Medical Policy

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Populations	Interventions	Comparators	Outcomes
Individuals: • With corneal blindness who have failed or are not candidates for corneal transplantation	Interventions of interest are: ▪ Boston Keratoprosthesis	Comparators of interest are: ▪ Penetrating keratoplasty	Relevant outcomes include: ▪ Change in disease status ▪ Morbid events ▪ Quality of life ▪ Treatment-related morbidity
Individuals: ▪ With corneal blindness who have failed or are not candidates for corneal transplantation	Interventions of interest are: ▪ Keratoprosthesis using the AlphaCor device	Comparators of interest are: ▪ Penetrating keratoplasty	Relevant outcomes include: ▪ Change in disease status ▪ Morbid events ▪ Quality of life Treatment-related morbidity
Individuals: ▪ With corneal blindness who have failed or are not candidates for corneal transplantation	Interventions of interest are: ▪ Osteo-odonto-keratoprosthesis	Comparators of interest are: ▪ Penetrating keratoplasty	Relevant outcomes include: ▪ Change in disease status ▪ Morbid events ▪ Quality of life Treatment-related morbidity

DESCRIPTION

A keratoprosthesis, consisting of a central optic held in a cylindrical frame, is an artificial cornea that is intended to restore vision to patients with severe bilateral corneal disease for whom a corneal transplant is not an option. The keratoprosthesis replaces the cornea that has been removed and is held in place by the surrounding tissue. Various biologic materials are being investigated to improve integration of the prosthetic into the eye.

Objective

The objective of this evidence review is to determine whether keratoprosthesis improves health outcomes in patients with corneal blindness who have failed or are not candidates for corneal transplantation.

Background

Cornea

The cornea, a clear, dome-shaped membrane that covers the front of the eye, is a key refractive element of sight. Layers of the cornea consist of the epithelium (outermost layer); Bowman layer; the stroma, which comprises approximately 90% of the cornea; Descemet membrane; and the endothelium.

Treatment

The established surgical treatment for corneal disease is penetrating keratoplasty, which involves making a large central opening through the cornea and then filling the opening with a full-thickness donor cornea. In certain conditions, such as Stevens-Johnson syndrome, ocular cicatricial pemphigoid, chemical injury, or prior failed corneal transplant, survival of transplanted cornea is poor. The keratoprosthesis was developed to restore vision in patients for whom a corneal transplant is not an option.

Keratoprosthetic devices consist of a central optic held in a cylindrical frame. The keratoprosthesis replaces the section of the cornea that has been removed, and, along with being held in place by the surrounding tissue, may be covered by a membrane to further anchor the prosthesis. A variety of biologic materials are being investigated to improve the integration of prosthetic corneal implants into the stroma and other corneal layers.

The Dohlman-Doane keratoprosthesis, most commonly referred to as the Boston Keratoprosthesis (KPro), is manufactured under the auspices of the Harvard Medical School affiliated Massachusetts Eye and Ear Infirmary. The Boston type 1 KPro uses a donor cornea between a central stem and a back plate. The Boston type 2 prosthesis is a modification of the type 1 prosthesis and is designed with an anterior extension to allow implantation through surgically closed eyelids. The AlphaCor, previously known as the Chirila keratoprosthesis (Chirila KPro), consists of a polymethylmethacrylate device with a central optic region fused to a surrounding sponge skirt; the device is inserted in a 2-stage surgical procedure.

Autologous keratoprostheses use a central polymethylmethacrylate optic supported by a skirt of either tibia bone or the root of a tooth with its surrounding alveolar bone. The most common is the osteo-odonto-keratoprosthesis, which uses osteodental lamina derived from an extracted tooth root and attached alveolar bone that has been removed from the patient’s jaw. Insertion of the osteo-odonto-keratoprosthesis device requires a complex staged procedure, in which the cornea is first covered with buccal mucosa. The prosthesis itself consists of a polymethylmethacrylate optical cylinder, which replaces the cornea, and is held in place by biologic support made from a canine tooth extracted from the recipient. A hole is drilled through the dental root and alveolar bone, and the polymethylmethacrylate prosthesis is placed within. This entire unit is placed into a subcutaneous ocular pocket and is then retrieved 6 to 12 months later for final insertion.

Hydroxyapatite, with a similar mineral composition to both bone and teeth (phosphate and calcium), may also be used as a bone substitute and as a bioactive prosthesis with the orbit. Collagen coating and scaffolds have also been investigated to improve growth and biocompatibility with the corneal epithelial cells, which form the protective layer of the eye. Many of these materials and devices are currently being tested in vitro or animal models.

REGULATORY STATUS

In 1992, the Boston KPro (Dohlman-Doane keratoprosthesis; Massachusetts Eye and Ear Infirmary) was approved by the U.S. Food and Drug Administration (FDA) through the premarket approval process for use in patients with severe corneal opacity. The device is used when standard corneal transplant has failed or would be unlikely to succeed. There are 2 types of Boston KPro. Type 1 is used in eyes when eyelids, blink mechanism, and tear film are intact. Type 2 is used with severe dry eye and in eyes with mucosal keratinization and obliteration of normal conjunctival fornices.

