MEDICAL POLICY

Medical Policy Title	**Amniotic Membrane Grafting/Transplantation (AMG/AMT) for Ophthalmologic Conditions**
Policy Number	**9.01.20**
Current Effective Date	**January 1, 2027**
Next Review Date	**August 2027**

Our medical policies are guides to evaluate technologies or services for medical necessity. Criteria are established through the assessment of evidence based, peer-reviewed scientific literature, and national professional guidelines. Federal and state law(s), regulatory mandates and the member's subscriber contract language are considered first in the determination of a covered service. (Link to Product Disclaimer)

POLICY STATEMENT(S)

I. Human amniotic membrane grafts with or without suture may be considered **medically necessary** when **ALL** the following are met:

A. Amniotic membrane product must be cleared or registered with the U.S. Food and Drug Administration (FDA) as a tissue product for application on the eye;

B. The use must be consistent with the FDA labeling; and

C. Used to treat **ANY** of the following ophthalmic indications:

1. Acute ocular surface injury (e.g., chemical, thermal or radiation injuries/burn);
2. Band keratopathy refractory to standard therapy (e.g., surgery, topical medications, bandage contact lens, or patching);
3. Bullous keratopathy with an epithelial defect;
4. Conjunctival defects refractory to medical or surgical treatment;
5. Corneal or scleral melting/thinning;
6. Corneal perforation/trauma when there is insufficient healthy tissue;
7. Corneal ulcer after adequate infection control for the purpose of healing the persistent epithelial defect;
8. Limbal stem cell deficiency;
9. Neurotrophic keratitis with ocular surface damage refractory to conservative therapy (e.g., patching, therapeutic contract lenses, and topical medications;
10. Persistent corneal epithelial defect (PED) refractory to conservative therapy;
11. Pterygium;
12. Recurrent corneal erosion refractory to standard therapy (e.g., bandage contact lens, patching, and topical medications);
13. Severe dry eye (Dry Eye Workshop Score [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);

14. Stevens-Johnson syndrome/Erythema multiforme.

II. Human amniotic membrane grafting is considered **not medically necessary** for the treatment of mild or moderate dry eye syndrome that does not meet the above criteria.

III. Amniotic membrane grafting is considered **investigational** for all other indications.

RELATED POLICIES

Corporate Medical Policy

7.01.35 Bioengineered Tissue Products for Wound Treatment and Surgical Interventions

11.01.03 Experimental or Investigational Services

POLICY GUIDELINE(S)

I. If an unspecified diagnosis code is being used, the supporting documentation must clearly describe in detail the indication the membrane is being used to treat.

II. Dry Eye Severity Grading (Dry Eye Workshop Score [DEWS])

Dry Eye Severity Level	1	2	3	4
Discomfort, Severity & Frequency	Mild and/or episodic occurs under environmental stress	Moderate episodic or chronic, stress or no stress	Severe Frequent or constant without stress	Severe and/or disabling and constant
Visual Symptoms	None or Episodic Mild Fatigue	Annoying and/or activity limiting Episodic	Annoying, chronic and/or constant limiting activity	Constant and/or possibly disabling
Conjunctival Injection	None to mild	None to mild	+/-	+/++
Conjunctival staining	None to mild	Variable	Moderate to marked	Marked
Corneal staining (severity/location)	None to mild	Variable	Marked central	Severe punctate erosions

Corneal/Tear signs	None to mild	Mild debris, decrease in meniscus	Filamentary keratitis, mucus clumping, increase in tear debris	Filamentary keratitis, mucus clumping, increase in tear debris
Lid/Meibomian glands	MGD variably present	MGD variably present	Frequent	Trichiasis, keratinization, symblepharon
TFBUT (sec)	Variable	≤10	≤5	Immediate
Schirmer score (mm/5 min)	Variable	≤10	≤5	≤2

III. Dry Eye Disease Management Algorithm (American Academy of Ophthalmology, AAO 2024)

A. Step 1

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

B. Step 2, if the above options are inadequate consider:

1. Non-preserved ocular lubricants to minimize preservative-induced toxicity.
2. Tea tree oil treatment for Demodex (if present).
3. Tear conservation.
4. Punctal occlusion.
5. Moisture chamber spectacles/goggles.
6. Overnight treatments (such as ointment or moisture chamber devices).
7. In-office, physical heating and expression of the meibomian glands.
8. In-office intense pulsed light therapy for meibomian gland dysfunction.

9. Prescription drugs to manage dry eye disease.
10. Topical antibiotic or antibiotic/steroid combination applied to the lid margins for anterior blepharitis (if present).
11. Topical corticosteroid (limited-duration).
12. Topical secretagogues.
13. Topical non-glucocorticoid immunomodulatory drugs (such as cyclosporine).
14. Topical lymphocyte function-associated antigen-1 (LFA-1) antagonist drugs (such as lifitegrast).
15. Oral macrolide or tetracycline antibiotics.

C. Step 3, if the above options are inadequate consider:
1. Oral secretagogues.
2. Autologous/allogeneic serum eye drops.
3. Therapeutic contact lens options.
4. Soft bandage lenses.
5. Rigid scleral lenses.

D. Step 4, if the above options are inadequate consider:
1. Topical corticosteroid for longer duration.
2. Amniotic membrane grafts.
3. Surgical punctal occlusion.
4. Other surgical approaches (eg, tarsorrhaphy, salivary gland transplantation).

