



MASSACHUSETTS

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## 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) (A56195)

#### 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** under the following conditions:

- as a treatment of progressive keratoconus, **or**
- as a treatment of corneal ectasia resulting from 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 Blue<sup>SM</sup> and Medicare PPO Blue<sup>SM</sup> Members

This is not a covered service.

Medical necessity criteria and coding guidance for **Medicare Advantage members living in Massachusetts** can be found through the link below.

[Local Coverage Determinations \(LCDs\) for National Government Services, Inc.](#)

Local Coverage Determination (LCD): Category III CPT® Codes (L33392) (A56195)

**Note:** To review the specific LCD, please remember to click “accept” on the CMS licensing agreement at the bottom of the CMS webpage.

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 at <https://www.cms.gov> for information regarding your specific jurisdiction.

## 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**.

	Outpatient
<b>Commercial Managed Care (HMO and POS)</b>	Prior authorization is <b>not required</b> .
<b>Commercial PPO and Indemnity</b>	Prior authorization is <b>not required</b> .
<b>Medicare HMO Blue<sup>SM</sup></b>	This is <b>not</b> a covered service.
<b>Medicare PPO Blue<sup>SM</sup></b>	This is <b>not</b> a covered service.

## 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:**

### CPT Codes

CPT codes:	Code Description
0402T	Collagen cross-linking of cornea, including removal of the corneal epithelium and intraoperative pachymetry, when performed (Report medication separately)

### HCPCS Codes

HCPCS codes:	Code Description
J2787	Riboflavin 5'-phosphate, ophthalmic solution, up to 3 mL

The following ICD Diagnosis Codes are considered medically necessary when submitted with the CPT and/or HCPCS codes above if medical necessity criteria are met:

### ICD-10 Diagnosis Codes

ICD-10-CM Diagnosis codes:	Code Description
H18.601	Keratoconus, unspecified, right eye
H18.602	Keratoconus, unspecified, left eye
H18.603	Keratoconus, unspecified, bilateral
H18.609	Keratoconus, unspecified, unspecified eye
H18.611	Keratoconus, stable, right eye

H18.612	Keratoconus, stable, left eye
H18.613	Keratoconus, stable, bilateral
H18.619	Keratoconus, stable, unspecified eye
H18.621	Keratoconus, unstable, right eye
H18.622	Keratoconus, unstable, left eye
H18.623	Keratoconus, unstable, bilateral
H18.629	Keratoconus, unstable, unspecified eye
H18.711	Corneal ectasia, right eye
H18.712	Corneal ectasia, left eye
H18.713	Corneal ectasia, bilateral
H18.719	Corneal ectasia, unspecified eye

## Description

### Treatment of Keratoconus and Ectasia

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 keratomileuses, although generally, results of these techniques have been poor. Implantation of intrastromal corneal ring segments (see evidence review 9.03.14) 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, penetrating keratoplasty is required.

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

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

1. Epithelium-off corneal collagen cross-linking (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 ultraviolet A 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-µm thick stroma (endothelium, anterior chamber, iris, lens, retina) are not exposed to an ultraviolet dose that is above the cytotoxic threshold.
2. Epithelium-on corneal collagen cross-linking (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 corneal collagen cross-linking treatment approved by the U.S. Food and Drug Administration (FDA) is the epithelium-off method. There are no FDA approved corneal collagen cross-linking treatments using the epithelium-on method. Corneal collagen cross-linking is being evaluated primarily for corneal stabilization in patients with progressive corneal thinning, such as keratoconus and

corneal ectasia following refractive surgery. Corneal collagen cross-linking may also have anti-edematous and antimicrobial properties.

## Summary

Corneal collagen cross-linking is a photochemical procedure approved by the U.S. Food and Drug Administration (FDA) for the treatment of progressive keratoconus and corneal ectasia. Keratoconus is a dystrophy of the cornea characterized by progressive deformation (steepening) of the cornea while corneal ectasia is keratoconus that occurs after refractive surgery. Both lead to functional loss of vision and need for corneal transplantation.

For individuals who have progressive keratoconus who receive corneal collagen cross-linking 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 endpoint (an intermediate outcome) of reducing maximum corneal curvature by 1 diopter (D) was achieved at month 3 and maintained at months 6 and 12 in corneal collagen cross-linking treated patients compared with sham controls. In both RCTs, the difference in mean change in maximum corneal curvature from baseline to 12 months was 1.9 D and 2.3 D, respectively, favoring the corneal collagen cross-linking treated patients. Several other studies measured visual acuity and found significant and lasting improvements in corrected visual acuity and other measures with corneal collagen cross-linking. Long-term follow-up for visual acuity outcomes is needed. The adverse events associated with corneal collagen cross-linking include corneal opacity (haze), corneal epithelial defects, and other ocular findings. Most adverse events resolved in the first month but continued in a few (1%-6%) patients 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 corneal collagen cross-linking using riboflavin and ultraviolet A, the evidence includes multiple RCTs and nonrandomized studies. Relevant outcomes are change in disease status, functional outcomes, and treatment-related morbidity. In both pivotal RCTs, the primary endpoint (an intermediate outcome) of reducing maximum corneal curvature by 1 D was achieved at month 3 and maintained at months 6 and 12 in the corneal collagen cross-linking treated patients compared with sham controls. In both RCTs, the difference in mean change in maximum corneal curvature from baseline to 12 months was 2.0 D and 1.1 D, respectively, favoring corneal collagen cross-linking treated patients. Other trials showed significant improvements not only in maximum corneal curvature but also visual acuity measures in the corneal collagen cross-linking groups compared with the control groups. The first and longest trial followed patients up to 3 years and saw continued improvement in visual acuity with corneal collagen cross-linking. Long-term follow-up for visual acuity outcomes is needed. The adverse events associated with corneal collagen cross-linking were the same for the ectasia trials as for the keratoconus. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

## Policy History

Date	Action
7/2020	Medically necessary statement clarified.
5/2020	BCBSA National medical policy review. Description, summary and references updated. Policy statements unchanged.
1/2020	Clarified coding information.
4/2019	BCBSA National medical policy review. Description, summary and references updated. Policy statements unchanged.
1/2019	Clarified coding information.
8/2018	Medically necessary statement clarified. 8/27/2018
4/2018	New references added from BCBSA National medical policy. Summary clarified.
8/2017	BCBSA National medical policy review. New medically necessary indications described. Investigational indications clarified. Clarified coding information. Effective 8/1/2017.
4/2016	New references added from BCBSA National medical policy.

1/2016	Clarified coding information.
6/2015	New references added from BCBSA National medical policy.
7/2014	New references added from BCBSA National medical policy.
5/2013	New references from BCBSA National medical policy.
2/2013	New policy describing ongoing non-coverage.

## 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](#)

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