In August 2002, the AlphaCor® (Chirila Keratoprosthesis) was cleared for marketing by the FDA through the 510(k) process. The FDA determined that this device was substantially equivalent to the Dolman-Doane keratoprosthesis. The AlphaCor® device is indicated as a keratoprosthesis in adults with corneal opacity when standard penetrating keratoplasty with donor tissue is not suitable, when patients have declined standard penetrating keratoplasty, or when adjunctive procedures to prevent graft rejection are contraindicated.

FDA product code: HQM

POLICY

A. The Boston (Dohlman-Doane) Keratoprosthesis (Boston KPro) may be considered **medically necessary** for the surgical treatment of severe corneal opacification in situations where cadaveric corneal transplants have failed or have a very low likelihood of success. (See Policy Guidelines)

B. All other types of permanent keratoprostheses are considered **experimental / investigational**.

Policy Guidelines

1. Implantation of a keratoprosthesis is considered a high-risk procedure associated with numerous complications and probable need for additional surgery. Therefore, the likelihood of regaining vision and the patient's visual acuity in the contralateral eye should be taken into account when considering the appropriateness of this procedure. Treatment should be restricted to centers experienced in treating this condition and staffed by surgeons adequately trained in techniques addressing implantation of this device.

2. Conditions under which cadaveric corneal transplants have a likelihood of failure include but are not limited to the following:
   - The cornea is severely opaque and vascularized AND
   - Best-corrected vision is 20/400 or less in the affected eye and 20/40 or less in the contralateral eye AND
   - No end-stage glaucoma or retinal detachment is present AND
   - The patient has **one** of the following indications:
     - History of 1 or more corneal transplant graft failures
     - Stevens-Johnson syndrome
     - Ocular cicatricial pemphigoid
     - Autoimmune conditions with rare ocular involvement
     - Ocular chemical burns
     - An ocular condition unlikely to respond favorably to primary corneal transplant surgery (e.g., limbal stem cell compromise or postherpetic anesthesia)

3. Note that patients should be able and expected to comply with postoperative care.

RATIONALE

This evidence review has been updated regularly with searches of the PubMed database. The most recent literature update was performed through December 13, 2020.

Evidence reviews assess the clinical evidence to determine whether the use of a technology improves the net health outcome. Broadly defined, health outcomes are length of life, quality of life, and ability to function including benefits and harms. Every clinical condition has specific outcomes that are important to patients and to managing the course of that condition. Validated outcome measures are necessary to ascertain whether a condition improves or worsens; and whether the magnitude of that change is clinically significant. The net health outcome is a balance of benefits and harms.

To assess whether the evidence is sufficient to draw conclusions about the net health outcome of a technology, 2 domains are examined: the relevance and the quality and credibility. To be relevant, studies must represent one or more intended clinical use of the technology in the intended population and compare an effective and appropriate alternative at a comparable intensity. For some conditions, the alternative will be supportive care or surveillance. The quality and credibility of the evidence depend on study design and conduct, minimizing bias and confounding that can generate incorrect findings. The randomized controlled trial is preferred to assess efficacy; however, in some circumstances, nonrandomized studies may be adequate. Randomized controlled trials are rarely large enough or long enough to capture less common adverse events and long-term effects. Other types of studies can be used for these purposes and to assess generalizability to broader clinical populations and settings of clinical practice.

The keratoprosthesis is intended for the relatively small number of patients with severe corneal damage who have lost vision and for whom a corneal transplant is not expected to result in satisfactory outcomes. These criteria generally refer to the population of patients who have failed one or more corneal transplants and who therefore have very few options to prevent blindness. Because this surgery is considered a salvage procedure with no acceptable alternative treatments, comparative studies are limited and/or lacking. The available literature primarily consists of retrospective case series. This evidence review examines the types of devices currently being tested in humans, focusing on reports that permit assessment of integration within the eye, durability, visual outcomes, and adverse events following implantation.

BOSTON (DOHLMAN-DOANE) KERATOPROSTHESIS

Clinical Context and Therapy Purpose

The purpose of Boston keratoprosthesis (KPro) in patients with corneal blindness who are not candidates for corneal transplantation is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The question addressed in this evidence review is: Does the use of Boston KPro in patients with corneal blindness who are not candidates for corneal transplantation improve net health outcomes?

The following PICO was used to select literature to inform this review.

Population

The relevant population of interest is patients with corneal blindness who are not candidates for corneal transplantation.

Interventions

The treatment being considered is Boston KPro, which is performed by an ophthalmologist or surgeon in an outpatient clinical setting or surgery center.

Patients with corneal blindness are actively managed by an ophthalmologist in an outpatient clinical setting.

Comparators

The comparator of interest is penetrating keratoplasty, which is performed by an ophthalmologist or surgeon in an outpatient clinical setting or surgery center.