DESCRIPTION

Human amniotic membrane is derived from the innermost layer of the placenta. It consists of a collagen-rich thick basement membrane and an avascular stroma and is used to reconstruct damaged ocular surfaces and promote wound healing. Its clinical benefits are attributed to anti-inflammatory, anti-fibrotic, anti-vascularization, and anti-scarring properties, and also to its ability to enhance epithelial healing.

Amnion can be processed in several ways. Heat or air-dried amniotic membrane loses some of its biologic properties and is not ideal for ocular surface rehabilitation. Lyophilized (freeze dried) tissue induces minimal change in its properties, however a cryopreserving method allows for greater retention of the membrane's structural, physiological, and biochemical properties responsible for its dramatic healing and easier handling intraoperatively.

There are multiple products available for amniotic membrane graft or transplantation (AMG or AMT) (e.g., Ambio2, Ambio5, AmbioDisk, AmnioGraft, Prokera Classic, Prokera Clear, Prokera Plus, Prokera

Slim).

SUPPORTIVE LITERATURE

Sridhar and Tripathy (2023) published a review of amniotic membrane grafting (AMG). The uses of AMG in ophthalmology include:

"1) Corneal diseases:

- Chemical injuries: Acute chemical injuries with a corneal epithelial defect and as a basement membrane for graft /SLET (simple limbal epithelial transplant) in acute chemical burns or LSCD (limbal stem cell deficiency)
- Stevens-Johnson syndrome (SJS)
- Bullous keratopathy
    - Aphakic/pseudophakic bullous keratopathy for pain relief with or without anterior stromal puncture
    - Epithelial defects: persistent epithelial defects, neurotrophic ulcers, recurrent corneal erosions, non-healing ulcers
- Small perforations and thinning: multi-layered AMG for tectonic purposes
- After superficial keratectomy for salzmann nodular degeneration, climatic droplet keratopathy, or superficial corneal scars

2) Conjunctiva

- Chemical and thermal injuries to help the healing of epithelial defect in acute burns or for surface reconstruction in chronic cases
- After trabeculectomy to repair leaking cystic bleb with bleb-thinning using subconjunctival AMG draping with the advancement of the conjunctiva
- Surface healing in acute SJS
- After pterygium excision to cover the bare sclera
- After OSSN (ocular surface squamous neoplasia) excision to cover the bare sclera
- Fornix and eyelid margin reconstruction
- Symblepheron release

3) Socket reconstruction

4) Cultivation of limbal stem cells

- In vivo as SLET
- In vitro as CLAT (conjunctival limbal autograft transplantation) or COMET (cultured oral mucosal epithelial transplant)

5) Retinal disorders

- To aid in the closure of recurrent macular holes, post-traumatic chronic macular holes, and recurrent macular holes in pathological myopia
- To promote the repair of retinal breaks".

Acute Ocular Surface Injury

A prospective, randomized, controlled trial (RCT) of 100 patients with chemical or thermal ocular burns was published by Tandon et al (2011). Half of the patients (n=50) had moderate ocular burns, and the remainder (n=50) had severe ocular burns. Both groups were individually randomized into control group (n=25) and study group (n=25). All but 8 of the patients had alkali or acid burns. The eyes in the study group underwent amniotic membrane transplantation (AMT) plus medical therapy while the control group had medical therapy alone. Epithelial healing, which was the primary outcome, was significantly improved in the group treated with AMT, but there was no significant difference between the 2 groups for final visual outcome, symblepharon formation, corneal clarity or vascularization. The authors concluded that AMT in eyes with acute ocular burns promotes faster healing of epithelial defects in patients with moderate grade burns.

A prospective, RCT by Tamhane et al (2005) evaluated AMT in acute ocular burns. Thirty-seven patients, 7 of whom had bilateral involvement (total, 44 eyes), participated in the trial. Twenty eyes were included in group A (AMT plus medical therapy), and 24 eyes were included in group B (controls, medical therapy only). Subjective ocular discomfort scores and size of epithelial defect were reduced significantly in eyes with moderate burns in the AMT group compared with controls, but there was no difference between the 2 groups in eyes with severe burns. The authors concluded that AMT in eyes with acute ocular burns has advantages in terms of reduction of pain and promotion of early epithelialization in patients with moderate grade burns, but not so in severe burns.

Westekemper et al (2017) published a multicenter, retrospective cohort study which analyzed the outcomes of patients receiving AMT after ocular chemical burn. Seventy-two yes from 54 patients were included in the cohort that were treated between 1998 and 2008 at participating centers. In 37 eyes (51.4%), AMT was applied within the first 6 days after injury. Mean follow-up time was 36.4 months (median 18.5; 1.3-117.3 months). Overall, 29 eyes (40.3%) achieved a best-corrected visual acuity of LogMAR 0.2 (0.63 decimal) or better at final visit. Complete 360° limbal stem cell deficiency (LSCD) occurred in 33 eyes (45.8%), while partial LSCD occurred in 21 eyes (29.2%). The authors concluded that AMT is an effective treatment in the management of acute ocular chemical burns with potential to improve vision.

