

## Medical Policy



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### Title: Keratoprosthesis

#### **Professional**

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### **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 (eg, prior failed corneal transplants, chemical injuries, or certain immunologic conditions) 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.

### **Background**

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

Descemet's membrane; and the endothelium. 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 full-thickness donor cornea. In certain conditions, such as Stevens-Johnson syndrome; cicatricial pemphigoid; chemical injury; or prior failed corneal transplant, survival of transplanted cornea is poor. The keratoprosthesis has been 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 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 I KPro uses a donor cornea between a central stem and a back plate. The Boston type II prosthesis is a modification of the type I 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 (PMMA) device with a central optic region fused with a surrounding sponge skirt; the device is inserted in a 2-stage surgical procedure.

Autologous keratoprostheses use a central PMMA 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 (OOKP), 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 OOKP device requires a complex staged procedure, in which the cornea is first covered with buccal mucosa. The prosthesis itself consists of a PMMA optical cylinder, which replaces the cornea, held in place by a biological support made from a canine tooth extracted from the recipient. A hole is drilled through the dental root and alveolar bone, and the PMMA 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 cornea epithelial cells, which form the protective layer of the eye. Many of these materials and devices are currently being tested in vitro or in animal models.

## Regulatory Status

A keratoprosthesis is a class II FDA device intended to provide a transparent optical pathway through an opacified cornea, in an eye that is not a reasonable candidate for a corneal transplant. Two permanent keratoprostheses have received 510(k) marketing clearance by FDA, the Boston KPro (Dohlman-Doane Keratoprosthesis) and the AlphaCor (Chirila keratoprosthesis) Both devices are indicated as permanent implantable keratoprostheses for eyes that are not corneal transplant candidates and are made of materials that have been proven to be biocompatible. According to the 510(k) summary, the AlphaCor keratoprosthesis was shown to be substantially equivalent to the Dohlman Doane Type I keratoprosthesis. FDA product code: HQM.

## POLICY

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. Best-corrected vision is  $\leq 20/400$  in the affected eye and  $\leq 20/40$  in the opposite eye  
AND
3. No end-stage glaucoma or retinal detachment is present  
AND
4. 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 (eg, limbal stem cell compromise or postherpetic anesthesia)

Note: 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.

## **Policy Guidelines**

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.

## **RATIONALE**

The most recent literature review was performed through January 13, 2015.

Assessment of efficacy for therapeutic interventions involves a determination of whether the intervention improves health outcomes. The optimal study design for a therapeutic intervention is a randomized controlled trial (RCT) that includes clinically relevant measures of health outcomes. Intermediate outcome measures, also known as surrogate outcome measures, may also be adequate if there is an established link between the intermediate outcome and true health outcomes. Nonrandomized comparative studies and uncontrolled studies can sometimes provide useful information on health outcomes, but are prone to biases such as noncomparability of treatment groups, the placebo effect, and variable natural history of the condition.

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. This generally refers to the population of patients who have failed 1 or more corneal transplants and who therefore have very limited options to prevent blindness. Because this is considered to be a salvage procedure with no acceptable alternative treatment, comparative studies are limited/lacking. The available literature primarily consists of retrospective case series. This literature review examines the types of devices currently being tested in humans, focusing on reports that allow assessment of integration within the eye, durability, visual outcomes, and adverse events following implantation.

## **Osteo-Odonto Keratoprosthesis**

A systematic review from 2012 included 8 case series describing surgical outcomes and complication rates of the osteo-odonto-keratoprosthesis (OOKP).<sup>1</sup> Sample sizes ranged from 4 to 181 eyes. (The 2 largest series follow. The study by Hughes et al described next was not included in the systematic review.) At 5 years, the anatomic survival rate was 87.8% (range, 67%-100%), and at 20 years, the anatomic survival rate was 81.0% (3 studies; range, 65%-98%). About half of the patients obtained visual acuity better than 6/18. Visual acuity in the other patients was not described.

The largest series is by Falcinelli et al in 2005, who reported on OOKP in 181 patients.<sup>2</sup> At a median follow-up of 12 years, survival analysis estimated that 18 years after surgery, the probability of retaining an anatomically intact OOKP was 85% with reasonable visual acuity.

