

Medical Policy

Corneal Collagen Cross-linking

Policy Number: 015

	Commercial and Qualified Health Plans	MassHealth	Medicare Advantage
Authorization required	X	X	X
Authorization not required			
Not covered			

Overview

The purpose of this document is to describe the guidelines Mass General Brigham Health Plan utilizes to determine medical appropriateness for corneal collagen cross-linking. The treating specialist must request prior authorization for the procedure.

Coverage Guidelines

Mass General Brigham Health Plan covers corneal collagen cross-linking for the treatment of progressive corneal thinning caused by progressive keratoconus or corneal ectasia following refractive surgery. Mass General Brigham Health Plan will **only authorize the epithelium-off corneal collagen cross-linking protocol**, as it is currently the only corneal collagen cross-linking approved by the Food and Drug Administration (FDA).

Mass General Brigham Health Plan covers medically necessary corneal collagen cross-linking treatment in the following instances:

1. For members with **progressive keratoconus** corneal collagen cross-linking is considered medically necessary when all of the following conditions are met:
 - a. Diagnosis of keratoconus based on keratometry and corneal mapping; and
 - b. Any of the following changes have occurred within 24 months:
 - i. increase of 1.00 diopters (D) or more in the steepest keratometry measurement; or
 - ii. increase of 1.00 D or more in manifest cylinder; or
 - iii. increase of 0.50 D or more in manifest refraction spherical equivalent (MRSE); and
 - c. Member is age 14 years or older; and
 - d. Corrected distance visual acuity (CDVA) worse than 20/20 with properly fitted spectacles or contact lenses; and
 - e. Corneal thickness 300 microns or more; and
 - f. No history of corneal or systemic disease that would interfere with healing post-procedure.
2. For members with a diagnosis of **corneal ectasia following refractive surgery**, corneal collagen cross-linking is considered medically necessary when all of the following conditions are met:
 - a. Member is age 14 years of age or older; and
 - b. Consistent axial topography pattern, including relative inferior steepening with inferior-superior difference of at least 1.5 diopters; and
 - c. Corrected distance visual acuity worse than 20/20; and
 - d. Corneal thickness of at least 300 micrometers at the thinnest area; and
 - e. No history of corneal or systemic disease that would interfere with healing post-procedure.

Exclusions

Mass General Brigham Health Plan does not provide coverage for corneal collagen cross-linking for conditions that do not meet the criteria noted above.

Medicare Variation

Mass General Brigham Health Plan uses guidance from the Centers for Medicare and Medicaid Services (CMS) for coverage determinations for its Medicare Advantage plan members. National Coverage Determinations (NCDs), Local Coverage Determinations (LCDs), Local Coverage Articles (LCAs) and documentation included in the Medicare manuals are the basis for coverage determinations. When there is no guidance from CMS for the requested service, Mass General Brigham Health Plan’s medical policies are used for coverage determinations.

Definitions

Corneal Collagen Cross-linking: A procedure used that uses riboflavin drops, ultraviolet light, and a photosensitizer to strengthen bonds in the cornea. Ultraviolet (UV) light is combined with riboflavin eye drops to create new collagen crosslinks in the cornea, strengthening and stabilizing the cornea. The viscous riboflavin solution is applied to the eye topically before and during UV irradiation using the KXL System.

Ectasia: 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.

Keratoconus: 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.

Codes

The following codes are included below for informational purposes only; inclusion of a code does not constitute or imply coverage or reimbursement.

This list of codes applies to commercial and MassHealth plans only.

Authorized CPT/HCPCS Codes	Code Description
0402T	Collagen cross-linking of cornea (including removal of the corneal epithelium and intraoperative pachymetry when performed)
J2787	Riboflavin 5'-phosphate, ophthalmic solution, up to 3 mL

Effective

November 2023: Annual update. Medicare Advantage added to table.
December 2022: Annual update. Criteria changed under both #1 and #2 to include list of conditions.
November 2021: Annual update. References updated.
November 2020: Annual update. References updated.
November 2019: Annual Update. References updated.
January 2019: Code update.
October 2018: Effective date.

References

Alnawaiseh M, Rosentreter A, Eveslage M, Eter N, Zumhagen L. Changes in Corneal Transparency After Cross-linking for Progressive Keratoconus: Long-term Follow-up. *Journal of Refractive Surgery* 2015;31(9):614–8.

Craig JA, Mahon J, Yellowlees A, Barata T, Glanville J, Arber M, Mandava L, Powell J, Figueiredo F. Epithelium-off photochemical corneal collagen cross-linkage using riboflavin and ultraviolet a for keratoconus and keratectasia:



a systematic review and meta-analysis. *Ocul Surf.* 2014 Jul;12(3):202-14. doi: 10.1016/j.jtos.2014.05.002. Epub 2014 May 14. PMID: 24999102.