Band Keratopathy Refractory to Standard Therapy

Anderson et al (2001) published a prospective, consecutive, uncontrolled case series that aimed to determine the safety and efficacy of AMT to restore corneal epithelium and reduce pain after surgical removal of band keratopathy. They included 15 patients (16 eyes) from two centers that underwent AMT as a graft after surgical removal of calcific deposits with or without the use of thylenediaminetetraacetic acid, with a mean follow up of 14.6 months. Pain from ocular surface instability was the presenting complaint in 14 of 15 (93.3%) patients and resolved in all cases after

the procedure even for those who experienced a recurrence of the calcific deposit. Fifteen of 16 eyes (93.7%) achieved epithelialization with a mean time to epithelial healing of 15.2 days. The only eye that failed to heal was subsequently diagnosed with total limbal stem cell deficiency. Visual acuity improved in five of nine (44%) sighted eyes and remained unchanged in four of nine (56%). No patient experienced any major surgical or medical complication after the procedure. The authors concluded that AMT is a safe and effective method to restore corneal epithelium after band keratopathy surgery.

Bullous Keratopathy with an Epithelial Defect

Paris FDS et al (2013) published a prospective, RCT that compared AMT with anterior stromal puncture (ASP) for the management of pain in patients with bullous keratopathy. Forty patients with pain from bullous keratopathy who were either waiting for a corneal transplant or had no potential for sight in the affected eye were randomized to the 2 treatments. (AMT and ASP) Symptoms had been present for approximately 2 years. AMT resulted in significantly more regular epithelial surface at 180 days follow-up, but there was no statistical difference between the treatments related to the presence of bullae or the severity or duration of pain. The authors concluded that AMT is similar to ASP in the relief of pain in symptomatic bullous keratopathy.

Georgiadis et al (2008) published a prospective, non-comparative interventional case series study to report the results of cryopreserved AMT for the management of bullous keratopathy. Consecutive cases with symptomatic bullous keratopathy for more than 12 months not amenable to conservative treatment were managed with amniotic membrane transplantation. They were recruited over a 5-year period (September 1999 to November 2004) in one referral center. Only one eye of each patient (the worse affected eye in bilateral cases) was operated with AMT being used as a patch. Eighty-one eyes completed the study with a mean follow up of 21 months. Seventy-one (87.6%) eyes became asymptomatic with healed epithelium, seven required repeated amniotic transplantation and three underwent penetrating keratoplasty. Visual acuity improved in 64 (79%) patients and remained unchanged in 14. No complications were recorded. This study is limited by a lack of a control arm however the authors concluded that AMT is efficient and safe treatment for bullous keratopathy, alleviating pain, promoting corneal epithelialization, and reducing conjunctival inflammation.

Stefaniu GI et al (2014) published a prospective, single-center, clinical study of AMT efficacy to improve symptoms of bullous keratopathy. They include 42 patients diagnosed with bullous keratopathy and operated between January 2009 and November 2013 with follow up mean of 22 months. In 37 cases, the symptoms improved; in 8 cases the minimum symptoms persisted and in 29 cases the symptoms completely disappeared. In 5 cases, there were no significant improvements, symptoms reappeared briefly after membrane resorption. Of the cases with unfavorable evolution, 11 out of 13 (84%) also presented secondary glaucoma. The authors concluded that AMT was efficient in improving bullous keratopathy symptoms.

Conjunctival Defects Refractory to Medical or Surgical Treatment

Sethi et al (2016) published a retrospective review of AMT for the repair of leaking blebs following mitomycin C (MMC) trabeculectomy. Seventeen eyes of 16 patients presenting with leaky cystic blebs

after undergoing trabeculectomy with MMC or combined cataract phacoemulsification and trabeculectomy with MMC were included. All patients were treated with amniotic membrane graft over the leaking area with conjunctival advancement without excision of the cystic bleb and had a minimum of 1-year follow-up. Success was defined as a final intraocular pressure (IOP) ≥ 6 and ≤ 21 mm Hg without glaucoma medications. Failure was defined as any patient with persistent bleb leak requiring additional procedures and/or the presence of hypotony (IOP<6 mm Hg ± clinical evidence of hypotony maculopathy). Mean follow-up time was 21.4 ± 7.3 months. All eyes had complete resolution of the bleb leak at the last follow up. Total success rate was 15/17 patients (88%). Eleven eyes (64.7%) met criteria for complete success. Two eyes (11.8%) met criteria for failure, as they presented with a pinpoint limbal leak requiring a suture at the slit lamp in the postoperative period. Mean IOP increased from 5.7 ± 2.8 mm Hg preoperatively to 13.1 ± 3.4 mm Hg at most recent follow-up while visual acuity improved from preop to most recent follow-up as well. The authors concluded the study showed amniotic membrane bleb draping with conjunctival advancement successfully restored bleb function, while facilitating fast resolution and stabilization of IOP and visual acuity.

Corneal or Scleral Melting/Thinning

Oh and Kim (2003) published a prospective, case series which evaluated the use of preserved scleral graft with amniotic membrane transplantation (AMT) for the surgical repair of scleromalacia. Eight eyes (8 patients) were grafted with a glycerin-preserved sclera onto the areas of scleral thinning with impending perforation and then covered them with an amniotic membrane with a thick basement membrane instead of a conjunctival flap. All patients experienced loss of ocular pain and inflammation, rapid reepithelialization of the ocular surface, and marked improvement in visual acuity. All of the scleral grafts remained intact, and no recurrence of scleromalacia was observed. The authors report preserved scleral graft with AMT was simple, fast, and effective and particularly advantageous when a large scleral defect or conjunctival scarring was present.

