Molina Clinical Policy
Corneal Collagen Cross-Linking (CXL)
Policy No. 328

Last Approval: 08/13/2025
Next Review Due By: August 2026

DISCLAIMER

This Molina Clinical Policy (MCP) is intended to facilitate the Utilization Management process. Policies are not a supplementation or recommendation for treatment; Providers are solely responsible for the diagnosis, treatment, and clinical recommendations for the Member. It expresses Molina's determination as to whether certain services or supplies are medically necessary, experimental, investigational, or cosmetic for purposes of determining appropriateness of payment. The conclusion that a particular service or supply is medically necessary does not constitute a representation or warranty that this service or supply is covered (e.g., will be paid for by Molina) for a particular Member. The Member's benefit plan determines coverage – each benefit plan defines which services are covered, which are excluded, and which are subject to dollar caps or other limits. Members and their Providers will need to consult the Member's benefit plan to determine if there are any exclusion(s) or other benefit limitations applicable to this service or supply. If there is a discrepancy between this policy and a Member's plan of benefits, the benefits plan will govern. In addition, coverage may be mandated by applicable legal requirements of a State, the Federal government or CMS for Medicare and Medicaid Members. CMS's Coverage Database can be found on the CMS website. The coverage directive(s) and criteria from an existing National Coverage Determination (NCD) or Local Coverage Determination (LCD) will supersede the contents of this MCP and provide the directive for all Medicare members. References included were accurate at the time of policy approval and publication.

OVERVIEW

Keratoconus is a corneal dystrophy characterized by localized thinning of the corneal stroma, leading to secondary ectasia (Wayman 2024). This progressive condition results in worsening myopia, irregular astigmatism, and deteriorating visual acuity, significantly impacting quality of life ([3]AAO 2024). Treatment is guided by disease severity. In mild cases, spectacles or soft contact lenses may be sufficient, while more advanced cases often require rigid gas permeable or scleral contact lenses ([3]AAO 2024). Keratoplasty, or corneal transplantation, is typically reserved for patients with advanced disease who experience suboptimal vision or develop intolerance to contact lenses (Hayes 2022). Initially, rigid lenses are used to flatten the cornea and help maintain its shape. As the disease progresses – or if lens therapy fails - penetrating keratoplasty (a full-thickness corneal transplant) may become necessary (Hayes 2022).

Various keratorefractive procedures have been explored as alternatives to transplantation. These techniques are generally classified as either subtractive or additive. Subtractive methods, such as laser-assisted in situ keratomileusis (LASIK), have demonstrated poor outcomes in keratoconus and therefore are not recommended. Additive procedures, like intracorneal ring segments (e.g., Intacs), involve surgical placement into the corneal stroma to flatten the central cornea and reinforce the cone. These devices are intended to stabilize cornea shape, slow disease progression, and potentially delay or prevent the need for transplantation. Nonetheless, approximately 20% of keratoconus patients eventually require corneal transplantation ([3]AAO 2024). While these interventions may reduce refractive errors, they do not modify the underlying pathology. As a result, patients with advanced disease often require transplantation to achieve functional vision (Hayes 2022).

Corneal Ectasia following refractive surgery – also known as keratectasia, iatrogenic keratoconus, or secondary keratoconus – is a progressive, long-term condition marked by corneal thinning and steepening, leading to optical irregularities and declining vision (Hayes 2022). It develops postoperatively, most commonly in older individuals ([2]AAO 2024), and is primarily linked to prior refractive procedures such as LASIK and photorefractive keratectomy (PRK) ([2]AAO 2024). The pathophysiology involves weakening of the corneal structure following surgery, leaving the cornea vulnerable to outward distension under intraocular pressure. Management options include corneal collagen cross-linking (CXL) to stabilize the cornea, along with visual correction using spectacles, rigid gas permeable contact lenses, intraocular lenses, or intracorneal ring segments (e.g., Intacs, Keraring, Ferrara ring, Myoring) (Hayes 2023). However, many patients experience discomfort or intolerance to rigid lens, and the effectiveness of ring implants may diminish overtime. Additional treatments include ablative or surgical options such as photorefractive keratectomy (PTK), phototherapy keratectomy, lamellar keratoplasty, and penetrating keratoplasty ([2]AAO 2024). Despite these options, Hayes (2022) notes that “none of these treatments change the course of the disease, and patients with advanced disease frequently require corneal transplantation.”