Patients with corneal blindness are actively managed by an ophthalmologist in an outpatient clinical setting.

Outcomes

The outcomes of interest are change in disease status, morbid events, quality of life, and treatment-related morbidity. Positive outcomes would be biointegration of the prosthetic by the body and improvement in visual acuity in the treated eye. Negative outcomes include infection, device extrusion, and permanent vision loss.

Follow-up of at least 2 years would be desirable to assess outcomes.

Study Selection Criteria

Methodologically credible studies were selected using the following principles:

1. To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
2. In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.
3. To assess long-term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.

Studies with duplicative or overlapping populations were excluded.

Review of Evidence

Systematic Reviews

In 2015, a systematic review from the American Academy of Ophthalmology identified 22 studies on the efficacy and safety of the Boston (Dohlman-Doane) Keratoprosthesis (Boston KPro).[1,] Studies were published in English and retrospective series had to include at least 25 eyes. The 22 studies included a total of 2,176 eyes; sample sizes in individual studies ranged from 30 to 300 eyes. The proportion of patients with visual acuity of 20/200 after surgery ranged from 54% to 84% in the 10 studies reporting this outcome. Five articles reported that 11% to 39% of treated eyes attained visual acuities of 20/40 or better. Reviewers noted that published data were skewed toward visual improvement. Fourteen articles reported retention rates (eyes retaining the KPro device without loss, extrusion or dehiscence of the device), and these rates ranged from 65% to 100% (mean, 88%). The most common reasons for KPro loss were corneal melts with device exposure or extrusion, endophthalmitis, infectious keratitis, or corneal ulceration. The most common complication was retroprosthetic membrane formation, which ranged from 1% to 65% (mean, 30%) in the 13 studies reporting complications.

A systematic review by Ahmad et al (2016) examined 26 studies on repeat penetrating keratoplasty vs Boston KPro implantation after failed penetrating keratoplasty.[2,] Studies selected focused on patients with corneal opacity who had failed one or more penetrating keratoplastys. Studies were excluded if they only selected patients with ocular surface disease. The primary outcome of interest was the proportion of patients with visual acuity of 20/200 or better at 2 or more years post-surgery. In a meta-analysis of 9 studies, the likelihood of 20/200 vision or better at least 2 years after repeat penetrating keratoplasty surgery was 42% (95% confidence interval [CI], 30% to 56%). A total of 104 eyes from 98 patients underwent KPro after failed penetrating keratoplasty surgery; 31 patients had only 1 previous penetrating keratoplasty. In a meta-analysis of data on KPro implantation after failed penetrating keratoplasty surgery, the probability of maintaining visual acuity of 20/200 or better at 2 years was 80% (95% CI, 68% to 88%). Among patients with a history of one failed penetrating keratoplasty, the probability of maintaining a visual acuity of 20/200 or better at 2 years was 74% (95% CI, 45% to 89%). (Reviewers did not specify the number of patients receiving KPro who were included in the analysis of 20/200 vision at 2 years.) In terms of complications after KPro following failed penetrating keratoplasty, at 2 years 29% of patients had elevated intraocular pressure and 8% needed surgery for glaucoma. In an analysis limited to patients undergoing KPro after 1 failed penetrating keratoplasty, complication rates ranging from 29% to 10% (which did not differ significantly from patients with KPro after >1 failed penetrating keratoplastys). Reviewers did not report the number of patients included in the complication analyses.

Case Series

Representative larger series include a report from the Boston Type 1 Keratoprosthesis Study Group (2013) that assessed retention of the KPro device in 300 eyes of 300 patients.[3] At a mean follow-up of 17.1 months (range, 1 week to 6 years), 93% of the keratoprostheses were retained. The probability of retention was 94% at 1 year and 89% at 2 years. Mean device durability was 3.8 years. Risk factors for keratoprosthesis loss were an autoimmune disease, ocular surface exposure, and a number of prior failed penetrating keratoplasty procedures. Additional data on this cohort were published in 2016.[4] Preoperative visual acuities, available for 47% of eyes, was 20/1205. During a mean follow-up of 17 months (range, 1 week to 6 years), visual acuity improved significantly for 85% of eyes to a final mean of 20/150. Median time to achieve visual acuity of 20/200 was 1 month, and this level of acuity lasted for a mean of 48 months among patients with sufficient follow-up.

Srikumaran et al (2014) reported on a mean follow-up of 46.7 months (range, 6 weeks to 8.7 years) for 139 eyes of 133 patients who had received a Boston KPro at 1 of 5 tertiary referral centers in the United States.[5] Twenty-seven percent of eyes underwent a primary KPro procedure while 73% had a prior donor graft failure. Postoperatively, visual acuity improved to at least 20/200 in 70% of eyes. The probability of maintaining visual acuity of at least 20/200 was 50%, and device retention was estimated at 67% at 7 years. The 7-year cumulative incidence of complications was 49.7% for retroprosthetic membrane formation, 21.6% for glaucoma surgery, 18.6% for retinal detachment, and 15.5% for endophthalmitis.

