissue Repair Society*. Jan-Feb 2016;24(1):112-26. doi:10.1111/wrr.12391

16. 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. *International wound journal*. Oct 2014;11(5):554-60. doi:10.1111/iwj.12329

17. 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. doi:10.1097/ico.0000000000001866

18. McDonald MB, Sheha H, Tighe S, et al. Treatment outcomes in the DRy Eye Amniotic Membrane (DREAM) study. *Clinical ophthalmology (Auckland, NZ)*. 2018;12:677-681. doi:10.2147/opth.S162203

19. Pachigolla G, Prasher P, Di Pascuale MA, McCulley JP, McHenry JG, Mootha VV. Evaluation of the role of ProKera in the management of ocular surface and orbital disorders. *Eye Contact Lens*. Jul 2009;35(4):172-5. doi:10.1097/ICL.0b013e3181a66a12

20. Paris Fdos S, Gonçalves ED, Campos MS, Sato EH, Dua HS, Gomes J. Amniotic membrane transplantation versus anterior stromal puncture in bullous keratopathy: a comparative study. *The British journal of ophthalmology*. Aug 2013;97(8):980-4. doi:10.1136/bjophthalmol-2013-303081

21. Parolini O, Soncini M, Evangelista M, Schmidt D. Amniotic membrane and amniotic fluid-derived cells: potential tools for regenerative medicine? *Regen Med*. Mar 2009;4(2):275-91. doi:10.2217/17460751.4.2.275

22. Serena TE, Carter MJ, Le LT, Sabo MJ, DiMarco DT. 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 and regeneration : official publication of the Wound Healing Society [and] the European Tissue Repair Society*. Nov-Dec 2014;22(6):688-93. doi:10.1111/wrr.12227

23. 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 1 2022;150(5):1128-1136. doi:10.1097/prs.0000000000009650

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24. 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. doi:10.2217/cer-2019-0142

25. 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. doi:10.1016/j.ophtha.2015.10.027

26. Shimberg MH. THE USE OF AMNIOTIC-FLUID CONCENTRATE IN ORTHOPAEDIC CONDITIONS. *Journal of Bone and Joint Surgery, American Volume*. 1938;20:167-177.

27. Smiell JM, Treadwell T, Hahn HD, Hermans MH. Real-world Experience With a Decellularized Dehydrated Human Amniotic Membrane Allograft. *Wounds*. Jun 2015;27(6):158-69.

28. 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.

29. 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. doi:10.1097/ICL.0b013e3182a2f8fa

30. 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. doi:10.1016/j.ophtha.2005.05.022

31. Tandon R, Gupta N, Kalaivani M, Sharma N, Titiyal JS, Vajpayee RB. Amniotic membrane transplantation as an adjunct to medical therapy in acute ocular burns. *The British journal of ophthalmology*. Feb 2011;95(2):199-204. doi:10.1136/bjo.2009.173716

32. Tettelbach W, Cazzell S, Reyzelman AM, Sigal F, Caporusso JM, Agnew PS. 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. *International wound journal*. Feb 2019;16(1):19-29. doi:10.1111/iwj.12976

33. 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. *International wound journal*. Feb 2019;16(1):122-130. doi:10.1111/iwj.13001

34. Toman J, Michael GM, Wisco OJ, Adams JR, Hubbs BS. Mohs Defect Repair with Dehydrated Human Amnion/Chorion Membrane. *Facial Plast Surg Aesthet Med*. Jan-Feb 2022;24(1):48-53. doi:10.1089/fpsam.2021.0167

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35. 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. doi:10.1136/bjsports-2015-095437

36. U.S. Food and Drug Administration. 510(k) Summary: ProKeraTM Bio-Tissue Inc. (K032104). 2003. Accessed January 3, 2024. https://www.accessdata.fda.gov/cdrh_docs/pdf3/K032104.pdf

37. 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. Accessed January 3, 2024. https://www.regulations.gov/document/FDA-2017-D-6146-0003

38. Vines JB, Aliprantis AO, Gomoll AH, Farr J. Cryopreserved Amniotic Suspension for the Treatment of Knee Osteoarthritis. *J Knee Surg*. Aug 2016;29(6):443-50. doi:10.1055/s-0035-1569481

39. 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. doi:10.1038/s41598-020-73672-2

40. Zelen CM, Gould L, Serena TE, Carter MJ, Keller J, Li WW. 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. *International wound journal*. Dec 2015;12(6):724-32. doi:10.1111/iwj.12395

41. 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 international*. Oct 2013;34(10):1332-9. doi:10.1177/1071100713502179

42. 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. *International wound journal*. Apr 2016;13(2):272-82. doi:10.1111/iwj.12566

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Coding:

CPT: 65778, 65779
HCPCS: A2001, Q4132, Q4133, Q4137, Q4138, Q4139, Q4140, Q4145, Q4148, Q4150, Q4151, Q4153, Q4154, Q4155, Q4156, Q4157, Q4159, Q4160, Q4162, Q4163, Q4168, Q4169, Q4170, Q4171, Q4173, Q4174, Q4176, Q4177, Q4178, Q4180, Q4181, Q4183, Q4184, Q4185, Q4186, Q4187, Q4188, Q4189, Q4190, Q4191, Q4192, Q4194, Q4198, Q4199, Q4201, Q4204, Q4205, Q4206, Q4208, Q4209, Q4210, Q4211, Q4212, Q4213, Q4214, Q4215, Q4216, Q4217, Q4218, Q4219, Q4220, Q4221, Q4224, Q4225, Q4227, Q4229, Q4230, Q4231, Q4232, Q4233, Q4234, Q4235, Q4236, Q4237, Q4238, Q4239, Q4240, Q4241, Q4242, Q4244, Q4245, Q4246, Q4247, Q4248, Q4249, Q4250, Q4251, Q4252, Q4253, Q4254, Q4255, Q4256, Q4257, Q4258, Q4259, Q4260, Q4261, Q4262, Q4263, Q4264, Q4265, Q4266, Q4267, Q4268, Q4269, Q4270, Q4271, Q4272, Q4273, Q4274, Q4275, Q4276, Q4277, Q4278, Q4279, Q4280, Q4281, Q4282, Q4283, Q4284, Q4285, Q4286, Q4287, Q4288, Q4289, Q4290, Q4291, Q4292, Q4293, Q4294, Q4295, Q4296, Q4297, Q4298, Q4299, Q4300, Q4301, Q4302, Q4303, Q4304, Q4311, Q4312, Q4313, Q4314, Q4315, Q4316, Q4317, Q4318, Q4319, Q4320, Q4321, Q4322, Q4323, Q4324, Q4325, Q4326, Q4327, Q4328, Q4329, Q4330, Q4331, Q4332, Q4333, Q4334, Q4335, Q4336, Q4337, Q4338, Q4339, Q4340, Q4341, Q4342, Q4343, Q4344, Q4345, V2790

History:	**Date:**	**Activity:**
Medical Policy Panel	05/21/24	Approved guideline
Medical Director (Dr. Sutanto)	04/16/24	Review with revisions

Policy Revisions:

10/07/24	Added:	HCPCS codes: Q4334, Q4335, Q4336, Q4337, Q4338, Q4339, Q4340, Q4341, Q4342, Q4343, Q4344, Q4345
07/09/24	Added:	HCPCS codes: Q4311, Q4312, Q4313, Q4314, Q4315, Q4316, Q4317, Q4318, Q4319, Q4320, Q4321, Q4322, Q4323, Q4324, Q4325, Q4326, Q4327, Q4328, Q4329, Q4330, Q4331, Q4332, Q4333

EVIDENCE-BASED CRITERIA	**ORIGINAL EFFECTIVE DATE: 05/21/24**
SECTION: SURGERY	**LAST REVIEW DATE: 05/21/24**
	CURRENT EFFECTIVE DATE: 10/07/24
	LAST CRITERIA REVISION DATE: 05/21/24
NEXT ANNUAL REVIEW DATE: 2ND QTR 2025	**ARCHIVE DATE:**

AMNIOTIC MEMBRANE AND AMNIOTIC FLUID

Non-Discrimination Statement:

Blue Cross Blue Shield of Arizona (BCBSAZ) complies with applicable Federal civil rights laws and does not discriminate on the basis of race, color, national origin, age, disability or sex. BCBSAZ provides appropriate free aids and services, such as qualified interpreters and written information in other formats, to people with disabilities to communicate effectively with us. BCBSAZ also provides free language services to people whose primary language is not English, such as qualified interpreters and information written in other languages. If you need these services, call (602) 864-4884 for Spanish and (877) 475-4799 for all other languages and other aids and services.

If you believe that BCBSAZ 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: BCBSAZ's Civil Rights Coordinator, Attn: Civil Rights Coordinator, Blue Cross Blue Shield of Arizona, P.O. Box 13466, Phoenix, AZ 85002-3466, (602) 864-2288, TTY/TDD (602) 864-4823, crc@azblue.com. You can file a grievance in person or by mail or email. If you need help filing a grievance BCBSAZ's 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/portal/lobby.jsf, or by mail or phone at: U.S. Department of Health and Human Services, 200 Independence Avenue SW., Room 509F, HHH Building, Washington, DC 20201, 1–800–368–1019, 800–537–7697 (TDD). Complaint forms are available at http://www.hhs.gov/ocr/office/file/index.html

Multi-Language Interpreter Services:

Spanish: Si usted, o alguien a quien usted está ayudando, tiene preguntas acerca de Blue Cross Blue Shield of Arizona, tiene derecho a obtener ayuda e información en su idioma sin costo alguno. Para hablar con un intérprete, llame al 602-864-4884.