In 2008, investigators from Spain published a retrospective review of 227 patients who underwent OOKP (n=145), or osteokeratoprosthesis (OKP; n=82) using tibial bone in patients

who lacked canine teeth to assemble the prosthesis.<sup>3</sup> A second publication in 2011 from the same study examined the impact of clinical factors on long-term functional and anatomic outcomes.<sup>4</sup> The primary diagnosis was chemical or thermal burn (48%), Stevens-Johnson syndrome or Lyell syndrome (13%), cicatricial pemphigoid (11%), trachoma (11%), and 17% other or not assignable. The mean preoperative decimal best-corrected visual acuity (BCVA) 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 BCVA of 0.05 or more, and anatomic survival was defined as retention of the keratoprosthesis lamina. Mean follow-up was 8.4 years for OOKP and 3.5 years for OKP. Anatomic success at 10 years was estimated to be 66% for OOKP and 47% for OKP. Functional success at 10 years was estimated to be 38% for OOKP and 17% for OKP. The best functional survival was in the Stevens-Johnson group, followed by chemical burn and trachoma. The least favorable prognosis was for the thermal burn group. 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 reported vitreoretinal complications of the OOKP in a retrospective review of 35 cases performed at 1 hospital in England between 1996 and 2005.<sup>5</sup> Original 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 patients (23%). These included vitreous hemorrhage (n=3), rhegmatogenous retinal detachment (n=3), retinal detachment complicating endophthalmitis after lamina resorption and optic extrusion (n=2), and intraoperative choroidal hemorrhage (1 patient). Retinal detachment with loss of vision occurred in 5 of the 8 patients. A 2009 publication of 36 patients treated at the same hospitals between 1996 and 2006 (likely to be an overlap of the patients reported by Hughes et al<sup>5</sup>) estimated that the probability of retaining visual acuity was 53% at 5 years and 44% at 9 years.<sup>6</sup> In addition to the vitreoretinal complications causing loss of vision, resorption of the bony lamina to the extent of causing visual or anatomic compromise occurred in 7 cases (19%).

### **Boston Keratoprosthesis (KPro or Dohlman-Doane)**

One of the largest studies on the Boston Keratoprosthesis (Boston KPro) is a prospective series of 265 eyes (265 patients) from 18 medical centers, published by the Boston Type 1 Keratoprosthesis Study Group in 2012.<sup>7</sup> The objective of this analysis was to evaluate the time to development of retroprosthetic membranes. Most eyes (85.4%) had undergone an average of 2.2 (range, 1-8) penetrating keratoplasties before keratoprosthesis implantation. The remaining eyes (14.6%) were considered to be at high risk for penetrating keratoplasty failure and had received a primary keratoprosthesis. At a mean of 17.8 months of follow-up, 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 found to be the indication for the keratoprosthesis, specifically, infectious keratitis had a hazard ratio of 3.20, and aniridia had a hazard ratio of 3.13.

A 2013 report from the Boston Type 1 Keratoprosthesis Study Group assessed retention of the device in 300 eyes of 300 patients.<sup>8</sup> At a mean duration of 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 survival time was 3.8 years. Risk factors for

keratoprosthesis loss were autoimmune disease, ocular surface exposure, and number of prior failed penetrating keratoplasties.

An earlier report from the Boston Type 1 Keratoprosthesis Study Group was published in 2006.<sup>9</sup> Thirty-nine surgeons were encouraged to mail standardized pre- and postoperative reports on their patients to a central collection site. Seventeen sites (44%) provided data on 133 patients (136 eyes). The number of patients with BCVA of 20/200 increased from 3.6% to 57%; 19% had postoperative vision of 20/40 or better. Postoperative complications were reported in 109 patients, with 35 occurrences of retroprosthetic membrane and 21 cases of high intraocular pressures. A limitation of this report is potential bias in the voluntary submission of data. In a small (N=24) prospective study, Cortina and Hallak found that quality of life measured by the National Eye Institute Visual Function Questionnaire–25 significantly improved following Boston KPro implantation (from a score of 44.6 preoperatively to 70.0 at a mean 6-month follow-up).<sup>10</sup>

Retrospective series of the Boston type I KPro have been reported from a number of U.S. institutions. Srikumaran et al reported mean follow-up of 46.7 months (range, 6 weeks to 8.7 years) on 139 eyes of 133 patients who had received a Boston KPro prosthesis at 1 of 5 tertiary referral centers in the United States.<sup>11</sup> Twenty-seven percent of eyes underwent a primary KPro procedure while 73% had experienced 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.