Both progressive keratoconus and postoperative corneal ectasia can result in significant visual impairment and commonly progress to the point of requiring transplantation. Since current therapies do not stop disease progression, corneal transplantation remains the definitive treatment option when functional vision is no longer attainable (Hayes 2023).

Corneal collagen cross-linking (CXL) is an FDA-approved, in-office procedure used to treat progressive keratoconus and corneal ectasia, with the goal of preserving visual function ([3]AAO 2024). CXL works by strengthening the cornea, slowing or halting the progressive thinning and steepening associated with keratoconus, other corneal diseases, or post-refractive surgery ectasia (Wayman 2024). The procedure induces collagen cross-links within the corneal stroma using a combination of riboflavin (vitamin B2) and ultraviolet A (UVA) light, resulting in increased biomechanical stiffness ([1]AAO 2024; Hayes 2022). While CXL enhances the structural integrity of the cornea, it does not directly improve visual acuity. There are two primary methods of CXL:

1. **Epithelium-off collagen crosslinking ("epi-off" CXL):** In the epi-off CXL procedure, the corneal epithelium is removed to allow better penetration of liquid riboflavin into the stroma ([1]AAO 2024). Riboflavin drops are applied to the corneal surface before and during UVA light exposure ([3]AAO 2024). Post-procedure care typically includes topical antibiotics and anti-inflammatory drops, with topical steroids used as needed. In some cases, a bandage contact lens may also be used temporarily. The procedure is done on one eye at a time and may be repeated if necessary. According to Wayman (2024), epi-off CXL is contraindicated in patients with active or prior herpes simplex keratitis, extremely thin corneas, or corneal hydrops. **While conventional CXL (C-CXL) is considered a procedure and not directly regulated by the FDA, any associated drugs, devices, or diagnostic tools used during the procedure are subject to FDA oversight.**

   Photrexa (riboflavin 5-phosphate ophthalmic solution) and Photrexa Viscous (riboflavin 5-phosphate in 20% dextran solution) have been FDA-approved for use with the KXL UVA light system for the treatment of progressive keratoconus (CDER 2016). Photrexa Viscous and Photrexa are photoenhancers indicated for use with the KXL System in CXL for the treatment of progressive keratoconus, according to the package insert. The original indication was expanded to include corneal ectasia following refractive surgery (FDA 2016).

2. **Epithelium-on CXL ("epi-on" or transepithelial):** The corneal epithelial surface is left intact (or only minimally disrupted), requiring a longer riboflavin loading time ([2]AAO 2024). According to the AAO ([1]2024), studies thus far have demonstrated lower effectiveness of CXL with this method. Currently, **no FDA-approved treatments exist using the epithelium-on approach of method of CXL.**

CXL can also be combined with other interventions, such as intrastromal corneal ring segments, PRK or phakic intraocular lens implantation, in a strategy referred to as "CXL-plus" (Hayes 2023). These combination therapies aim to enhance visual acuity; however, the evidence supporting their efficacy remains limited (Hayes 2023).

Epithelium-off CXL ("epi-off") Treatment

- CXL with riboflavin 5'-phosphate ophthalmic solution (Photrexa 0.146%; Photrexa Viscous 0.146% in Dextran 20%) and UVA irradiation (KXL System) reduces clinical progression and improves visual acuity in individuals with progressive keratoconus or post-refractive surgery corneal ectasia. However, it remains uncertain whether it significantly reduces the long-term need for corneal transplantation. Randomized Controlled Trials (RCTs) have shown that corneal CXL can reduce or even reverse corneal steepening in the short term, improving vision. However, long-term outcomes remain unclear.
- Relevant outcome measures include disease progression, functional vision, and procedure-related morbidity. Studies report improvements in corneal thickness and visual maintained over two to three years (Moghadam et al. 2019).
- Some retrospective studies have indicated positive 10-year outcomes; however these findings are limited by small sample sizes and incomplete data across patient groups. Larger prospective studies are needed to better assess long-term effectiveness and potential complications.