A prospective series of 265 eyes (265 patients) from 18 medical centers, published by the Boston Type 1 Keratoprosthesis Study Group (2012), focused on the time to development of retroprosthetic membranes.[6] Most eyes (85.4%) had undergone an average of 2.2 (range, 1-8) penetrating keratoplastys before keratoprosthesis implantation. The remaining eyes (14.6%) were considered at high-risk for penetrating keratoplasty failure and had received a primary keratoprosthesis. At a mean follow-up of 17.8 months, retroprosthetic membranes had formed in 31.7% of eyes. The mean time to development of retroprosthetic membranes was 216.7 days (range, 7 days to 4 years). Risk factors were the indication for the keratoprosthesis. Specifically, infectious keratitis had a hazard ratio of 3.2 (95% CI, 1.7 to 6.2) and aniridia had a hazard ratio of 3.1 (95% CI, 1.1 to 8.9).

Dunlap et al (2010) retrospectively analyzed 122 patients (126 eyes) at 2 centers who received a Boston type 1 KPro between 2004 and 2007.[7] For most patients, the affected eye had a visual acuity of less than 20/400, and the contralateral eye did not have better vision. Of the 126 eyes, 112 had a history of multiple failed corneal grafts, and 14 had received the keratoprosthesis as a primary procedure due to the presence of limbal stem cell deficiency or significant ocular surface diseases. Following implantation, 96 (76%) eyes had improved vision, 22 (17.4%) eyes did not improve, and 8 (6.3%) eyes lost vision. At 3-month follow-up, 54% of eyes had 20/200 vision or better, with 18% achieving 20/40 or better. In approximately 45% of the eyes, visual acuity remained less than 20/400. The percentage of patients with improved visual outcomes was lower than in other published studies, due in part to the presence of comorbid conditions (e.g., glaucoma, retinal detachment).

Adverse Events

Odorcic et al (2015) published a literature review on fungal infections after Boston type 1 KPro.[8] They identified 15 relevant publications, primarily retrospective case series. Annual rates of fungal infections reported in these studies ranged from 0.9 to 2 per 100 patients. The largest case series assessed 291 eyes, and the cumulative incidence of fungal endophthalmitis was 2.4% over 10 years.

Chan et al (2016) retrospectively reviewed 110 patients (128 eyes) who received a Boston type 1 KPro, focusing on corneal melts, leaks, and extrusions.[9] Mean follow-up was 29 months (range, 3-77 months). Melt-related complications requiring surgical repair occurred in 16% (20/128) of eyes; seven of these eyes had multiple episodes. The average time to a melt complication was 13 months after KPro implantation. Risk factors significantly associated with melt-related complications were previous infectious keratitis, and conjunctival deficiency caused by Stevens-Johnson syndrome, mucous membrane pemphigoid, or previous chemical injury.

Posterior segment complications were reported by Goldman et al (2013)[10] Of 83 eyes (93 procedures) with follow-up of at least 6 months (range, 6-84 months), 38 (40.9%) eyes had at least 1 postoperative posterior segment complication, which included retinal detachment (16.9%), choroidal detachment (16.9%), and sterile vitritis (14.5%). Visual acuity was worse in eyes that experienced posterior segment complications than in eyes that did not.

Section Summary: Boston Keratoprosthesis

Numerous case series and systematic reviews of these series have assessed thousands of eyes implanted with the Boston KPro device. A 2015 systematic review of KPro efficacy included 22 series with a total of 2,176 eyes. Studies with longer follow-up (i.e., at least 2 years) have shown improved visual outcomes in a substantial percentage of patients with Boston KPro. This procedure is high-risk and is associated with numerous complications (e.g., the growth of retroprosthetic membranes) and a probable need for additional surgery, thus careful patient selection is important.

ALPHACOR DEVICE

Clinical Context and Therapy Purpose

The purpose of AlphaCor keratoprosthesis in patients with corneal blindness who are not candidates for corneal transplantation is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The question addressed in this evidence review is: Does the use of AlphaCor keratoprosthesis in patients with corneal blindness who are not candidates for corneal transplantation improve net health outcomes?

The following PICO was used to select literature to inform this review.

Population
The relevant population of interest is patients with corneal blindness who are not candidates for corneal transplantation.

Interventions
The treatment being considered is AlphaCor keratoprosthesis, which is performed by an ophthalmologist or surgeon in an outpatient clinical setting or surgery center.

Patients with corneal blindness are actively managed by an ophthalmologist in an outpatient clinical setting.

Comparators
The comparator of interest is penetrating keratoplasty, which is performed by an ophthalmologist or surgeon in an outpatient clinical setting or surgery center.

Patients with corneal blindness are actively managed by an ophthalmologist in an outpatient clinical setting.

