



CIGNA HEALTHCARE COVERAGE POSITION

**Subject Amniotic Membrane Transplant
for the Treatment of Ocular
Conditions**

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Coverage Position

CIGNA HealthCare covers amniotic membrane transplantation (AMT) as medically necessary for the treatment of ocular conditions when there is failure, contraindication, or intolerance to medical therapy (e.g., lubricants/artificial tears, topical and systemic steroids and antibiotics, eyelid taping, patches).

General Background

Disease or severe ocular injuries can compromise ocular surfaces and deplete the stem-cell population that repairs the damaged corneal epithelium, leading to pain, scarring, vascularization, and loss of sight. In addition, there are a number of conditions affecting the conjunctiva and the eyelids that can cause pain and corneal injury, as well as interfere with the normal appearance and function of the eye.

Treatment of ocular injuries includes (Lemp, 2002):

- elimination of underlying problems
- control of inflammation
- prevention of additional loss of tissue
- protection of ocular surfaces with a bandage contact lens
- possible surgery or corneal transplant

When medical therapies fail, the type of surgery (i.e., ocular surface reconstruction) indicated is dependent upon the “extent of involvement of the cornea (i.e., epithelium, basement membrane or stroma), extent of limbal ischemia, conjunctival necrosis and intact tear supply” (Chandra, et al., 2005).

Amniotic membrane (AM), the innermost layer of the fetal membrane, exhibits properties that are helpful in wound healing, particularly of ocular injuries, and has been proposed for various clinical indications for ocular reconstruction. AM consists of an endodermal layer of epithelia cells, a basement membrane and an avascular stromal matrix. The tissue is obtained by consent from planned Caesarean sections on patients who are seronegative (i.e., hepatitis B and C, syphilis and human immunodeficiency virus). The avascular matrix inhibits blood vessel growth in adjacent tissues, decreases cell death, and promotes differentiation and cellular migration to the affected areas. It exhibits anti-inflammatory properties and suppresses expression of transforming growth factor, minimizing scar tissue during the healing process. In addition, AM does not express antigens, thereby reducing the risk of an immune-mediated reaction to the transplanted tissue and decreasing the need for immunosuppressive drugs (Lemp, 2002; John, 2003; Gomes, et al., 2005; Dogru and Tsubota, 2005; Royal College of Ophthalmologists [RCO]).

AM may be applied by inlay, overlay or “filling.” Inlay involves suturing a piece of AM slightly larger than the affected area onto the cornea. The AM is placed epithelial side up to provide a new surface on which corneal epithelial cells may grow (i.e., a graft), acting as a replacement for the damaged basement membrane. Overlay involves placing AM over the entire cornea, limbus and perilimbal area. This allows the AM to function as a biological contact lens (i.e., a patch) which protects the damaged cornea. In overlay, the side up is not important. Filling is used when multiple layers of AM are needed to fill a deep cavity as seen in an ulcer (Wang, et al., 2004; Dogru and Tsubota, 2005). AMT may include the application of more than one layer of AM. The most common complications seen after surgical placement of AM are dehiscence, irritation and pain. Infection, dislodged or loose AM, hemorrhage and early disintegration have also been reported. It is not a good substance for use as a graft due to the lack of mechanical strength and resultant wound leakage (Fernandes, et al., Aug 2005; Wang, et al., 2004; RCO).

AMT has been proposed as a treatment option for numerous ocular conditions, including: (Anderson, et al., 2003; Gomes, et al., 2005):

- acute inflammatory conditions
- bullous keratopathy
- chemical and thermal injury
- conjunctival cicatrization or scar
- conjunctival surface reconstruction
- conjunctivochalasis
- corneal ulceration
- corneal perforations
- contracted socket
- entropion surgery
- glaucoma surgery/complications
- limbal stem cell deficiency (partial or total, combined with stem cell graft)
- persistent epithelial defects
- pterygium
- Stevens-Johnson Syndrome
- symblepharon lysis
- trabeculectomy bleb leakage or revision
- tumors

Optimal AMT techniques for different ocular conditions, definitive patient-selection criteria, the relative benefit of AMT compared with other surgical or transplantation options, the durability of the treatment effect, and the range and frequency of complications as reported in large patient populations have not been firmly established. (John, 2003; Letko, et al., 2001; Essex, et al., 2004; Tosi, et al., 2005).