Navajo: Díí kwe'é atah nílínigíí Blue Cross Blue Shield of Arizona haada yit'éego bína'ídíłkidgo éí doodago Háida bíjá anilyeedígíí t'áadoo le'é yína'ídíłkidgo beehaz'áanii hóló díí t'áá hazaadk'ehjí háká a'doowołgo bee haz'ą doo bąąh íłínígóó. Ata' halne'ígíí kojį' bich'į' hodíilnih 877-475-4799.

Chinese: 如果您，或是您正在協助的對象，有關於插入項目的名稱 Blue Cross Blue Shield of Arizona 方面的問題，您有權利免費以您的母語得到幫助和訊息。洽詢一位翻譯員，請撥電話 在此插入數字 877-475-4799。

Vietnamese: Nếu quý vị, hay người mà quý vị đang giúp đỡ, có câu hỏi về Blue Cross Blue Shield of Arizona quý vị sẽ có quyền được giúp và có thêm thông tin bằng ngôn ngữ của mình miễn phí. Để nói chuyện với một thông dịch viên, xin gọi 877-475-4799.

Arabic:
إن كان لديك أو لدى شخص تساعده أسئلة بخصوص Blue Cross Blue Shield of Arizona، فلديك الحق في الحصول على المساعدة والمعلومات الضرورية بلغتك من دون اية تكلفة. للتحدث مع مترجم اتصل ب 877-475-4799.

AMNIOTIC MEMBRANE AND AMNIOTIC FLUID

Multi-Language Interpreter Services:

Tagalog: Kung ikaw, o ang iyong tinutulangan, ay may mga katanungan tungkol sa Blue Cross Blue Shield of Arizona, may karapatan ka na makakuha ng tulong at impormasyon sa iyong wika ng walang gastos. Upang makausap ang isang tagasalin, tumawag sa 877-475-4799.

Korean: 만약 귀하 또는 귀하가 돕고 있는 어떤 사람이 Blue Cross Blue Shield of Arizona 에 관해서 질문이 있다면 귀하는 그러한 도움과 정보를 귀하의 언어로 비용 부담없이 얻을 수 있는 권리가 있습니다. 그렇게 통역사와 얘기하기 위해서는 877-475-4799 로 전화하십시오.

French: Si vous, ou quelqu'un que vous êtes en train d'aider, a des questions à propos de Blue Cross Blue Shield of Arizona, vous avez le droit d'obtenir de l'aide et l'information dans votre langue à aucun coût. Pour parler à un interprète, appelez 877-475-4799.

German: Falls Sie oder jemand, dem Sie helfen, Fragen zum Blue Cross Blue Shield of Arizona haben, haben Sie das Recht, kostenlose Hilfe und Informationen in Ihrer Sprache zu erhalten. Um mit einem Dolmetscher zu sprechen, rufen Sie bitte die Nummer 877-475-4799 an.

Russian: Если у вас или лица, которому вы помогаете, имеются вопросы по поводу Blue Cross Blue Shield of Arizona, то вы имеете право на бесплатное получение помощи и информации на вашем языке. Для разговора с переводчиком позвоните по телефону 877-475-4799.

Japanese: ご本人様、またはお客様の身の回りの方でも、Blue Cross Blue Shield of Arizona についてご質問がございましたら、ご希望の言語でサポートを受けたり、情報を入手したりすることができます。料金はかかりません。通訳とお話される場合、877-475-4799 までお電話ください。

Farsi:
اگر شما، یا کسی که شما به او کمک میکنید ، سوال در مورد Blue Cross Blue Shield of Arizona ، داشته باشید حق این را دارید که کمک و
اطلاعات به زبان خود را به طور رایگان دریافت نمایید 877-475-4799
[تماس حاصل نمایید.

Assyrian:
[illegible] Blue Cross Blue Shield of Arizona [illegible]
[illegible] 877-475-4799.

Serbo-Croatian: Ukoliko Vi ili neko kome Vi pomažete ima pitanje o Blue Cross Blue Shield of Arizona, imate pravo da besplatno dobijete pomoć i informacije na Vašem jeziku. Da biste razgovarali sa prevodiocem, nazovite 877-475-4799.

Thai: หากคณ หรอคนทคณกาลงชวยเหลอมคาถามเกยวกบ Blue Cross Blue Shield of Arizona
คณมสทธทจะไดรบความชวยเหลอและขอมลในภาษา ของคณไดโดยไมมคาใชจาย พดคยกบลาม โทร 877-475-4799