Outcomes
The outcomes of interest are change in disease status, morbid events, quality of life, and treatment-related morbidity. Positive outcomes would be biointegration of the prosthetic by the body and improvement in visual acuity in the treated eye. Negative outcomes include infection, device extrusion, and permanent vision loss.

Follow-up of at least 2 years would be desirable to assess outcomes.

Study Selection Criteria
Methodologically credible studies were selected using the following principles:

1. To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
2. In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.
3. To assess long-term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.

Studies with duplicative or overlapping populations were excluded.

Review of Evidence
Studies have suggested that, with the AlphaCor device, thinning or "melting" of the anterior corneal surface can lead to loss of biointegration.[11,12,] This complication appears most prevalent in patients with ocular herpes, hence, the AlphaCor device is contraindicated in these patients.

Several case series have evaluated the AlphaCor. One of the larger was published by Hicks et al (2003).[11] It included 40 devices implanted in 38 patients. At an average 30-month follow-up, 42% of eyes had visual acuity better than 20/200. Hoffart et al (2015) evaluated the AlphaCor device implanted in 12 patients.[13] At a mean follow-up of 25 months, 8 (67%) of devices were retained, and patients had a mean gain in best-corrected visual acuity of 2.5 lines. The most common complication was corneal necrosis, observed in 7 (59%) patients, two of whom had a history of ocular herpes.

Section Summary: AlphaCor Device

Only a few published case series have evaluated the AlphaCor device, and hence there are insufficient data on improvements in vision outcomes this device. Moreover, the device has been associated with complications, including thinning or melting of the anterior corneal surface and corneal necrosis.

OSTEO-ODONTO-KERATOPROSTHESIS

Clinical Context and Therapy Purpose

The purpose of osteo-odonto-keratoprosthesis in patients with corneal blindness who are not candidates for corneal transplantation is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The question addressed in this evidence review is: Does the use of osteo-odonto-keratoprosthesis in patients with corneal blindness who are not candidates for corneal transplantation improve net health outcomes?

The following PICO was used to select literature to inform this review.

Population

The relevant population of interest is patients with corneal blindness who are not candidates for corneal transplantation.

Interventions

The treatment being considered is osteo-odonto-keratoprosthesis. This is a staged procedure requiring a multidisciplinary approach involving dentists, ophthalmologists, and radiologists. The entire procedure takes place over a span of 6 to 12 months.

Patients with corneal blindness are actively managed by an ophthalmologist in an outpatient clinical setting.

Comparators

The comparator of interest is penetrating keratoplasty, which is performed by an ophthalmologist or surgeon in an outpatient clinical setting or surgery center.

Patients with corneal blindness are actively managed by an ophthalmologist in an outpatient clinical setting.

Outcomes

The outcomes of interest are change in disease status, morbid events, quality of life, and treatment-related morbidity. Positive outcomes would be biointegration of the implant by the body and improvement in visual acuity in the treated eye. Negative outcomes include infection, device extrusion, and permanent vision loss.

Follow-up of at least 5 years, preferably longer, would be desirable to assess outcomes.

Study Selection Criteria

Methodologically credible studies were selected using the following principles:

1. To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
2. In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.
3. To assess long-term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.

Studies with duplicative or overlapping populations were excluded.

Review of Evidence

A systematic review by Tan et al (2012) included 8 case series describing surgical outcomes and complication rates of the osteo-odonto-keratoprosthesis.[14,] Sample sizes ranged from 4 to 181 eyes. None of the studies was conducted in the United States. At 5 years, the pooled anatomic survival rate was 88% (range, 67%-100%) and, at 20 years, based on pooled data from 3 series, the anatomic survival rate was 81% (range, 65%-98%). About half of the patients obtained visual acuity better than 6/18. Visual acuity in the other patients was not described.

One of the largest case series (included in the Tan systematic review) is that by Falcinelli et al (2005), who reported on osteo-odonto-keratoprosthesis in 181 patients.[15,] At a median follow-up of 12 years, survival analysis estimated that the probability of retaining an anatomically intact osteo-odonto-keratoprosthesis 18 years after surgery with reasonable visual acuity was 85%.

In 2008, investigators from Spain retrospectively reviewed 227 patients who underwent osteo-odonto-keratoprosthesis (n=145) or osteokeratoprosthesis (n=82) using tibial bone in patients who lacked canine teeth to assemble the prosthesis.[16,] A second publication in 2011 from the same study examined the impact of clinical factors on long-term functional and anatomic outcomes.[17,] The primary diagnosis was chemical or thermal burn (48%), Steven-Johnson syndrome and Lyell syndrome (13%), cicatricial pemphigoid (11%), trachoma (11%), and other or not assignable (17%). Mean preoperative decimal best-corrected visual acuity was 0.00062 (range, light perception to 0.10). (On the decimal visual acuity scale, 0 = no light perception, 0.00001 = light perception, 0.0001 = light projection, and 0.001 = counting fingers.) Functional survival was defined as best-corrected visual acuity of 0.05 or more, and anatomic survival as retention of the keratoprosthesis lamina. Mean follow-up was 8.4 years for osteo-odonto-keratoprosthesis and 3.5 years for osteokeratoprosthesis. Anatomic success at 10 years was estimated to be 66% for osteo-odonto-keratoprosthesis and 47% for osteokeratoprosthesis. Functional success at 10 years was estimated to be 38% for osteo-odonto-keratoprosthesis and 17% for osteokeratoprosthesis. The best functional survival was in the Stevens-Johnson group, followed by chemical burn and trachoma. The least favorable prognosis was thermal burn. Complications included extrusion of the keratoprosthesis (28%), retinal detachment (16%), uncontrolled glaucoma (11%), infection (9%), retroprosthetic membrane (5%), and vitreous hemorrhage (3%). In cases without complications, functional survival was 57% at 5 years and 42% at 10 years.