Eissa SA, Yassin A. Prospective, randomized contralateral eye study of accelerated and conventional corneal cross-linking in pediatric keratoconus. *Int Ophthalmol.* 2019 May;39(5):971-979. doi: 10.1007/s10792-018-0898-y. Epub 2018 Mar 21. PMID: 29564806.

Fard AM, Reynolds AL, Lillvis JH, Nader ND. Corneal collagen cross-linking in pediatric keratoconus with three protocols: a systematic review and meta-analysis. *J AAPOS.* 2020 Dec;24(6):331-336. doi: 10.1016/j.jaapos.2020.08.013. Epub 2020 Dec 3. PMID: 33279597.

HAYES Directory Report™. Comparative effectiveness review. Corneal Crosslinking for treatment of keratoconus. PA: HAYES, Inc., ©2018 Winifred S. Hayes, Inc. Feb 2018.

Hersh PS, Greenstein SA, Fry KL. Corneal collagen crosslinking for keratoconus and corneal ectasia: One-year results. *J Cataract Refract Surg.* Jan 2011;37(1):149-160. PMID 21183110.

Hersh PS, Stulting RD, Muller D, et al. U.S. multicenter clinical trial of corneal collagen crosslinking for treatment of corneal ectasia after refractive surgery. *Ophthalmology.* Oct 2017;124(10):1475-1484. PMID 28655538

Kobashi H, Rong SS. Corneal Collagen Cross-Linking for Keratoconus: Systematic Review. *BioMed Research International.* 2017;2017:8145651. doi:10.1155/2017/8145651.

Madeira C, Vasques A., et al. Transepithelial accelerated versus conventional corneal collagen crosslinking in patients with keratoconus: a comparative study. *Clinical Ophthalmology* 2019;Volume 13:445–52

Marafon SB, Kwitko S, Marinho DR. Long-term results of accelerated and conventional corneal cross-linking. *Int Ophthalmol.* 2020 Oct;40(10):2751-2761. doi: 10.1007/s10792-020-01462-w. Epub 2020 Jun 13. PMID: 32535751.

Meiri Z, Keren S, Rosenblatt A, et al. Efficacy of corneal collagen cross-linking for the treatment of keratoconus: a systematic review and meta-analysis. *Cornea.* Mar 2016;35(3):417-428. PMID 26751990

National Institute for Health and Care Excellence (NICE). Photochemical corneal collagen cross-linkage using riboflavin and ultraviolet A for keratoconus and keratectasia [IPG466]. 2013; <https://www.nice.org.uk/guidance/ipg466>. Accessed October 1, 2019

Poli M, Lefevre A, Auxenfans C, Burillon C. Corneal Collagen Cross-linking for the Treatment of Progressive Corneal Ectasia: 6-Year Prospective Outcome in a French Population. *Am J Ophthalmol.* 2015;160(4):654-662.e1. doi:10.1016/j.ajo.2015.06.027.

Shajari M, Kolb CM, Agha B, et al. Comparison of standard and accelerated corneal cross-linking for the treatment of keratoconus: a metaanalysis. *Acta Ophthalmol.* 2019 Feb;97(1):e22-e35. doi: 10.1111/aos.13814. Epub 2018 May 31.

Singh T, Taneja M, Murthy S, Vaddavalli PK. Evaluation of safety and efficacy of different protocols of collagen cross linking for keratoconus. *Rom J Ophthalmol.* 2020 Apr-Jun;64(2):158-167. PMID: 32685782; PMCID: PMC7339692.

Syakakis E, Karim R, Evans JR, et al. Corneal collagen cross-linking for treating keratoconus. *Cochrane Database Syst Rev.* Mar 24 2015;3(3):CD010621. PMID 25803325

Tian, Mingxia MS a; Ma, Ping MD b; Zhou, Weiyan MD b; Feng, Jie MS a; Mu, Guoying MD. Outcomes of corneal crosslinking for central and paracentral keratoconus. *Medicine.* March 2017 96:10(e6247)



Turhan SA, Yargi B, Toker E. Efficacy of Conventional Versus Accelerated Corneal Cross-linking in Pediatric Keratoconus: Two-Year Outcomes. *J Refract Surg.* 2020 Apr 1;36(4):265-269. doi: 10.3928/1081597X-20200302-01. PMID: 32267958.

Vinciguerra P, Rosetta P, Legrottaglie EF, et al. Iontophoresis CXL With and Without Epithelial Debridement Versus Standard CXL: 2-Year Clinical Results of a Prospective Clinical Study. *J Refract Surg.* 2019 Mar 1;35(3):184-190.

Wan Q, Wang D, Ye H, Tang J, Han Y. A review and meta-analysis of corneal cross-linking for post-laser vision correction ectasia. *Journal of Current Ophthalmology.* 2017;29(3):145-153. doi:10.1016/j.joco.2017.02.008.