Rosetta and Gupta (2026) published a single-center, non-randomized, controlled, retrospective, comparative study which assessed whether application of cryopreserved amniotic membrane (AM) improves recovery after collagen cross-linking (CXL) using the Dresden protocol in patients with progressive keratoconus. They included consecutive patients with progressive keratoconus who underwent epi-off CXL followed by bandage contact lens (BCL) or cryopreserved AM (Prokera Slim). Patients were assessed preoperatively and at 1 week, 1 month, 3 months, and 6 months postoperatively. Outcomes included best-corrected visual acuity (BCVA), maximum keratometry (Kmax), complete re-epithelialization, and complications. A total of 108 eyes from 71 patients underwent CXL performed by a single surgeon and were included in the study analysis. Of these, 62 eyes of 46 patients (31 males, 15 females) received AM after CXL, and 46 eyes of 39 patients (24 males, 15 females) received only BCL after CXL. At 6 months follow up, a significantly greater proportion of eyes in the AM group returned to baseline BCVA versus the BCL group (85.7% vs 64.9%, $p < 0.05$). BCVA logMAR was significantly better in the AM treatment group compared to the BCL group at 6-months (0.19 ± 0.21 vs 0.31 ± 0.28, respectively; $p=0.046$). The change in Kmax values was comparable between the groups at all time points. The proportion of eyes with a healed epithelial defect at 1 week postoperatively was comparable between the groups (69.6% BCL vs

66.1% AM, p = 0.71). There were three complications (one each of infiltrative keratitis, infectious keratitis, and persistent epithelial defect) in the BCL group and none in the treatment group (p = 0.07). This study is limited by its retrospective design and non-randomization, and short follow up time of 6 months. The authors concluded that the use of AM after epi-off CXL resulted in no post-op complications and improved BCVA at 6 month follow up compared to BCL.

Corneal Perforation / Trauma When There is Insufficient Healthy Tissue

Mancini et al (2026) published a prospective observational study which included 50 eyes (50 patients) with autoimmune or inflammatory ocular surface disease presenting with corneal perforations ≤3 mm. Sutureless AMT was applied, and complete anatomical closure was achieved in all cases (100%), with a mean healing time of 14.2 days. Corneal thinnest point increased significantly from 215 ± 38 µm at baseline to 402 ± 39 µm at 6 months (p = 0.000031). No patients developed intraocular complications or required additional surgical interventions. The authors concluded that AMT was tolerated well, safe, and effective for managing small-diameter corneal perforations (≤3 mm) in patients with severe ocular surface disease.

Solomon et al (2002) published a large retrospective interventional case series to describe the clinical outcome of AMT for nontraumatic corneal perforations, descemetoceles, and deep ulcers. Thirty-four eyes of 33 consecutive patients operated on for nontraumatic corneal perforations or descemetoceles at four academic departments of ophthalmology. Three or four layers of amniotic membrane (AM) were applied over the ulcer bed and anchored with 10-0 nylon interrupted or running sutures. A large AM piece was used as a patch to cover the entire corneal surface. Associated autoimmune disorders included rheumatoid arthritis (n = 6), Stevens-Johnson syndrome (n = 3), ocular cicatricial pemphigoid (n = 2), systemic lupus erythematosus (n = 1), and one eye with Mooren's ulcer, as well as neurotrophic, or exposure keratopathy (n = 10), postinfectious nonhealing ulcers (n = 6), and post-surgery (n = 5). The mean follow-up period was 8.1 months. A successful result was observed in 28 of 34 eyes (82.3%). Of the successful cases, 23 eyes needed one AMT procedure, whereas 5 eyes needed two procedures to achieve a successful result. In five eyes, a subsequent definitive surgical procedure such as penetrating keratoplasty or lid surgery was needed. Failure was observed in six eyes with rheumatoid arthritis, neurotrophic keratopathy, or graft melting. The authors found in this early study that AMT is an effective method for managing nontraumatic corneal perforations and descemetoceles. It can serve as either permanent therapy or as a temporizing measure until the inflammation has subsided and a definitive reconstructive procedure can be performed.

Corneal Ulcer After Adequate Infection Control for The Purpose of Healing the Persistent Epithelial Defect

Liu et al (2019) conducted a meta-analysis and systematic review of 18 studies (390 eyes, 385 patients) to evaluate the corneal epithelium healing rate (CEHR) and vision improvement rate (VIR) after AMT in the treatment of corneal ulceration. The authors analyzed the differences in the CEHR and VIR between the 2 groups of infective and noninfective corneal ulcerations. There were 3 subgroups: single-layered inlay, multilayered inlay, and sandwich (SAN). All but one of the studies was conducted outside of the U.S. There was one RCT with 30 patients, the remainder of the studies were prospective or retrospective case series. Corneal healing was obtained in 97% (95% CI, 0.94 to

0.99; p=.089) of patients evaluated. In the 12 studies (222 eyes) that reported on vision, the vision improvement rate was improved in 113 eyes (53%; 95% CI, 0.42 to 0.65; p<.001). There were no significant differences in either the CEHR or the VIR between the 2 groups of infective and noninfective corneal ulcerations. Among the 3 subgroups of single-layered inlay, multilayered inlay, and SAN, the differences in both CEHR and VIR were statistically significant. The authors concluded that this meta-analysis also concluded that AMT was effective in the treatment of corneal ulceration.

