Medical Policy
Corneal Collagen Cross-linking

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Policy Number: 905
BCBSA Reference Number: 9.03.28
NCD/LCD: Local Coverage Determination (LCD): Category III CPT® Codes (L33392)

Related Policies
Implantation of Intrastromal Corneal Ring Segments, #235

Policy
Commercial Members: Managed Care (HMO and POS), PPO, and Indemnity

Corneal collagen cross-linking using riboflavin and ultraviolet A may be considered MEDICALLY NECESSARY as a treatment of progressive keratoconus or corneal ectasia after refractive surgery in patients who have failed conservative treatment (eg spectacle correction, rigid contact lens).

Corneal collagen cross-linking using riboflavin and ultraviolet A is considered INVESTIGATIONAL for all other indications.

Medicare HMO BlueSM and Medicare PPO BlueSM Members

This is not a covered service.

Local Coverage Determination (LCD): Category III CPT® Codes (L33392)

For medical necessity criteria and coding guidance for Medicare Advantage members living outside of Massachusetts, please see the Centers for Medicare and Medicaid Services website for information regarding your specific jurisdiction at https://www.cms.gov.

Prior Authorization Information
Inpatient
- For services described in this policy, precertification/preauthorization IS REQUIRED for all products if the procedure is performed inpatient.

Outpatient
- For services described in this policy, see below for products where prior authorization might be required if the procedure is performed outpatient.
CPT Codes / HCPCS Codes / ICD Codes

Inclusion or exclusion of a code 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 as it applies to an individual member.

Providers should report all services using the most up-to-date industry-standard procedure, revenue, and diagnosis codes, including modifiers where applicable.

The following codes are included below for informational purposes only; this is not an all-inclusive list.

The above medical necessity criteria MUST be met for the following codes to be covered for Commercial Members: Managed Care (HMO and POS), PPO, and Indemnity:

<table>
<thead>
<tr>
<th>CPT Codes</th>
<th>Code Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>0402T</td>
<td>Collagen cross-linking of cornea (including removal of the corneal epithelium and intraoperative pachymetry when performed)</td>
</tr>
</tbody>
</table>

The following ICD Diagnosis Codes are considered medically necessary when submitted with the CPT code above if medical necessity criteria are met:

<table>
<thead>
<tr>
<th>ICD-10-CM Diagnosis codes:</th>
<th>Code Description</th>
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</thead>
<tbody>
<tr>
<td>H18.601</td>
<td>Keratoconus, unspecified, right eye</td>
</tr>
<tr>
<td>H18.602</td>
<td>Keratoconus, unspecified, left eye</td>
</tr>
<tr>
<td>H18.603</td>
<td>Keratoconus, unspecified, bilateral</td>
</tr>
<tr>
<td>H18.609</td>
<td>Keratoconus, unspecified, unspecified eye</td>
</tr>
<tr>
<td>H18.611</td>
<td>Keratoconus, stable, right eye</td>
</tr>
<tr>
<td>H18.612</td>
<td>Keratoconus, stable, left eye</td>
</tr>
<tr>
<td>H18.613</td>
<td>Keratoconus, stable, bilateral</td>
</tr>
<tr>
<td>H18.619</td>
<td>Keratoconus, stable, unspecified eye</td>
</tr>
<tr>
<td>H18.621</td>
<td>Keratoconus, unstable, right eye</td>
</tr>
<tr>
<td>H18.622</td>
<td>Keratoconus, unstable, left eye</td>
</tr>
<tr>
<td>H18.623</td>
<td>Keratoconus, unstable, bilateral</td>
</tr>
<tr>
<td>H18.629</td>
<td>Keratoconus, unstable, unspecified eye</td>
</tr>
<tr>
<td>H18.711</td>
<td>Corneal ectasia, right eye</td>
</tr>
<tr>
<td>H18.712</td>
<td>Corneal ectasia, left eye</td>
</tr>
<tr>
<td>H18.713</td>
<td>Corneal ectasia, bilateral</td>
</tr>
<tr>
<td>H18.719</td>
<td>Corneal ectasia, unspecified eye</td>
</tr>
</tbody>
</table>
**Description**

**KERATOCONUS AND ECTASIA**

Keratoconus is a bilateral dystrophy characterized by progressive ectasia (paracentral steepening and stromal thinning) that impairs visual acuity. While frequently diagnosed at a young age, the progression of keratoconus is variable. Results from a longitudinal study with 7 years of follow-up showed that, over the study period, there was a decrease of 2 high- and 4 low-contrast letters in best-corrected visual acuity (BCVA).\(^1\)\(^,\)\(^2\) About 1 in 5 patients showed a decrease of 10 or more letters in high-contrast visual acuity and one-third of patients showed a decrease of 10 or more letters in low-contrast visual acuity. Over 8 years of follow-up, there was a mean increase of 1.44 diopters (D) in First Definite Apical Clearance Lens (a rigid contact lens to measure corneal curvature) and 1.6 D in flatter keratometric reading.

Ectasia (also known as keratectasia, iatrogenic keratoconus, or secondary keratoconus) is a serious long-term complication of laser in situ keratomileusis (LASIK) surgery and photorefractive keratectomy. It is similar to keratoconus, but occurs postoperatively and primarily affects older populations. It may result from unrecognized preoperative keratoconus or, less frequently, from the surgery itself. Similar to keratoconus, it is characterized by progressive thinning and steepening of the cornea, resulting in corneal optical irregularities and loss of visual acuity.