Further research is required to determine whether corneal CXL improves long-term outcomes and to evaluate other crucial factors, such as defining the inclusion and exclusion criteria for progression of disease, types and number of prior refractive procedures (including non-laser based refractive procedures), optimal timing between CXL and previous surgery, and how initial versus post-treatment corneal thickness affects outcomes (CDER 2016).

COVERAGE POLICY

Epithelium-off CXL using riboflavin and ultraviolet A for the treatment of progressive keratoconus or corneal ectasia resulting from refractive surgery may be **considered medically necessary** when ALL the following clinical criteria are met:

1. Member is age 14 years or older

2. Diagnosis of ONE of the following supported by clinical documentation:
   a. Progressive keratoconus (thinning of the cornea)
   b. Corneal ectasia (corneal thinning and protrusion) after refractive surgery (e.g., LASIK or PRK)

   NOTE: In keratoconus and ectatic disease, diagnostic metrics include corneal topography, corneal pachymetry, corneal epithelial thickness, posterior corneal topography, wavefront analysis, and corneal biomechanics. Documentation may include any of the listed diagnostic metrics.

2. Member meets ONE of the following according to specific diagnosis:
   a. Progressive Keratoconus
      i. At least ONE of the following changes have occurred within the 24 months:
         a) Increase of 1.00 diopters (D) or more in the steepest keratometry measurement
         b) Increase of 1.00 D or more in manifest cylinder
         c) Increase of 0.50 D or more in manifest refraction spherical equivalent (MRSE)
      ii. Corrected distance visual acuity worse than 20/20 with properly fitted spectacles or contact lenses
      iii. Corneal thickness ≥ 300 microns
   b. Corneal ectasia resulting from refractive surgery (e.g., LASIK) and ALL the following:
      i. Corrected distance visual acuity worse than 20/20
      ii. Corneal thickness of at least 300 microns at the thinnest area

3. Requested treatment for ONE of the following. Documentation required:
   a. Left eye
   b. Right eye

4. Absence of ALL the following contraindications:
   a. Visual disturbance from a significant central corneal opacity or other eye disease (e.g., herpetic keratitis, neurotrophic keratopathy)
   b. History of corneal or systemic disease that would interfere with healing after the procedure (e.g., chemical injury or delayed epithelial healing in the past)
   c. Corneal thickness of < 300 microns
   d. Prior herpetic infection (due to possible viral reactivation)
   e. Concurrent infection
   f. Severe corneal scarring or opacification
   g. History of corneal surgery, including intracorneal ring segments
   h. History of poor epithelial wound healing; or History of corneal disease that would interfere with healing after the procedure, such as chemical injury or delayed epithelial healing in the past
   i. Severe ocular surface disease (e.g., dry eye)
   j. Autoimmune disorders known to impair corneal healing (e.g., rheumatoid arthritis, systemic lupus erythematosus, Sjögren's syndrome, ocular cicatricial pemphigoid, Behçet's disease, Stevens–Johnson syndrome, and granulomatosis with polyangiitis)

Continuation of Therapy
Repeat treatment in the same eye is considered **experimental, investigational, and unproven** due to insufficient evidence in the peer-reviewed medical literature to establish long-term safety, efficacy, and effect on net health outcomes.

DOCUMENTATION REQUIREMENTS. Molina Healthcare reserves the right to require that additional documentation be made available as part of its coverage determination; quality improvement; and fraud; waste and abuse prevention processes. Documentation required may include, but is not limited to, patient records, test results and credentials of the provider ordering or performing a drug or service. Molina Healthcare may deny reimbursement or take additional appropriate action if the documentation provided does not support the initial determination that the drugs or services were medically necessary, not investigational, or experimental, and otherwise within the scope of benefits afforded to the member, and/or the documentation demonstrates a pattern of billing or other practice that is inappropriate or excessive.