### Outcomes

In 2010, Dunlap et al reported a retrospective analysis from 122 patients (126 eyes) at 2 centers who received a Boston type I keratoprosthesis between 2004 and 2007.<sup>12</sup> For most patients, the affected eye had a visual acuity of less than 20/400, and the other eye did not have better vision. Of the 126 eyes, 112 had a history of multiple failed corneal grafts, and 14 received the keratoprosthesis as a primary procedure due to the presence of limbal stem cell deficiency or the presence of significant ocular surface diseases. Following implantation, 22 eyes (17.4%) did not have improved vision and 8 eyes (6.3%) lost vision, leaving 76% of eyes with improved 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 noted to be lower than in other published studies, due in part to the presence of comorbid conditions, which included glaucoma and retinal detachment.

In 2009, Bradley et al reported outcomes from all of the 30 eyes (28 patients) who had previously received a Boston type I keratoprosthesis at their institution; 6 of the eyes had been included in the multicenter study described earlier.<sup>13</sup> Preoperative diagnoses were failed graft (26 eyes [87%]), chemical injury (3 eyes [10%]), and Stevens-Johnson syndrome (1 eye [3%]). Each eye had undergone an average of 2.6 prior corneal transplants (range, 0-7). Twenty eyes (66%) had preoperative glaucoma. Preoperative BCVA ranged from 20/150 to light perception (<20/200 in 83% of eyes). At an average follow-up of 19 months (range, 1-48 months) anatomic retention of the initial keratoprosthesis was 83%, with 5 failures (corneal melting in 4 eyes, infectious keratitis in 1 eye). The number of patients with BCVA of 20/200 or better increased

from 14% preoperatively to 77% postoperatively; 23% of patients achieved postoperative vision of 20/40 or better. In the 16 eyes followed up for at least 1 year, 12 (75%) achieved BCVA better than 20/200 and 4 (25%) achieved BCVA better than 20/40. The most common nonsurgical complication was retroprosthetic membrane formation (43% of eyes), followed by increased intraocular pressure (27%), corneal melt (17%), infectious keratitis (17%), endophthalmitis (10%), progression of glaucoma (7%), choroidal effusion or hemorrhage (7%), vitreous hemorrhage (3%), iris prolapse (3%), sterile vitritis (3%), posterior capsular opacity (3%), high myopic refraction (3%), hyphema (3%), and phthisis bulbi (3%). Keratoprosthesis replacement was performed at least once in 5 eyes (17% of patients).

Harissi-Dagher and Dohlman performed a retrospective study of 30 eyes (30 patients) with severe ocular trauma (6 mechanical trauma, 21 chemical burns, 3 thermal burns) implanted with a Boston KPro type I prosthesis at the Massachusetts Eye and Ear Infirmary since 1990.<sup>14</sup> Patients were followed up for an average of 35 months (range, 1-108 months). Anatomic success (retention of the prosthesis) was achieved in 5 of 5 of the mechanical trauma patients, 14 of 17 of the chemical burn patients, and 3 of 3 of the thermal burn patients. In addition to repeat KPro implantation in 3 patients (2 with early models), repair procedures for leaks were performed in 8 chemical burn eyes. Preoperative visual impairment was near total, with visual acuity ranging from counting fingers to light perception. Postoperatively, 80% of patients achieved BCVA of 20/400 or better, and 53% achieved BCVA of 20/60 or better. There was some attrition in visual acuity over time, primarily from progression of glaucoma in eyes with chemical burns. The authors noted that glaucoma progression is difficult to control in these patients because of damage to the trabecular meshwork and to the retinal ganglion cell layer and nerve fiber layer and that damage to the eye behind the cornea cannot always be diagnosed until the medium (eg, opaque cornea) is cleared. Aquavella et al reported on a case series of 25 patients who received a Dohlman-Doane device.<sup>15</sup> With a follow-up time ranging from 2 to 12 months, 20 of the 25 patients had a visual acuity of 20/400 or better, with 12 patients achieving better than 20/40 vision. There were no dislocations or extrusions, and no reoperations were required within the 2- to 12-month follow-up.