Yin et al (2020) compared epithelialization and visual outcomes of 24 patients (24 eyes) with corneal infectious ulcers and visual acuity of less than 20/200 who were treated with (n=11) or without (n=13) self-retained amniotic membrane. Utilization of amniotic membrane was initiated in their institution in 2018, allowing a retrospective comparison of the 2 treatment groups. Complete epithelialization occurred more rapidly (3.56 ± 1.78 weeks vs. 5.87 ± 2.20 weeks; p=.01) and was reached in significantly more patients (72.7% vs. 23.1%; p=.04). The group treated with amniotic membrane plus the standard therapy had more patients with clinically significant (>3 lines) improvement in visual acuity (81.8% vs. 38.4%; p=.047) and greater total improvement in visual acuity (log MAR, 0.7 ± 0.6 vs. 1.6 ± 0.9; p=.016) compared to the control group. The authors concluded that in-office sutureless AMT is an effective adjuvant therapy in treating sight-threatening infectious corneal ulcers by promoting faster corneal epithelialization and overall better recovery of the VA.

Limbal Stem Cell Deficiency

Gomes et al (2003) published a prospective interventional cohort study that evaluated AMT outcomes for ocular surface reconstruction in chemical burn with limbal stem cell deficiency. Twenty eyes of 20 consecutive patients with limbal stem cell deficiency secondary to ocular chemical injury underwent AMT with or without adjunctive limbal transplantation using limbal tissue from either the healthy contralateral eye (CLAU) or a living related donor (lr-CLAL). They were divided into 2 groups according to the severity of limbal deficiency: group 1 (partial limbal deficiency [PLD]), composed of four eyes, which received AMT alone, and group 2 (total limbal deficiency [TLD]), composed of 16 eyes, which received AMT and conjunctival and limbal stem cell transplantation. With a mean follow-up time of 19 months (range, 8-27 months), satisfactory ocular surface reconstruction was obtained in 15 eyes (75%), with reduced inflammation and vascularization of the ocular surface and a mean epithelialization time of 3.3 weeks. Success was observed in all cases of partial limbal stem cell deficiency (PLD) and in 68.75% (11 eyes) of cases of total limbal stem cell deficiency (TLD). Surgical failure was observed in five severe cases (31.25%). A significant visual improvement was observed in all cases after surgery, except for 2 eyes that maintained preoperative visual acuity. The authors concluded that AMT was efficient adjunct for ocular surface reconstruction in chemical burns with PLD and when performed in conjunction with limbal stem cell transplantation, AMT is effective in most cases of TLD.

Kheirkhah et al (2008) reported on the use of AMT in 11 eyes of 9 patients who had limbal stem cell deficiency in a retrospective noncomparative interventional case series. Patients underwent superficial keratectomy to remove the conjunctivalized pannus followed by AMT using fibrin glue. An additional ProKera patch was used in 7 patients. The surgery was repeated in three eyes for residual pannus.

During a mean follow-up of 14.2 months, all eyes maintained a smooth and stable corneal epithelial surface without recurrent erosion or persistent epithelial defect and showed less stromal cloudiness and vascularization. Best-corrected visual acuity improved in nine eyes (81.8%). Corneal epithelialization proceeded by epithelial growth over AMT (n = 4), accompanied by dissolution of AMT (n = 4) or a combination of both (n = 3). No complication was noted regarding initial or repeated uses of fibrin glue.

Pachigolla et al (2009) reported a series of 20 patients who received a ProKera implant for ocular surface disorders; 6 of the patients had limbal stem cell deficiency with a history of chemical burn. Following treatment with ProKera, 3 of the 6 patients had a smooth corneal surface and improved vision to 20/40. The other 3 patients had final visual acuity of 20/400, counting fingers, or light perception.

Neurotrophic Keratitis with Ocular Surface Damage Refractory to Conservative Therapy

Khokhar et al (2005) reported on an RCT of 30 patients (30 eyes) with refractory neurotrophic corneal ulcers who were randomized to AMT transplantation (n=15) or conventional treatment with tarsorrhaphy (n=11) or bandage contact lens (n=4). At the 3-month follow-up, 11 (73%) of 15 patients in the AMT group showed complete epithelialization compared with 10 (67%) of 15 patients in the conventional group. The median time for complete epithelialization was 21 days in both groups. Both groups showed an improvement in the best-corrected visual acuity. The authors concluded this study showed both AMT and conventional management are effective treatment.

Suri et al (2013) conducted a retrospective chart review of patients who had ProKera (Bio-Tissue, Inc.) from June 2008 and May 2012 at 3 ophthalmology practices to evaluate the indications and outcomes of sutureless AMT in the management of ocular surface disorders. There were 35 eyes of 33 patients included of which neurotrophic keratopathy was reported in 11 eyes (31.4%) and complete or partial success was seen in a total of 64% of patients with neurotrophic keratopathy. The mean duration of treatment prior to ProKera insertion was 51 days. Five of the 11 patients (45.5%) were considered to have had a successful outcome. Two eyes (2/11, 18.2%) showed partial improvement. The authors concluded that favorable outcomes in treating neurotrophic keratopathy were seen in nearly two thirds of eyes.