DRUG INFORMATION

ROUTE OF ADMINISTRATION: Photrexa-Photrexa Viscous Kit: Photrexa 0.146%; Photrexa Viscous 0.146% in Dextran 20% (6 mL) [contains dextran]. Photrexa is administered during the CXL procedure.

DRUG CLASS: Corneal Collagen Cross-Linking Agent, Ophthalmic; Ophthalmic Agent

FDA-APPROVED USES
Photrexa (riboflavin 5'-phosphate ophthalmic solution) 0.146% and Photrexa Viscous (riboflavin 5'-phosphate in 20% dextran ophthalmic solution) is indicated for the treatment of (CDER 2014):

- **Keratoconus, progressive:** Treatment of progressive keratoconus with the KXL System in corneal collagen cross-linking
  The FDA issued a new drug application (NDA) approval for Photrexa Viscous (riboflavin 5'-phosphate in 20% dextran ophthalmic solution) 0.146%, and Photrexa (riboflavin 5'phosphate ophthalmic solution) 0.146%, to be used with the KXL System (Avedro, Inc., Waltham, MA), a UV light source, for the treatment of progressive keratoconus (CDER 2016).
- **Corneal ectasia following refractive surgery:** Treatment of corneal ectasia following refractive surgery with the KXL System in corneal collagen cross-linking (FDA 2016).
  The FDA supplemented the NDA approval for the treatment of corneal ectasia following refractive surgery. The NDA noted that the safety and effectiveness of corneal collagen crosslinking has not been established in patients age < 14 years and the clinical trials did not include patients who were age 65 years or older (FDA 2016, reviewed 2019).

Refer to the prescribing information for specific dosage and administration instructions which indicates usage only of the conventional epi-off CXL protocol since the KXL® system has not been approved for the use with any other protocol (e.g., transepithelial "epithelium-on") or for other indications (e.g., infectious keratitis, corneal ulcers).

COMPENDIAL APPROVED OFF-LABELED USES: None

SUMMARY OF MEDICAL EVIDENCE

The peer-reviewed medical evidence for corneal collagen cross-linking (CXL) for the treatment of keratoconus and corneal ectasia includes randomized controlled trials (RCTs), prospective cohort studies, retrospective comparative analyses, and systematic reviews. Key outcomes reported include disease progression, changes in corneal topography and thickness, visual acuity, and procedure-related adverse events. Collectively, evidence suggests that CXL slows or stops progression of keratoconus and post-refractive ectasia, primarily through topographic flattening of the cornea. The procedure is generally considered safe, with delayed epithelial healing and transient corneal haze being the most frequently reported conditions.

The U.S. Food and Drug Administration (FDA) approved epithelium-off (epi-off) CXL using riboflavin (Photrexa or Photrexa Viscous) and UVA light (KXL system) for the treatment of progressive keratoconus and corneal ectasia following refractive surgery. This approval was supported by three pivotal prospective, open-label, randomized, sham-controlled trials involving a total of 384 patients aged 14 years and older (Table 1). These studies – UVX-001, UVX-002, and UVX-003—included patients with either keratoconus or post-refractive surgery ectasia. The trials initially assessed maximum keratometry (Kmax) reduction at 3 months, but this endpoint was later extended to 12 months due to the delayed remodeling response of the corneal stroma post-CXL. Each patient received a single CXL treatment in one eye and was followed for 12 months.