Hughes et al (2008) reported on vitreoretinal complications of the osteo-odonto-keratoprosthesis in a retrospective review of 35 patients performed at 1 hospital in England between 1996 and 2005.[18] Diagnoses were Stevens-Johnson syndrome in 15 patients, chemical injury in 5, mucous membrane pemphigoid in 3, and topical medication toxicity in 3. Follow-up at a mean 57 months (range, 13-105 months) revealed 9 vitreoretinal complications in 8 (23%) patients, which included vitreous hemorrhage, retinal detachment, and intraoperative choroidal hemorrhage. A 2008 report on 36 patients treated at the same hospital between 1996 and 2006 (likely to have reported patients assessed by Hughes[18]) estimated that the probability of retaining visual acuity was 53% at 5 years and 44% at 9 years.[19] In addition to the vitreoretinal complications causing loss of vision, resorption of the bony lamina led to visual or anatomic compromise in 7 (19%) cases.

Section Summary: Osteo-Odonto-Keratoprosthesis

A 2012 systematic review identified 8 case series evaluating osteo-odonto-keratoprosthesis, all of which were conducted outside of the United States, and no subsequent studies were identified. Pooled analyses of case series data found high anatomic survival rates at 5 and 20 years. However, vision outcomes were not well-described. The systematic review reported that half of the patients obtained visual acuity better than 6/18. Osteo-odonto-keratoprosthesis is a complex surgical procedure and has been associated with a number of complications, including extrusion of the keratoprosthesis, retinal detachment, and vitreoretinal complications.

Summary of Evidence

For individuals who have corneal blindness and have failed or are not candidates for corneal transplantation who receive a Boston Keratoprosthesis (Boston KPro), the evidence includes case series and systematic reviews. Relevant outcomes are change in disease status, morbid events, quality of life, and treatment-related morbidity. Numerous case series have been published. Together, studies have assessed thousands of eyes. A 2015 systematic review of Boston KPro efficacy included 22 series with a total of 2,176 eyes. Systematic reviews and case series with longer follow-up (i.e., at least 2 years) have shown improvement in visual outcomes in a substantial percentage of patients with Boston KPro. This procedure is high-risk and associated with numerous complications (e.g., the growth of retro prosthetic membranes) and a probable need for additional surgery, thus careful patient selection is important. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have corneal blindness and have failed or are not candidates for corneal transplantation who receive a keratoprosthesis using the AlphaCor device, the evidence includes case series. Relevant outcomes are change in disease status, morbid events, quality of life, and treatment-related morbidity. Only a few published case series have evaluated the AlphaCor device. There are insufficient data on improvement in vision outcomes using the AlphaCor device. Moreover, the device has been associated with complications, including thinning or melting of the anterior corneal surface and corneal necrosis. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have corneal blindness and have failed, or are not candidates for corneal transplantation who receive an osteo-odonto-keratoprosthesis, the evidence includes case series and a systematic review. Relevant outcomes are change in disease status, morbid events, quality of life, and treatment-related morbidity. A 2012 systematic review of case series, all conducted outside of the United States, found high anatomic survival rates at 5 and 20 years, but vision outcomes were not well-described. Osteo-odonto-keratoprosthesis is a complex surgical procedure and has been associated with a number of complications, including extrusion of the keratoprosthesis, retinal detachment, and vitreoretinal complications. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

SUPPLEMENTAL INFORMATION

The purpose of the following information is to provide reference material. Inclusion does not imply endorsement or alignment with the evidence review conclusions.

Clinical Input From Physician Specialty Societies and Academic Medical Centers

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

In response to requests, input was received from 1 specialty society and 4 academic medical centers while this policy was under review in 2009. Reviewers generally supported a limited role for the Boston Keratoprosthesis in select patients. Some reviewers recommended use without first attempting a transplant under specific conditions that have a poor prognosis for corneal transplant; however, others found this controversial. Some reviewers recommended use only in patients with limited visual acuity in the contralateral eye. Overall, input indicated that the Boston Keratoprosthesis should be reserved for cases in which no other alternative (i.e., corneal transplantation) is available for treatment of corneal opacification.