U.S. Food and Drug Administration (FDA)

In 2001, the FDA established a registry and implemented regulations to ensure safety for the public in the use of human cells, tissues, and cellular- and tissue-based products. This regulation included the use of AM in the eye. The tissue must be obtained, processed, maintained and distributed in accordance with these regulatory guidelines (FDA, 2001). AMNIOGRAFT® (Bio-Tissue, Inc. Miami, FL) and AmbioDry2™ (OKTO Ophtho, Costa Mesa, CA) are examples of AM products which are governed under the FDA human cell and tissue regulatory guidelines. AmbioDry2 is a processed, dehydrated, sterilized AM allograft product derived from the submucosal of the placenta and includes a basement membrane and stromal matrix (OKTO Ophtho, 2006).

ProKera™ (Bio-Tissue, Inc., Miami, FL) is an example of a 510(k) Class II approved ophthalmic conformer with amniotic membrane. It is a device with AMNIOGRAFT clipped into it. The device is “intended for use in eyes in which the ocular surface cells are damaged, or underlying stroma is inflamed and scarred.” The device is placed between the eyeball and the eyelid to maintain space, and to prevent closure and adhesions. Because the device conforms snugly over the cornea and under the eyelid, sutures are not needed (Bio-Tissue, 2006; FDA, 2003).

Bullous Keratopathy

Characterized by corneal stromal edema, bullous keratopathy is a condition caused by corneal endothelial decompensation. Corneal endothelial decompensation can occur as a result of trauma, intraocular surgery, glaucoma and other diseases of endothelial dystrophy. Pain and discomfort are the most common symptoms. With good visual potential, keratoplasty is the only curative treatment. With poor visual potential, treatment modalities may include bandage contact lenses, stromal puncture, keratotomy, or conjunctival flap. It has been proposed that AMT may be a viable treatment option for patients with painful recurrent epithelial defects with poor visual potential (Chansanti and Horatanaruang, 2005).

Chansanti and Horatanaruang (2005) retrospectively evaluated 17 eyes with bullous keratopathy in patients complaining of intractable pain and discomfort. Outcomes included relief of pain, epithelial healing and visual acuity. Follow-up ranged from 1–36 months. Postoperatively, 14 eyes experienced pain relief, and 15 eyes demonstrated complete corneal epithelial healing. Visual acuity improved in three patients, remained unchanged in 12 patients and deteriorated in two patients. Three patients experienced recurrent bullous keratopathy and re-grafting, which resulted in pain relief. In comparison to conjunctival flap, the authors stated that AMT is an easier technique to perform and does not induce limbal stem cell proficiency. Chansanti and Horatanaruang noted that limitations of the study included retrospective, descriptive review, small number of cases and evaluation of symptoms subjectively; large cases of randomized controlled trials may be needed.

Chemical and Thermal Burns

Ocular burns are classified as chemical or thermal. Chemical burns may result from exposure to alkaline or acidic agents and can result in extensive and permanent damage to the eye. Thermal burns result from hot liquids, gases or molten metals. Eighty-four percent of ocular burns are chemical in nature. Depending upon the extent of the burn, damage can result in corneal conjunctivalization, vascularization, mucous deficiency, severe dry eye and fibrosis. Burns may be accompanied by limbal stem cell deficiency, which is characterized by conjunctival ingrowth, chronic inflammation and epithelial defects which can be recurrent or persistent. Corneal neovascularization, corneal scarring, symblepharon, and severe dry eye may also occur. Corneal epithelial defect is the most challenging problem, and treatment to promote rapid epithelialization is an important strategy. Other treatment goals include reducing the severity of the damage and inflammation and prevention of progressive tissue melting. Medical treatment may include the use of topical and systemic ascorbate, citrate, tetracycline and steroids. Surgical options include glued-on hard contact lens, tenoplasty, tissue adhesives and keratoplasty. AMT has been proposed as a treatment option for chemical burns (Prabhasawat, et al., 2007; Arora, et al., 2005; Ivekovic, et al., 2005).