Persistent Corneal Epithelial Defect (PED) Refractory to Conservative Therapy

Sell et al (2023) published results of a nonrandomized, large, multicenter, retrospective, interventional comparative clinical study comparing cryopreserved suture less amniotic membrane (C-SAM) and dehydrated SAM (D-SAM) outpatient treatment outcomes for persistent epithelial defects (PED). The inclusion criteria were as follows: (1) PEDs treated (2) outpatient with (3) either C-SAM or D-SAM. PEDs were defined as epithelial defects present for ≥7 days after failing prior conservative therapy. The primary outcome measure was the resolution or improvement of a PED. The secondary outcomes included analysis of treatment failures and identification of adverse events. A total of 220 PEDs from 204 eyes (197 patients) treated with either C-SAM or D-SAM met the inclusion criteria. A total of 100 PEDs (45.5%) resolved after single amniotic membrane administration, 46.5% (59 of 127) in the C-SAM group and 44.1% (41 of 93) in the D-SAM group

(*P* = .727). Forty-nine PEDs neither improved nor resolved without a significant difference between the C-SAM (21.3%) and D-SAM groups (23.7%, *P* = .673). The most common adverse events in the cryopreserved group were pain/ring dysesthesia (n = 10, 7.9%), perforation (n = 3, 2.4%), lost ring (n = 2, 1.6%), and worsened PED from ring trauma (n = 2, 1.6%). In the dehydrated group, infectious or sterile infiltrate (n = 9, 9.7%), scrolled or displaced amnion (n = 6, 6.5%), and pain (n = 4, 4.3%) were the most common adverse effects. There was no statistically significant difference for PED resolution, PED improvement, PEDs that did not resolve/improve, or those requiring surgery between the 2 groups for initial SAM. Limitations include a non-randomized, retrospective design. The authors concluded that the data demonstrated that both C-SAMs and D-SAMs were equally effective in the treatment of PEDs failing conservative medical treatment. They noted that suture less AMT was safe and well tolerated.

Letko et al (2001) published an influential early prospective interventional study that helped determine the effect of AMT on PED and to compare the efficacy between inlay and overlay techniques. They included 30 patients (30 eyes) for whom all previous therapies had failed, including bandage contact lenses and tarsorrhaphy. The AMT was placed on the surface of the cornea in overlay (group A) or inlay (group B). The PED healed after the first AMT in 21 eyes (70%) within an average of 25.5 days after surgery and recurred in 6 eyes (29%). Among the 22 eyes treated with an overlay AMT (group A), the PED healed after the first AMT in 14 eyes (64%) within an average of 24.5 days and recurred in 4 eyes (29%). Among the 8 eyes treated with an inlay AMT (group B), the PED healed within an average of 27.4 days after AMT, which did not statistically significantly differ from group A (P = .72). The PED healed after the first AMT in 7 eyes (88%) and recurred in 2 (29%) of 7 eyes. Limitations of this study include a lack of control group and small sample sizes. The authors concluded that the study showed that AMT is beneficial in the treatment of PED when all other conventional management has failed. They did not find any difference between overlay and inlay techniques in terms of healing time and recurrence rate.

Lee and Tseng (1997) published an early experience from a single expert center, prospective, interventional case series which aimed to determine if AMT could be used as an alternative substrate for treating PED with sterile ulceration. AMT was performed in 11 eyes of 11 consecutive patients with corneal ulcers of different causes that had persisted for a mean ± SD of 17.5 ± 13.9 weeks. Ten patients healed in 3.9 ± 2.3 weeks (P < .01) without recurrence for 9.0 ±5.9 months. One patient failed to heal because of preexisting corneal perforation pursuant to severe rheumatoid arthritis. Limitations of the study include a small sample size and no control group. The authors showed that AMT was a viable option as an alternative method for treating PED refractory to conventional treatment and before considering treatment by conjunctival flaps or tarsorrhaphy.

Pterygium

A 2016 Cochrane review and meta-analysis of 20 RCTs (total N=1866 patients) assessed the safety and effectiveness of conjunctival autograft (with or without adjunctive therapy) compared with amniotic membrane graft (with or without adjunctive therapy) for pterygium (Clearfield 2016). The authors found that with pterygium excision, conjunctival autograft is associated with a lower risk of recurrence at six months after surgery than amniotic membrane transplant. Analysis of repeat

surgery, vision-related quality of life, and direct and indirect costs of surgery was unable to be completed due to an insufficient number of studies reporting these outcomes. Comparison of these two procedures in such outcome measures bears further investigation.

Kaufman et al (2013) on behalf of The American Academy of Ophthalmology published a technology assessment on options and adjuvants for pterygium surgery. Reviewers identified 4 RCTs comparing conjunctival or limbal autograft procedure with amniotic membrane graft, finding that conjunctival or limbal autograft was more effective than AMT graft in reducing the rate of pterygium recurrence though use of adjuvants was more beneficial than bare sclera excision of pterygium.

Chang et al (2024) conducted a meta-analysis to evaluate the effects of different pterygium surgery techniques on ocular surface. A total of 33 articles were analyzed for ocular surface disease index, tear film break-up time, and score of corneal fluorescein staining. All parameters in AMT showed better improvement in early stage and they showed non-inferior improvements in the long term compared with conjunctival autograft, while pterygium excision showed the worst ocular surface.