### Indications

A 2009 study reported expanding indications and outcomes from a consecutive series of 50 eyes of 49 patients implanted with the Boston type I keratoprosthesis and a donor cornea.<sup>16</sup> In addition to the single patient with bilateral prostheses, 31% of patients had good preoperative vision (visual acuity of 20/40 or better) in the contralateral eye. Patients had to meet the following criteria to be considered a candidate for keratoprosthesis implantation: visually significant corneal opacification (BCVA  $\leq$ 20/200); poor candidacy for repeat corneal transplantation because of a history of 2 or more failed transplantations, extensive corneal limbal stem cell failure with or without corneal vascularization and scarring, or both; and adequate visual potential for meaningful visual restoration. Exclusion criteria included: adequate potential for a successful outcome after penetrating keratoplasty; the presence of a comorbid ocular condition associated with a minimal chance of recovering meaningful vision, such as a chronic retinal detachment or near end-stage glaucoma; the presence of comorbid ocular conditions associated with an unacceptably high risk of postoperative complications, such as inadequate eyelid function, severe ocular surface desiccation, ocular surface keratinization, recalcitrant intraocular inflammation, patient inability or unwillingness to comply with the routine postoperative regimen, or a combination thereof. Of the 50 eyes that underwent implantation of the Boston KPro, 42 had a history of prior corneal transplantation, varying between 1 and 5 prior

transplantations (mean, 2.3). Preoperative visual acuity was 20/200 or worse in all eyes, with vision of counting fingers, hand movements, or light perception in 42 eyes (88%). Glaucoma was present in 38 eyes (76%) undergoing keratoprosthesis implantation, and tube shunt implantation was performed simultaneously with keratoprosthesis implantation in 45% of the eyes with preexisting glaucoma. A total of 57 Boston type I KPros were implanted in 50 eyes. Two eyes were excluded due to the early death of 1 patient and replacement of the type I KPro with a type II KPro in another patient. Nine of the 57 keratoprostheses implanted were removed, resulting in a retention rate of 84% during an average follow-up of 17 months (range, 3-49 months). Three of the 9 were removed in the first 6 months after surgery, and 5 were removed between 1 and 2 years after surgery. The final postoperative vision was improved over the preoperative vision in 38 eyes (79%), unchanged in 9 eyes (9%), and decreased in 1 eye (2%; from counting fingers preoperatively to light perception postoperatively). The percentage of eyes with postoperative visual acuity of 20/100 or better was 67% of 45 eyes followed up for at least 6 months (90% follow-up), 75% of 28 eyes (56%) followed up to 1 year, 69% of 13 eyes (26%) at 2 years, and all of the 7 eyes (14%) followed up for at least 3 years. In 38 eyes (76%), 1 or more postoperative complications developed. The most common postoperative complications were retroprosthetic membrane formation (44% of eyes) and persistent epithelial defects (38% of eyes). This detailed report provides information on visual outcomes and complications in a well-described patient population. The major limitation of this study is the small number of subjects who were followed up for more than 6 months.

Use of the Boston KPro has been reported in children and in patients with herpetic keratitis, autoimmune disease, aniridia, atopic keratoconjunctivitis, medication toxicity, and other corneal dystrophies.<sup>17</sup> The device has a lower retention rate when used for highly inflammatory, cicatricial, and autoimmune ocular disorders. Also reported is use of the KPro as a primary treatment in eyes considered to have little or no chance of success with penetrating keratoplasty.<sup>18</sup> The most common preoperative diagnosis was primary or secondary limbal stem cell disease (71.4%), including chemical/thermal injury (28.6%), aniridia (23.8%), and Stevens-Johnson syndrome (4.8%). Retention rate of the keratoprosthesis was 90.5% at a mean follow-up of 14.6 months (range, 6-36.3 months).