The utility of AMT as an adjunct to medical therapy in treating acute ocular burns was evaluated in a randomized controlled clinical trial of 37 patients with 44 injured eyes (Tamhane, et al., 2005). Twenty eyes were treated with AMT, and 24 eyes, which acted as the control group, were treated with conventional medical therapy. Results were measured over an 18-month follow-up period. Subjective ocular discomfort scores were reduced significantly in eyes with moderate burns in the AMT group

compared to controls, but no difference was found between the two groups in patients with severe burns. There was a significant decrease in the size of epithelial defects by day seven in patients with moderate burns who underwent AMT compared to controls. There was no difference in this parameter between the two groups in patients with severe burns. After three months, there was no overall difference between the two groups in visual acuity, symblepharon formation, corneal vascularization, and tear function tests.

In a small case series, Arora et al. (2004) reported on 15 patients treated with AMT for chemical burns who experienced immediate postoperative pain relief. Epithelialization was seen in nine eyes within one to four weeks postoperatively. Ten eyes experienced improved visual acuity. Nine eyes developed symblepharon, and twelve eyes demonstrated limbal stem cell deficiency and superficial corneal vascularization.

Prabhasawat et al. (2007) conducted a retrospective review of 21 eyes with grade II to IV acute ocular burns treated with AMT (n=13) compared to eyes (n=8) treated with conventional therapy (i.e., soft bandage contact lens). The conventional therapy group experienced an overall 87.5% success rate, 100% in grade II and 0% in grade III (n=1) burns. No grade IV patients were placed in the conventional group. The shorter the time span between the burn and the AMT, the quicker complete epithelialization occurred. Tejwani et al. (2007) retrospectively reviewed 72 eyes of 69 patients with acute (n=24) and chronic (n=48) chemical (i.e., acid [n=18] and alkaline [n=52]) and thermal ocular burns (n=2) treated with AMT. Twenty-one chronic burns underwent a second AMT, 10 underwent a third AMT and three underwent a fourth AMT. Overall success rate for acute cases was 87.5%, 72.9% for chronic cases, 94.3% for epithelial defect healing, 88.2% for symptomatic relief, 59.7% for ocular surface reconstruction, and 55% for limbal stem cell function improvement. Success was not achieved for 4.2% of acute cases and 12.5% of chronic cases.

A small comparative study reported outcomes of ocular burns treated with AMT (n=5), stem cell transplantation (LSCT), and AMT plus LSCT. Epithelialization occurred three weeks postoperatively in the AMT group and two weeks in the LSCT group with an improvement in visual acuity experienced by all patients (Ivekovic, et al., 2005).

Contracted Socket

Contracted socket involves shrinkage or loss of conjunctiva resulting in shrinkage and fibrosis of the socket. Typically, additional tissue is needed, usually through grafting, to prepare the socket for prosthesis. Mucous membrane grafting is the preferred surgical intervention for this condition. However, other grafts (e.g., skin, dermis fat, and forearm) have been attempted. Disadvantages of these methods include the lack of availability from the donor site and foul smelling discharge with conjunctival and mucous grafts. It has been proposed that AMT may be an alternative graft procedure for this condition (Kumar, et al., 2006; Poonyathalange, et al., 2005).

In the first study of its kind, Kumar et al. (2006) reported on the outcomes of a prospective, randomized controlled trial of 20 eyes with ophthalmic contracted sockets following enucleation or evisceration. Patients were randomly assigned to either group A, treated with AMT, or group B, treated by mucous membrane grafting. Prostheses were fitted six to eight weeks postoperatively. Outcomes were measured in terms of volume, fornices' lengths, and patient satisfaction. Twelve months following surgery, the relative increase in the fornix and volume outcomes was significantly different, with group A experiencing more comfort. There was no significant difference in complications between the two groups. A well-fitted prosthesis was accomplished in eight patients in both groups. The authors concluded that AMT was "superior in terms of less contracture, less morbidity, better patient comfort and easier availability." However, it was observed that AMT was helpful in reducing only lesser degrees of fibrosis, and Kumar et al. recommended its use be restricted to mild and moderate contracted sockets.