Practice Guidelines and Position Statements

Guidelines or position statements will be considered for inclusion in 'Supplemental Information' if they were issued by, or jointly by, a US professional society, an international society with US representation, or National Institute for Health and Care Excellence (NICE). Priority will be given to guidelines that are informed by a systematic review, include strength of evidence ratings, and include a description of management of conflict of interest.

American Academy of Ophthalmology

The 2018 Preferred Practice Parameter on ocular edema and opacification by the American Academy of Ophthalmology did not provide specific recommendations on the keratoprosthesis, but discussed the technology and its current use:[20,]

"Significant improvements in the design and postoperative management of the Boston type 1 keratoprosthesis has resulted in a steady rise in the number of these procedures performed both in the United States and abroad. Reduced incidence of postoperative stromal necrosis and bacterial endophthalmitis due to the chronic use of protective soft contact lenses and topical antibiotics has resulted in improved retention and visual outcomes and has had a positive impact on surgeons' perceptions of when to recommend keratoprosthesis. Once considered a procedure of last resort in patients with severe bilateral visual impairment, it is now being used for a variety of unilateral and bilateral indications, such as ocular trauma, herpetic keratitis, aniridia, and Stevens-Johnson syndrome. More recently, as corneal surgeons have gained a greater appreciation of the failure rate of repeat corneal transplantation, a role for a keratoprosthetic in cases of multiple graft failure has become clearer. Despite earlier suggestions, keratoprosthetics are not considered ideal for pediatric cases, particularly as primary treatment.…

"Patients with severe dry eye and autoimmune ocular surface diseases...remain a difficult management group despite the other successes of the Boston type 1 keratoprosthetic. Primary placement of the Boston keratoprosthesis in this group of patients results in a higher rate of epithelial defects, scleral and corneal necrosis, extrusion, and endophthalmitis. Some surgeons advocate ocular surface reconstruction with combined keratolimbal allografts or living related allografts prior to placement of the keratoprosthesis. This can potentially lead to improved outcomes in this group. The Boston type 2 keratoprosthetic designed to be used through the eyelid and the osteo-odonto-keratoprosthesis have been implanted with some success in this group of patients."

U.S. Preventive Services Task Force Recommendations

Not applicable.

Ongoing and Unpublished Clinical Trials

Some currently ongoing trials that might influence this review are listed in Table 1.

Table 1. Summary of Key Trials

NCT No.	Trial Name	Planned Enrollment	Completion Date
Ongoing			
NCT02084745	Timing of Glaucoma Drainage Device With Boston KPro Surgery (GDD-KPro)	40	Mar 2025

NCT: national clinical trial.

CODING

The following codes for treatment and procedures applicable to this policy are included below for informational purposes. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

CPT/HCPCS

65770	Keratoprosthesis
C1818	Integrated keratoprosthesis
L8609	Artificial cornea

CD-10 Diagnoses (Effective October 1, 2015)

H17.11	Central corneal opacity, right eye
H17.12	Central corneal opacity, left eye
H17.13	Central corneal opacity, bilateral
H54.0X	Blindness, both eyes, different category levels

H54.10	Blindness, one eye, low vision other eye, unspecified eyes
H54.413A	Blindness right eye category 3, normal vision left eye
H54.414A	Blindness right eye category 4, normal vision left eye
H54.415A	Blindness right eye category 5, normal vision left eye
H54.42A3	Blindness left eye category 3, normal vision right eye
H54.42A4	Blindness left eye category 4, normal vision right eye
H54.42A5	Blindness left eye category 5, normal vision right eye
L51.1	Stevens-Johnson syndrome
T26.61xA	Corrosion of cornea and conjunctival sac, right eye, initial encounter
T26.61xD	Corrosion of cornea and conjunctival sac, right eye, subsequent encounter
T26.61xS	Corrosion of cornea and conjunctival sac, right eye, sequela
T26.62xA	Corrosion of cornea and conjunctival sac, left eye, initial encounter
T26.62xD	Corrosion of cornea and conjunctival sac, left eye, subsequent encounter
T26.62xS	Corrosion of cornea and conjunctival sac, left eye, sequela
T85.318A	Breakdown (mechanical) of other ocular prosthetic devices, implants and grafts, initial encounter
T85.318D	Breakdown (mechanical) of other ocular prosthetic devices, implants and grafts, subsequent encounter
T85.318S	Breakdown (mechanical) of other ocular prosthetic devices, implants and grafts, sequela
T85.328A	Displacement of other ocular prosthetic devices, implants and grafts, initial encounter
T85.328D	Displacement of other ocular prosthetic devices, implants and grafts, subsequent encounter
T85.328S	Displacement of other ocular prosthetic devices, implants and grafts, sequela
T85.398A	Other mechanical complication of other ocular prosthetic devices, implants and grafts, initial encounter
T85.398D	Other mechanical complication of other ocular prosthetic devices, implants and grafts, subsequent encounter
T85.398S	Other mechanical complication of other ocular prosthetic devices, implants and grafts, sequela
T85.79xA	Infection and inflammatory reaction due to other internal prosthetic devices, implants and grafts, initial encounter
T85.79xD	Infection and inflammatory reaction due to other internal prosthetic devices, implants and grafts, subsequent encounter
T85.79xS	Infection and inflammatory reaction due to other internal prosthetic devices, implants and grafts, sequela
T85.83xA	Hemorrhage due to internal prosthetic devices, implants and grafts, not elsewhere classified, initial encounter
T85.83xD	Hemorrhage due to internal prosthetic devices, implants and grafts, not elsewhere classified, subsequent encounter
T85.83xS	Hemorrhage due to internal prosthetic devices, implants and grafts, not elsewhere classified, sequela
T85.84xA	Pain due to internal prosthetic devices, implants and grafts, not elsewhere classified, initial encounter
T85.84xD	Pain due to internal prosthetic devices, implants and grafts, not elsewhere classified, subsequent encounter
T85.84xS	Pain due to internal prosthetic devices, implants and grafts, not elsewhere classified, sequela
T85.89xA	Other specified complication of internal prosthetic devices, implants and grafts, not elsewhere classified, initial encounter
T85.89xD	Other specified complication of internal prosthetic devices, implants and grafts, not elsewhere classified, subsequent encounter
T85.89xS	Other specified complication of internal prosthetic devices, implants and grafts, not elsewhere classified, sequela
T86.840	Corneal transplant rejection
T86.841	Corneal transplant failure
T86.842	Corneal transplant infection