### **Complications**

Longer term vision outcomes and complications with the Boston type I KPro was reported by Greiner et al in 2011.<sup>19</sup> Included in the series were all of the 40 eyes of 35 patients who received a Boston KPro between 2004 and 2010 at their institution. Preoperative diagnoses included failed corneal transplants (47.5%), chemical injury (25%), and aniridia (12.5%). Preoperative visual acuity ranged from 20/150 to light perception and was 20/400 or less in 38 eyes (95%). Follow-up evaluations were performed at 1, 3, 6, 9, and 12 months and then annually, with a mean duration of follow-up of 33.6 months (range, 5-72 months). Of 36 eyes followed for at least 1 year, 32 (89%) achieved postoperative BCVA of 20/200 or more. The percentage of eyes that retained BCVA of 20/200 or more was 59% (19/32) at 1 year, 59% (16/27) at 2 years, 50% (7/14) at 3 years, and 29% (2/7) at 4 years or longer. The most common reason for vision loss (54% of the 13 eyes when BCVA  $\geq$ 20/200 was not retained) was end-stage glaucoma. Other complications included glaucoma drainage device erosion (22.5%), retroprosthetic membrane formation (55%), endophthalmitis (12.5%), and corneal melt (15%). In a separate publication, this group of investigators reported that of 25 eyes implanted with both the Boston type I KPro and glaucoma drainage devices, conjunctival breakdown occurred in association with 10 implants

in 9 eyes.<sup>20</sup> The authors note that glaucoma continues to be one of the most difficult postoperative management challenges in patients with a Boston type I keratoprosthesis.

Posterior segment complications were reported by Goldman et al in 2013.<sup>21</sup> Of 83 eyes (93 procedures) with follow-up of at least 6 months (range, 6-84 months), 38 eyes (40.9%) 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 compared with eyes that did not. Pujari et al reported outcomes from 29 eyes of 26 patients who received the Boston type II keratoprosthesis between 2000 and 2009 at the Massachusetts Eye and Ear Infirmary.<sup>22</sup> The type II keratoprosthesis is a modification of the original prosthesis, with an anterior extension to allow implantation through surgically closed eyelids and is generally reserved for patients with significant symblepharon or ankyloblepharon, ocular surface keratinization, and absence of normal lid function. Preoperative diagnoses were mucous membrane pemphigoid (51.7%), Stevens-Johnson syndrome/toxic epidermal necrolysis (41.4%), and other ocular surface disease (6.9%). In patients who had more than 1 year of follow-up (mean of 3.7 years), loss of visual acuity was found to occur due to retinal detachment (17.4%), end-stage glaucoma (8.7%), choroidal detachment (8.7%), endophthalmitis (4.3%), and unknown (21.7%). Fourteen eyes (48.3%) required treatment for retroprosthetic membranes. Of the total of 29 eyes, 12 (41.4%) either underwent reimplantation of the device or experienced partial or total extrusion of the keratoprosthesis during follow-up, corresponding to a hazard rate of 0.11 per person-year.

### **Other Devices**

Studies suggest that with the AlphaCor device, thinning or “melting” of the anterior corneal surface can lead to loss of biointegration.<sup>23,24</sup> This complication appears most prevalent in patients with ocular herpes, therefore the AlphaCor device is contraindicated in these patients. In 1 study, the percentage of eyes with visual acuity of better than 20/200 was 42% at an average 30-month follow-up.<sup>23</sup> No additional studies with the AlphaCor were identified in literature updates.

The BOKOP device is similar in concept to the AlphaCor device in that a microporous polymer is used to promote host tissue integration. However, the results with this device have been disappointing. In 1 case series of 11 patients with 5-year follow-up, the authors concluded that the BOKOP keratoprosthesis was only able to restore vision for a short postoperative period.<sup>25</sup> Limited success was due to instability of the device and postoperative complications.

### **Clinical Input Received 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 KPro in selected patients. Some reviewers recommended use without first attempting a transplant in specific conditions that have a poor prognosis for corneal transplant; however, other input indicated that this is controversial. Some reviewers recommended use only

in patients who have limited visual acuity in the contralateral eye. Overall, input indicated that the Boston Keratoprosthesis is reserved for cases in which no other alternative (ie, corneal transplantation) is available for treatment of corneal opacification.

### **Summary of Evidence**

Successful development of a keratoprosthesis requires durable clarity, retention, and bioincorporation. The published literature reveals ongoing modifications of the design of the keratoprosthesis, both in terms of the optics and the techniques used for anchoring the optic in place, the surgical technique, and the postoperative management. Randomized trials are unlikely due to very limited indications for this device and a lack of alternative treatments. Patients can serve as their own controls because the comparison of pre- and postoperative visual acuity has some validity given the predictable clinical course and relative lack of confounding factors. As a result, case series with pre- and postcomparisons are the primary type of evidence available; these types of studies are likely to remain small due to the low volume of the procedure.