Recurrent Corneal Erosion Refractory to Standard Therapy

Huang et al (2013) conducted a retrospective study to evaluate the efficacy of AMT in treating recurrent corneal erosion (RCE). Eleven eyes of 9 consecutive patients with RCE received epithelial debridement and placement of ProKera (Bio-Tissue, Inc, Miami, Florida, USA). Complete epithelialization was noted in all eyes in 4 to 7 days. During the follow up of 13.7 ± 2.2 months, 10 eyes became symptom-free, one eye recurred and required repeated treatment. Afterwards, all eyes were asymptomatic and regained a smooth and stable corneal epithelium. Best corrected visual acuity (BCVA) improved in 10 eyes from 20/60 to 20/20 and 1 eye remained 20/20 as before the treatment. The authors concluded this review supports debridement and Prokera placement in the office to treat RCE.

Dry Eye Syndrome

Travé-Huarte and Wolffsohn (2024) published a manufacturer (NuVision Biotherapies Ltd., UK) sponsored RCT investigating long-term efficacy of dehydrated amniotic membrane (dAM, Omnigen) delivered via a specialized bandage contact lens (sBCL, OmniLenz) for managing moderate-to-severe dry eye disease (DED). Participants (n=70) with moderate-to-severe DED, were randomized to receive either a 1-week bilateral treatment of either dAM applied under a sBCL or sBCL alone. Both groups demonstrated improved ocular surface disease index scores. At 6 months, there was no statistical difference between treatment groups.

McDonald et al (2018) conducted the DRy Eye Amniotic Membrane (DREAM) study which was a retrospective study of 84 patients (97 eyes) with severe dry eye despite maximal medical therapy who were treated with Prokera self-retained amniotic membrane. A majority of patients (86%) had superficial punctate keratitis. Other patients had filamentary keratitis (13%), exposure keratitis (19%), neurotrophic keratitis (2%), and corneal epithelial defect (7%). Treatment with Prokera for a mean of 5.4 days (range, 2 to 11) resulted in an improved ocular surface and reduction in the DEWS score from 3.25 at baseline to 1.44 at 1 week, 1.45 at 1 month, and 1.47 at 3 months (p=.001). Ten percent of eyes required repeated treatment. There was no significant difference in the number of

topical medications following Prokera treatment. Limitations of the study include author employment by Bio-Tissue Inc., distributors of Prokera, short term follow up, no control group, and retrospective subjective patient reported data.

Stevens-Johnson Syndrome

One prospective, RCT from India by Sharma et al (2016) assigned 25 patients (50 eyes) with acute ocular Stevens-Johnson syndrome to AMT plus medical therapy (n=25, antibiotics, steroids, or lubricants) or medical therapy alone (n=25). The AMT was prepared locally and applied with fibrin glue rather than sutures. Application of AMT in the early stages of Stevens-Johnson syndrome resulted in improved visual acuity (p=.042), better tear breakup time (p=.015), improved Schirmer test results (p<.001), and less conjunctival congestion (p=.03). In the AMT group at 180 days, there were no cases of corneal haze, limbal stem cell deficiency, symblepharon, ankyloblepharon, or lid-related complications. These outcomes are dramatically better than those in the medical therapy alone group, which had 11 (44%) cases with corneal haze (p=.001), 6 (24%) cases of corneal vascularization and conjunctivalization (p=.03), and 6 (24%) cases of trichiasis and metaplastic lashes. The authors concluded that this RCT showed AMT is a useful adjunct to conventional medical therapy in maintaining BCVA and a stable ocular surface in cases of acute ocular SJS. Furthermore, the adjunctive use of AMT also helps to prevent intermediate-term ocular cicatricial sequelae.

Shanbhag et al (2020) reported long term outcomes of AMT and self-retained Prokera amniotic membrane in Steven's Johnson syndrome /toxic epidermal necrolysis. Data of 55 eyes of 29 patients were analyzed. All 55 eyes received the first amniotic membrane at a median interval of 5 days after onset of skin rash. Fifty-six percent of eyes (31/55) received AMT while 44% (24/55) received Prokera. Forty percent of eyes (22/55) required a repeat AMT or Prokera placement. Median follow-up after initial AM was 2.5 years. At last follow-up, the best-corrected visual acuity was ≥ 20/40 in 87% of eyes (48/55). The most common complications in the chronic phase were meibomian gland disease and dry eye, seen in 78% of eyes (43/55) and 58% of eyes (32/55) respectively. The authors concluded that this retrospective review of patient medical records and long-term results show early use of amniotic membrane to treat Stevens Johnson syndrome/toxic epidermal necrolysis is effective in mitigating severe vision loss though eyelid related complications and dry eye may remain a common problem.

Rashad et al (2024) published a retrospective cohort study which compared a glued/sutureless technique for AMT with the traditional sutured technique in patients with Stevens Johnson syndrome/toxic epidermal necrolysis. They included 12 years of data from a hospital network of patients who received AMT for acute Stevens Johnson syndrome/toxic epidermal necrolysis. A total of 23 patients (45 eyes) were included: 14 patients (27 eyes) in the AMT suture group and 9 patients (18 eyes) in the AMT glue group. There was no difference between the two groups in BCVA at the most recent visit (p=0.5112) or development of a severe ocular complication (p=1.000). The glue method was shorter in duration than the suture method (p<0.001). Random effects model additionally indicated that there was no difference in BCVA at most recent follow-up between patients who had received glued versus sutured AMT (p=0.1460). The authors found both techniques to be effective at stabilizing the ocular surface and mitigating chronic ocular complications.