A small retrospective study by Poonyathalange et al. (2005) analyzed 20 patients with contracted eye sockets. Traditionally, forniceal reconstruction was achieved with mucosal transplantation, which involves a limited, available amount of graft material, prolonged operative time, a donor site, and donor site pain. In this study, AMT resulted in an 80% successful prosthetic fitting rate with no serious complications. The authors stated that AMT could be a useful treatment modality in forniceal reconstruction, resulting in a high success rate, low complication rate, and no donor is needed.

Corneal Ulceration

When the surface of the cornea is injured or compromised, a corneal ulceration, or keratitis, may develop. A corneal ulcer is a nonpenetrating erosion on the outer layer of the cornea. These ulcers may develop as a result of trauma, foreign body, severe dry eye or a local infection (i.e., bacterial, fungal, *acanthamoeba* [a parasite] and herpes simplex). Presenting symptoms usually include pain, impaired vision, photophobia, excessive tearing, burning, itching and/or discharge. Treatment will be based upon the underlying cause and presenting symptoms and may include: antibiotic, antiviral, or antifungal eye drops, corticosteroids eye drops, artificial tears, lubricants, patching, and/or therapeutic lenses. In severe cases, corneal transplantation, conjunctival flap or tarsorrhaphy may be indicated (National Institutes of Health, 2006; Hick, et al., 2005; Khokhar, et al., 2005). AMT has been proposed as a treatment option for this population in an effort to avoid complications seen with other surgical interventions (e.g., tissue inflammation from glue toxicity, diminished vision, poor cosmesis, and graft failure).

Khokhar et al. (2005) conducted a randomized controlled trial of the treatment of patients with refractory neurotrophic corneal ulcers of varying etiology. Unresponsive to four weeks of medical management, patients were randomized to a group (n=15) treated with conventional management with tarsorrhaphy (n=11) or bandage contact lens (n=4) or to the AMT group (n=15). Outcomes were measured by epithelialization time, duration of healing of corneal ulcers and visual acuity. Postoperatively, patients were treated with ofloxacin eye drops, artificial tears, and steroids. At the end of three months of follow-up, complete epithelialization and healing of corneal ulcer was seen in 10 control group patients and 11 AMT patients. Changes in visual acuity were not statistically significant between the two groups. One AMT eye developed corneal perforation 28 days postoperatively. The authors noted that both conventional management and AMT were effective methods of treatment, and that, "In eyes with post-herpes infection neurotrophic keratitis, AMT seems to be more effective than conventional treatment."

Two retrospective reviews (n=23–33) reported outcomes for the use of AMT for the treatment of corneal ulceration secondary to corneal perforation, descemetocele, neurotrophic keratitis, autoimmune disease and other conditions. Although four to six patients failed treatment, useful vision was maintained in a subgroup of patients, and Hick et al. reported an 80% overall success rate (Chen, et al., 2006; Hick, et al., 2005). A third retrospective review by Fuchsluger et al. (2007) compared the efficacy of AMT to botulinum toxin type A-induced ptosis and perforating keratoplasty. Group A initially received AMT followed by AMT or keratoplasty (n=92), group 2 received AMT followed by botulinum (n=32), and group 3 was initially treated with botulinum followed by AMT or keratoplasty (n=13). With a follow-up range of 1–60 months, the overall rate of reoperation was 45.3%, 44.6% for group 1 (reduced to 30.4% following a second AMT), 34.4% for group 2, and 69.25 for group 3 (reduced to 23.1% following AMT application).