T86.848	Other complications of corneal transplant
T86.849	Unspecified complication of corneal transplant

REVISIONS

07-09-2009	Policy added to the bcbsks.com web site. No policy changes were made.
11-19-2012	Description section updated
	In Policy section: ▪ Policy statement revised from the experimental / investigational position of: "Temporary and permanent keratoprostheses are considered experimental / investigational." To the medically necessary position of: "A. The permanent Boston Keratoprosthesis (Boston KPro) may be considered medically necessary for the treatment of corneal blindness under the following conditions: 1. The cornea is severely opaque and vascularized; AND 2. The patient has had two or more prior failed corneal transplants. Patients should be expected to be able to be compliant with postoperative care. B. A permanent keratoprosthesis for all other conditions is considered experimental / investigational. C. All other types of permanent keratoprostheses are considered experimental / investigational. D. The medical necessity of a temporary keratoprosthesis will be considered on a case-by-case basis."
	Rationale section updated
	In Coding section: ▪ Added the following diagnosis codes: 369.00-369.08, 369.60-369.69, 371.03, 695.13, 940.2, 940.3, 996.51, 996.69, 996.79
	References updated
06-07-2013	Rationale section updated
	References updated
02-05-2014	ICD-10 Diagnoses Codes added
08-20-2015	Policy published 07-21-2015 and effective 08-20-2015.
	Description section updated
	In Policy section: ▪ In Item A removed "The patient has had two or more prior failed corneal transplants." ▪ In Item A added the following indications: "Best-corrected vision is ≤20/400 in the affected eye and ≤20/40 in the opposite eye; AND No end-stage glaucoma or retinal detachment is present; AND The patient has one of the following indications: a. Multiple corneal transplant graft failures b. Stevens-Johnson syndrome c. Ocular cicatricial pemphigoid d. Autoimmune conditions with rare ocular involvement e. Ocular chemical burns f. An ocular condition unlikely to respond favorably to primary corneal transplant surgery (e.g., limbal stem cell compromise or postherpetic anesthesia)"
	Rationale section updated
	References updated
10-01-2017	In Coding section: ▪ Added ICD-10 Codes: H54.0X, H54.413A, H54.414A, H54.415A, H54.42A3, H54.42A4, H54.42A5 ▪ Removed ICD-10 Code: H54.0, H54.41, H54.42

10-25-2019	Policy published 09-25-2019. Policy effective 10-25-2019.
	Description section updated
	In Policy section: ▪ In Item A removed "permanent" and added "Dohlman-Doan", "opacification in situations where cadaveric corneal transplants have failed or have a very low likelihood of success" and "(See Policy Guidelines" to read "The Boston (Dohlman-Doane) Keratoprosthesis (Boston KPro) may be considered medically necessary for the surgical treatment of severe corneal opacification in situations where cadaveric corneal transplants have failed or have a very low likelihood of success. (See Policy Guidelines)" ▪ In Item A moved the failed or low likelihood of success list to the Policy Guidelines section. Removed Item B "A permanent keratoprosthesis for all other conditions is considered experimental / investigational." ▪ Removed Item D "The medical necessity of a temporary keratoprosthesis will be considered on a case-by-case basis." ▪ Updated the Policy Guidelines to include the failed or low likelihood of success list.
	Rationale section updated
	References updated
05-05-2021	Description section updated
	Rationale section updated
	References updated

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