PROFESSIONAL GUIDELINE(S)

American Academy of Ophthalmology (AAO) published a technology assessment of the efficacy of amniotic membrane grafting (AMG) for the treatment of chemical and thermal ocular surface injuries (AAO 2025). They state:

- "The available level II evidence suggests that AMG is efficacious in the management of acute ocular surface burns in hastening corneal re-epithelialization when compared with medical therapy alone for moderate burns."
- "Evidence reviewed in this assessment suggests that in mild to moderate ocular surface burns, AMG plus medical therapy yields a greater percent reduction of epithelial defect size, a faster rate of re-epithelialization, and faster resolution of epithelial defects than medical therapy alone."
- "In contrast, most eyes with severe ocular surface burns reported in the 4 level II studies did not re-epithelialize more rapidly than controls treated with medical therapy alone. These findings suggest that the addition of AMG to medical therapy in severe ocular surface burns may not reliably enhance re-epithelialization."
- "In addition, level II evidence suggests that AMG is not a sufficient adjunctive therapy to improve visual acuity outcomes in moderate to severe ocular surface burns."

AAO's Dry Eye Syndrome Preferred Practice Pattern (Amescua 2024) do not recommend amniotic membrane grafting as first line treatment for dry eye syndrome. In step 4 for staged management and treatment recommendations for dry eye syndrome AAO states if the above (steps 1-3) are inadequate consider amniotic membrane grafts. The practice pattern does not discuss AMT in any further detail.

The Tear Film and Ocular Surface Society (TFOS) DEWS III management and therapy report recommends amniotic membrane grafting for severe and refractory cases of dry eye syndrome (Jones 2025).

REGULATORY STATUS

Amniotic membrane must be cleared by, or registered with, the U.S. Food and Drug Administration (FDA) for application of the eye.

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, title 21, parts 1270 and 1271.

CODE(S)

- Codes may not be covered under all circumstances.
- Code list may not be all inclusive (AMA and CMS code updates may occur more frequently than policy updates).
- (E/I)=Experimental/Investigational

- (NMN)=Not medically necessary/appropriate

CPT Codes

Code	Description
65778	Placement of amniotic membrane on the ocular surface; without sutures
65779	Placement of amniotic membrane on the ocular surface; single layer, sutured
65780	Ocular surface reconstruction; amniotic membrane transplantation, multiple layers
65781	Ocular surface reconstruction; limbal stem cell allograft (e.g., cadaveric or living donor)
65782	Ocular surface reconstruction; limbal conjunctival autograft (includes obtaining graft)

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HCPCS Codes

Code	Description
V2790	Amniotic membrane for surgical reconstruction, per procedure
Q4334	AmnioPlast 1, per sq cm (add-on, list separately in addition to primary procedure)
Q4335	AmnioPlast 2, per sq cm (add-on, list separately in addition to primary procedure)
Q4369	AmnioPlast 3, per sq cm (add-on, list separately in addition to primary procedure)

ICD10 Codes

Code	Description
H04.121-H04.129	Dry eye syndrome (code range) *MN for severe dry eye syndrome, NMN for mild-moderate dry eye syndrome
H11.001 - H11.069	Pterygium of eye (code range)
H15.89 - H15.9	Other disorders of sclera (code range)
H16.001 - H16.079	Corneal ulcer (code range)
H16.121 - H16.129	Filamentary keratitis (code range)

Code	Description
H16.231 - H16.239	Neurotrophic keratoconjunctivitis (code range)
H18.10 - H18.13	Bullous keratopathy (code range)
H18.421 - H18.429	Band keratopathy (code range)
H18.831 - H18.839	Recurrent erosion of cornea (code range)
H18.891 - H18.899	Other specified disorders of cornea (includes limbal stem cell deficiency) (code range)
L51.0	Nonbullous erythema multiforme
L51.1	Stevens-Johnson syndrome
L51.3	Stevens-Johnson syndrome-toxic epidermal necrolysis overlap syndrome
L51.9	Erythema multiforme, unspecified
T26.00XA - T26.92XS	Burn and corrosion of cornea and conjunctival sac (code range)

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SEARCH TERMS

Not Applicable

CENTERS FOR MEDICARE AND MEDICAID SERVICES (CMS)

Amniotic membrane transplantation is not addressed in National or Regional Medicare coverage determinations or policies.

PRODUCT DISCLAIMER

- Services are contract dependent; if a product does not cover a service, medical policy criteria do not apply.
- If a commercial product (including an Essential Plan or Child Health Plus product) covers a specific service, medical policy criteria apply to the benefit.
- If a Medicaid product covers a specific service, and there are no New York State Medicaid guidelines (eMedNY) criteria, medical policy criteria apply to the benefit.
- If a Medicare product covers a specific service, and there is no national or local Medicare coverage decision for the service, medical policy criteria apply to the benefit.

POLICY HISTORY/REVISION

Committee Approval Dates	
01/01/27	
Date	**Summary of Changes**
01/01/27	• Original effective date