Pterygium

Pterygium is an ocular disease characterized by fibrovascular overgrowth of degenerative conjunctiva on the cornea. The size of the growth varies, and may interfere with vision if it extends over the cornea. The growth can be caused by dry eye or irritation from wind, dust and/or ultraviolet light. Symptoms include: redness, inflammation, blurred vision, irritation, dryness, itching, and burning. Pterygium is typically treated with eye drops or ointment and may be surgically removed for visual disturbance or persistent discomfort. Surgical intervention may involve a conjunctival transplant or the application of an antimetabolite solution (e.g., mitomycin C). AMT alone, or as an adjunct, has been proposed as a treatment alternative for pterygium. Recurrence is the most common complication following excision of primary pterygia ((Nakamura, et al., 2006; American Academy of Ophthalmology [AAO], 2005; Ma, et al., 2005).

Küçükerdönmez et al. (2007) conducted a randomized controlled trial to compare the surgical and cosmetic outcomes of AMT (n=27 primary pterygia, 11 recurrent pterygia) compared to conjunctival autografting (n=28 primary pterygia, 12 recurrent pterygia). Postoperatively, topical antibiotics, steroids and lubricants were administered. Follow-up occurred for a minimum of six months. Six to eight months postoperatively, groups 1 and 2 experienced recurrence in three eyes each. In group 1, there was an overall recurrence rate of 7.5% (3.6% with primary pterygia and 16.7% with recurrent pterygia). In group 2, the overall recurrence rate was 7.9% (3.7% with primary pterygia and 18.2% with recurrent pterygia). There were no statistically significant differences between the two groups for recurrence rate (p=1.00) and time to recurrence (p=0.673). The authors reported better cosmetic results with conjunctival autografting, but noted that "selected cases with large pterygium lesions, or patients with glaucoma who

may have the need of filtering surgery in the future, can be treated using the AMT technique.” A limitation of the study is the small patient population.

Ma et al. (2005) conducted a randomized controlled trial to compare the treatment of pterygia with AM graft (AMG) alone (n=48 eyes) to AMG plus intraoperative mitomycin C (AMG+MC, n=47 eyes) after excision of recurrent pterygia. Ages ranged from 26–82 years. Preoperative evaluation identified four eyes with symblepharon in each group. Postoperatively, patients were treated with oral and topical medications, and lubricants as needed. Eye examinations occurred monthly for the first four months, then bimonthly from the fifth month to the end of the first year. Follow-up ranged from 12–87 months. In the AMG group, six conjunctival and six corneal recurrences developed compared to four conjunctival and six corneal recurrences in the AMG-MC group. The conjunctival and the corneal recurrence rates between the two groups were not statistically significant. Symblepharon was identified in six AMG patients and two AMG-MC patients following surgery. Complications included conjunctival cyst, massive subconjunctival hematoma, diplopia secondary to symblepharon, and pyogenic granuloma. Limitations of the study include the small patient population, preoperative presence of symblepharon, and the use of postoperative adjuvant therapies (i.e., topical and oral medications).

Two case series reported favorable outcomes with the use of AMT for the treatment of pterygium. Nakamura et al. (2006) evaluated the use of sterilized, freeze-dried AM (FD-AM) transplantation for pterygium surgery in 13 eyes. At six-month follow-ups, reported outcomes included: complete epithelialization within one to two weeks; early resolution of ocular inflammation; no recurrence of pterygium; and no ocular complications. Solomon et al. (2001) reported three- to nine-month outcome data on 54 patients. The recurrence rate (i.e., grade 4, corneal recurrence) for primary pterygia was 3.0%, 9.5% for secondary pterygia and 5.6% overall. Removal of the semilunar fold in 32 patients resulted in longer survival times (P = 0.063), and failure rate was reported in only two patients (P = 0.046).

Fernandes et al. (2005) retrospectively reviewed 920 records (989 eyes) of patients with primary and recurrent pterygia. Of the 920 patients, 105 had undergone AMT. Recurrence rates following AMT were 10.9% for primary pterygia and 37.5% for recurrent pterygia. Overall, the recurrence rate for AMT alone was 26.7%, and conjunctival autograft [CAG] with AMT was 15% compared to 12.2–20% for other surgical procedures (i.e., bare sclera, primary closure, CAG, conjunctival limbal autograft [CLAG], and bare sclera plus mitomycin C). Ma et al. (2000) conducted a retrospective comparison of patients who had undergone AMT (n=80 eyes) as an adjunct therapy for primary pterygium compared to independent studies in which pterygium were treated with conjunctival autograft (n=56 eyes) and excision followed by topical mitomycin C (n=54 eyes). The AMT group was treated postoperatively with topical ointment, oral indomethacin, antacids and lubricants. Following treatment of the AMT group, the outcomes were compared to two groups who had been previously treated. There were no significant differences in the outcomes of the three groups. The recurrence rates were 3.8% for the AMT group, 5.4% for the conjunctival autograft group, and 3.7% for the topical mitomycin C group.