Some large case series focus on the use of the osteo-odonto-keratoprosthesis (OOKP) in Europe. The OOKP device is not widely used in the United States. Anatomic retention with the OOKP appears good, but restoration of vision is not well-reported.

Based on the literature and clinical input, the Boston KPro is the most widely used and accepted keratoprosthesis in the United States at this time. Anatomic retention and visual success of this device at long term are uncertain, but short-term visual outcomes with the Boston KPro show improvement in a substantial percentage of patients. This remains a high-risk procedure that is associated with numerous complications (eg, growth of retroprosthetic membranes) and a probable need for additional surgery. Complications with other designs of keratoprostheses appear to be worse than those associated with the Boston KPro. Therefore, given the available evidence, the clinical input, and the absence of alternative treatment options, the Boston KPro may be considered medically necessary for patients with corneal opacification who have failed corneal transplantation or who have a condition not amenable to good outcomes from corneal transplant.

### **Practice Guidelines and Position Statements**

The U.K.'s National Institute for Clinical Excellence concluded in 2004 that, "Current evidence on the safety and efficacy of insertion of hydrogel keratoprosthesis does not appear adequate for this procedure to be used without special arrangements for consent and for audit or research."<sup>26</sup>

### **U.S. Preventive Services Task Force Recommendations**

Not applicable.

**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

ICD-9 Diagnoses

369.00-369.08	Blindness and low vision; Profound impairment, both eyes
369.60-369.69	Blindness and low vision; profound impairment, one eye
371.03	Central opacity of cornea
695.13	Stevens-Johnson syndrome
940.2	Alkaline chemical burn of cornea and conjunctival sac
940.3	Acid chemical burn of cornea and conjunctival sac
996.51	Mechanical complication of other specified prosthetic device, implant, and graft; due to corneal graft
996.69	Infection and inflammatory reaction due to internal prosthetic device, implant, and graft; Due to other internal prosthetic device, implant, and graft
996.79	Other complications of internal (biological) (synthetic) prosthetic device, implant, and graft; Due to other internal prosthetic device, implant, and graft

ICD-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: <ul style="list-style-type: none"> <li>▪ 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:               <ol style="list-style-type: none"> <li>1. The cornea is severely opaque and vascularized; AND</li> <li>2. The patient has had two or more prior failed corneal transplants.</li> </ol> </li> </ul>

	<p>Patients should be expected to be able to be compliant with postoperative care.</p> <p>B. A permanent keratoprosthesis for all other conditions is considered experimental / investigational.</p> <p>C. All other types of permanent keratoprostheses are considered experimental / investigational.</p> <p>D. The medical necessity of a temporary keratoprosthesis will be considered on a case-by-case basis."</p>
	Rationale section updated
	<p>In Coding section:</p> <ul style="list-style-type: none"> <li>▪ 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</li> </ul>
	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
	<p>In Policy section:</p> <ul style="list-style-type: none"> <li>▪ In Item A removed "The patient has had two or more prior failed corneal transplants."</li> <li>▪ In Item A added the following indications: "Best-corrected vision is <math>\leq 20/400</math> in the affected eye and <math>\leq 20/40</math> in the opposite eye; AND No end-stage glaucoma or retinal detachment is present; AND The patient has one of the following indications: <ul style="list-style-type: none"> <li>a. Multiple corneal transplant graft failures</li> <li>b. Stevens-Johnson syndrome</li> <li>c. Ocular cicatricial pemphigoid</li> <li>d. Autoimmune conditions with rare ocular involvement</li> <li>e. Ocular chemical burns</li> <li>f. An ocular condition unlikely to respond favorably to primary corneal transplant surgery (eg, limbal stem cell compromise or postherpetic anesthesia)"</li> </ul> </li> </ul>
	Rationale section updated
	References updated
10-01-2017	<p>In Coding section:</p> <ul style="list-style-type: none"> <li>▪ Added ICD-10 Codes: H54.0X, H54.413A, H54.414A, H54.415A, H54.42A3, H54.42A4, H54.42A5</li> <li>▪ Removed ICD-10 Code: H54.0, H54.41, H54.42</li> </ul>

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