**Treatment**

The initial treatment for keratoconus often consists of hard contact lenses. A variety of keratorefractive procedures have also been attempted, broadly divided into subtractive and additive techniques. Subtractive techniques include photorefractive keratectomy or laser in situ keratomileusis (LASIK), although generally, results of these techniques have been poor. Implantation of intrastromal corneal ring segments (see policy #235) is an additive technique in which the implants are intended to reinforce the cornea, prevent further deterioration, and potentially obviate the need for penetrating keratoplasty. Penetrating keratoplasty (ie, corneal grafting) is the last line of treatment. About 20% of patients with keratoconus will require corneal transplantation. All of these treatments attempt to improve the refractive errors, but are not disease-modifying.

Treatment options for ectasia include intraocular pressure-lowering drugs, and intracorneal ring segments. Frequently, a penetrating keratoplasty is required.

None of the currently available treatment options for keratoconus and corneal ectasia halt the progression of disease and corneal transplantation is the only option available when functional vision can no longer be achieved.

Corneal collagen cross-linking (CXL) has the potential to slow the progression of disease. It is performed with the photosensitizer riboflavin (vitamin B2) and ultraviolet A (UVA) irradiation. There are 2 protocols for CXL.

1. Epithelium-off CXL (also known as “epi-off”): In this method, about 8 mm of the central corneal epithelium is removed under topical anesthesia to allow better diffusion of the photosensitizer riboflavin into the stroma. Following de-epithelialization, a solution with riboflavin is applied to the cornea (every 1-3 minutes for 30 minutes) until the stroma is completely penetrated. The cornea is then irradiated for 30 minutes with ultraviolet A 370 nm, a maximal wavelength for absorption by riboflavin, while the riboflavin continues to be applied. The interaction of riboflavin and UVA causes the formation of reactive oxygen species, leading to additional covalent bonds (cross-linking) between collagen molecules, resulting in stiffening of the cornea. Theoretically, by using a homogeneous light source and absorption by riboflavin, the structures beyond a 400-micron thick stroma (endothelium, anterior chamber, iris, lens, retina) are not exposed to an ultraviolet dose that is above the cytotoxic threshold.

2. Epithelium-on CXL (also known as “epi-on” or transepithelial): In this method, the corneal epithelial surface is left intact (or may be partially disrupted) and a longer riboflavin loading time is needed.

Currently, the only CXL treatment approved by the Food and Drug Administration (FDA) is the epithelium-off method. There are no FDA-approved CXL treatments using the epithelium-on method. CXL is being
evaluated primarily for corneal stabilization in patients with progressive corneal thinning, such as keratoconus and corneal ectasia following refractive surgery. CXL may also have anti-edematous and antimicrobial properties.

Summary
For individuals who have progressive keratoconus who receive CXL using riboflavin and ultraviolet A, the evidence includes multiple randomized controlled trials (RCTs), systematic reviews, and nonrandomized studies. Relevant outcomes are change in disease status, functional outcomes, and treatment-related morbidity. In both pivotal RCTs, the primary end point (an intermediate outcome) of reducing maximum corneal curvature (Kmax) by 1 diopter (D) was achieved at month 3 and maintained at months 6 and 12 in CXL-treated patients, compared to sham controls. In the 2 RCTs, the difference in mean change in Kmax from baseline to 12 months was 1.9 and 2.3 D, respectively, favoring the CXL-treated patients. Long-term follow-up for visual acuity outcomes are needed. The adverse events associated with CXL include corneal opacity (haze), corneal epithelial defects, and other ocular findings. Most adverse events resolved in the first month but, in a few (1%-6%) patients, continued for 6 to 12 months. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals who have corneal ectasia after refractive surgery who receive CXL using riboflavin and ultraviolet A, the evidence includes multiple RCTs, systematic reviews, and nonrandomized studies. Relevant outcomes are change in disease status, functional outcomes, and treatment-related morbidity. In both pivotal RCTs, the primary end point (an intermediate outcome) of reducing Kmax by 1 D was achieved at month 3 and maintained at months 6 and 12 in the CXL-treated patients compared to sham controls. In the 2 RCTs, the difference in mean change in Kmax from baseline to 12 months was 2.0 and 1.1 D, respectively, favoring CXL-treated patients. Long-term follow-up for visual acuity outcomes are needed. The adverse events associated with CXL include corneal opacity (haze), corneal epithelial defects, and other ocular findings. Most adverse events resolved in the first month, but, in a few (1%-6%) patients, continued for 6 to 12 months. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

Policy History

<table>
<thead>
<tr>
<th>Date</th>
<th>Action</th>
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<tbody>
<tr>
<td>4/2016</td>
<td>New references added from BCBSA National medical policy.</td>
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<tr>
<td>1/2016</td>
<td>Clarified coding information.</td>
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<tr>
<td>6/2015</td>
<td>New references added from BCBSA National medical policy.</td>
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<td>7/2014</td>
<td>New references added from BCBSA National medical policy.</td>
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<tr>
<td>5/2013</td>
<td>New references from BCBSA National medical policy.</td>
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<tr>
<td>2/2013</td>
<td>New policy describing ongoing non-coverage.</td>
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Information Pertaining to All Blue Cross Blue Shield Medical Policies
Click on any of the following terms to access the relevant information:
- Medical Policy Terms of Use
- Managed Care Guidelines
- Indemnity/PPO Guidelines
- Clinical Exception Process
- Medical Technology Assessment Guidelines

References


7. Avedo Inc. Avedro Briefing Package for Joint Meeting of the Dermatologic and Ophthalmic Drugs Advisory Committee and Ophthalmic Device Panel of the Medical Devices Advisory Committee NDA 203324; Photorexa Viscous and Photorexa (riboflavin ophthalmic solution) and KXL System (UVA light source) Avedo, Inc. 2015; http://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/Drugs/Dermatologica