Stevens-Johnson Syndrome (SJS)

SJS, also known as Lyell syndrome or toxic epidermal necrolysis, is an erythema skin disorder that is generally self-limited and nonprogressive. It is an inflammatory disorder of the skin involving at least two mucous membranes, generally lasting two to three weeks. However, if unresponsive to treatment, systemic toxicity may occur and be accompanied by malaise, fever, headache and fluid imbalance. SJS may also involve the eyes, and it is hypothesized that ocular involvement may be associated with a genetic predisposition. The exact cause of the disease is unknown, but can be precipitated by bacteria, viruses, fungi and drug usage (e.g., penicillin, sulfonamides, salicylates, topical ophthalmic ointments). Herpes simplex virus and mycoplasma are often seen with SJS. As the disease progresses, mucous membranes of the mouth and eyes are most frequently and most severely affected. With ocular involvement, the lids become swollen, ulcerated and crusted. In severe cases, purulent drainage, conjunctivitis, and dry eye may occur. Major ocular problems, including symblepharon, conjunctival scarring, corneal ulceration, corneal neovascularization and limbal stem cell deficiency may occur during the cicatricial stage. Treatment depends upon the severity of the condition and may include lubricants, artificial tears, ointments, corticosteroids, antibiotics, buccal mucous membrane grafts, stem cell transplantation and AMT (Gomes, et al., 2003; Sugar, 2004; Kunimoto, et al., 2004b).

Gomes et al. (2003) conducted a study involving ten patients, age range 9–64 years, with total limbal stem cell and conjunctival deficiency due to SJS. Excision of cicatricial tissue was followed by placement of the amniotic membrane and living related corneal limbal/conjunctival transplantations. Postoperatively, patients used topical eye medication, artificial tears, autologous serum drops, and wore special dry-eye glasses. Follow-up occurred weekly for the first two months, then twice a month for six months and monthly thereafter, range 12–24 months. The appearance of corneal epithelial without defect, normal fluorescein permeability, absence of conjunctiva-derived goblet cells, decreased corneal vascularization, and improvement in visual acuity were considered successful procedures. Two eyes (20%) obtained successful reconstruction, four eyes failed (40%) and infection occurred in four eyes. Visual acuity was achieved in four eyes (40%), maintained in five eyes (50%) and decreased in one eye (10%). High postoperative complications, especially infection, jeopardized favorable outcomes.

Other Indications: AMT has been proposed as a treatment option for various other ocular conditions. These conditions include: porous stem orbital implant exposure (Chen and Cui, 2007); severe bacterial keratitis (Gicquel, 2007); conjunctival scarring and adhesions due to symblepharon, exposed Ahmed valve, tumor and pterygium (Maharajan, et al., 2007); persistent epithelial defects (Saw, et al., 2007); herpes necrotizing stromal keratitis (Shi, et al., 2007); extensive ocular surface neoplasia (Gunduz, et al., 2006); dystrophic epidermolysis bullosa (EB), laryngo-onychocutaneous syndrome and measles-related keratitis in children (Goyal, et al., 2006); persistent hydrops related to keratoconus (Wylegala, et al., 2006); repair of severe conjunctival dehiscence (Mocan and Azar, 2005); and defects created after excision for conjunctival intraepithelial neoplasia and tumors (Wang, et al., 2004).

Rauscher et al. (2007) conducted a randomized controlled trial to compare the long-term results of AMT to conjunctival advancement for repair of late-onset glaucoma filtering bleb leakage. Due to more recurrent leakage and bleb failure with AMT, recruitment was halted after 30 subjects. With a median follow-up of 80 months (range 26–102 months), there were seven AMT failures compared to four conjunctival failures; all failures required surgical intervention. The AMT group recorded a final intraocular pressure of 10.9 ± 0.9 millimeters of mercury (mm HG) compared to 12.7 ± 1.3 mm HG for the conjunctival group ($p=0.28$). Postoperatively, the conjunctival group experienced diplopia, persistent ptosis, and cysts of the Tenon capsule compared to no complications in the AMT group. The authors noted that AMT “should be considered when there is preoperative ptosis or inadequate conjunctiva for standard advancement.”

Evidence from a number of uncontrolled studies and case series also suggested that AMT can be effective in the reconstruction and healing of ocular conditions in patients with corneal, conjunctival, or lid defects that have not responded to medical treatment (Miyai, et al., 2005; Jain and Rastogi, 2004; Prabhasawat, et al., 2000; Azuara-Blanco, et al., 1999; Tseng, et al., 1998; Shimazaki, et al., 1997).

Although there is limited evidence comparing AMT with other treatment modalities for ocular conditions, small case series, large retrospective reviews and medical textbooks indicate that AMT is a safe and effective treatment option in a select patient population with hard-to-treat ocular conditions that are unresponsive to conventional medical therapies (e.g., lubricants/artificial tears, topical and systemic steroids and antibiotics, eyelid taping) and non-AMT surgical intervention (e.g., excision, buccal mucosa grafts, tarsorrhaphy, conjunctival flap).

Professional Societies/Organizations

In their recommendations for the management of herpes zoster, the Infectious Disease Society of America lists AMT as one surgical option for the treatment of chronic problems secondary to herpes ophthalmicus (Dworkin, et al., 2007).

In a report on the progress of eye and vision research, the National Eye Institute (1999–2006) states that the use of AMT, based upon previous reports of the success of AMT when used with a variety of other eye diseases, may improve outcomes with photorefractive keratectomy (PKR) when used for the treatment of corneal ulcers. They explain that AMT promotes healing and reduces inflammation and scarring, and its use as a bandage or dressing to promote healing and reduce inflammation has been demonstrated. AMT may also help reduce corneal haze after PKR and “has important implications for use in enhancing corneal healing after damage by injury, disease or infection.”

In their guidelines on AMT, the Royal College of Ophthalmologists (ROC) states that AMT has been successfully used in a number of procedures “either as a 'substrate' to replace the damaged ocular tissue or as a 'patch' (biological dressing), or a combination of both.” They also note that the full potential of AMT is not yet known, and randomized trials are indicated.

The American Academy of Ophthalmology (AAO) notes that AMT was proposed as a treatment option for recurring pterygia in a study by Tsang et al. (2001) but states that not all corneal surgeons agree with the findings as they “have not been able to replicate his results” (AAO, 2003).

Summary

Amniotic membrane transplant (AMT) has been proposed as a treatment option for numerous ocular conditions. Some studies concluded that AMT was as good as conventional medical therapy; some proposed AMT as an adjunctive therapy; and still others stated that AMT may be considered as a treatment option before other surgical procedures (e.g., keratoplasty or conjunctival flap). In general, the available evidence is in the form of retrospective reviews or case series with small, heterogeneous patient populations and short-term follow-up. However, these studies, professional societies and medical textbook sources support AMT as a safe and effective treatment option for ocular conditions unresponsive to medical therapy (e.g., lubricants/artificial tears, topical and systemic steroids and antibiotics, eyelid taping) and non-AMT surgical interventions (e.g., excision, buccal mucosa grafts, tarsorrhaphy, conjunctival flap).

Coding/Billing Information

Note: This list of codes may not be all-inclusive.

Covered when medically necessary:

CPT* Codes	Description
65780	Ocular surface reconstruction; amniotic membrane transplantation

HCPCS Codes	Description
V2790	Amniotic membrane for surgical reconstruction, per procedure

ICD-9-CM Diagnosis Codes	Description
	Multiple/varied

*Current Procedural Terminology (CPT®) © 2007 American Medical Association: Chicago, IL.

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