FDA approval of Photrexa Viscous and Photrexa was based on 3 prospective, open-label, sham-controlled trials with a total of 384 patients ≥14 years old with progressive keratoconus (Table 1). The studies were titled Safety and Effectiveness of the UV-X System for Corneal Collagen Cross-Linking in Eyes with Corneal Ectasia or Progressive Keratoconus (UVX-001 Keratoconus and UVX-001 Ectasia) (a combined trial), Safety and Effectiveness of the UV-X System for Corneal Collagen Cross-Linking in Eyes With Progressive Keratoconus (UVX-002) for keratoconus, and Safety and The identical protocol was used for all 3 trials. Initially, the primary endpoint was a 1-D reduction in maximum corneal curvature at month 3. Because corneal stromal remodeling associated with the healing response following CXL requires 6 to 12 months to stabilize, the primary endpoint was adjusted from 3 to 12 months. Patients received a single treatment and were followed for 12 months. CXL-treated eyes had significant reductions in corneal curvature at 6 and 12 months compared to sham-treated eyes; these improvements were generally correlated with improvements in best corrected visual acuity (BCVA). This endpoint was more appropriate for assessing the long-term clinical benefits of corneal collagen cross-linking. Only 1 eye per patient was assigned as the experimental eye in each of the 3 trials. These trials included patients with corneal ectasia diagnosed following LASIK or PRK, as well as those with progressive keratoconus. Inclusion criteria for these trials required documented progression of keratoconus within the previous 24 months, defined by one or more of the following: a ≥1.0 diopter (D) increase in the steepest keratometry, a ≥1.0 D increase in manifest cylinder, a ≥0.50 D myopic shift in spherical equivalent, or a ≥0.1 mm decrease in the back optical zone radius in rigid contact lens users. Sham eyes received topical anesthetic and riboflavin drops without epithelial debridement or UVA exposure. For sham subjects who crossed over to active treatment at 3 or 6 months, their last pre-treatment Kmax value was carried forward, which likely underestimated the extent of untreated disease progression. At 12 months, Photrexa-treated eyes in UVX-001 showed a mean Kmax reduction of 1.0 D, while sham-treated eyes demonstrated a 1.0 D increase, for a net treatment effect of -2.0 D. In UVX-003, the corresponding figures were a 0.5 D reduction in treated eyes versus a 0.5 D increase in sham eyes, yielding a net effect of -1.1 D. These improvements were correlated with gains in best corrected visual acuity (BCVA). A safety analysis submitted to the FDA included data from 512 treated eyes (293 with keratoconus and 219 with ectasia). Adverse events included corneal haze, epithelial defects, punctate keratitis, striae, pain, dry eye, photophobia, and blurred vision. Most events resolved within 6 months, though corneal opacity persisted at 12 months in up to 6% of ectasia patients.

Table 1.

Summary of Pivotal Trial Characteristics and Results Study	Study	Design	Dates	Patients (N or n) Total = 384	Difference in Mean Change in Kmax From Baseline to 12 Months (95% CI)
Unpublished	UVX-001	RCT	2008-2010	Keratoconus (58) Ectasia (49)	-1.9 D (-3.4 to -0.3) -2.0 D (-3.0 to -1.1)
Hersh et al (2011)	UVX-002	RCT	2008-2010	Keratoconus only (147)	-2.3 D (-3.5 to -1.0)
Safety and Effectiveness of the UV-X System for Corneal Collagen Cross-Linking in Eyes with Progressive Keratoconus; ClinicalTrials.gov Identifier: NCT00647699 In UVX-002: Hersh et al (2011) reported early trial results that included data from 49 of 147 patients in the UVX-002 trial and 22 of 130 patients in the UVX-003 trial. These results are not noted.					
Hersh et al (2011)	UVX-003	RCT	2008-2011	Ectasia only (130)	-1.1 D (-1.9 to -0.3)
Safety and Effectiveness of the UV-X System for Corneal Collagen Cross-Linking in Eyes with Corneal Ectasia After Refractive Surgery; ClinicalTrials.gov Identifier: NCT00674661 In UVX-003: 4 patients in the collagen cross-linking group had missing baseline Kmax values and were excluded from the analysis.					

Abbreviations: CI: confidence interval; D: diopter; Kmax: maximum corneal curvature; RCT: randomized controlled trial

Randomized Controlled Trials

Koppen et al. (2024) conducted a prospective, randomized, controlled, open-label, multicenter trial to evaluate the safety and efficacy of epithelium-on (epi-on) corneal crosslinking (CXL) in patients with keratoconus. The study enrolled 2,228 patients, of which 1,922 (86.3%) had a diagnosis of keratoconus. Subjects were randomized into three treatment groups using different UVA energy protocols, all with the same riboflavin delivery and epi-on technique. Primary outcomes included changes in corrected distance visual acuity (CDVA), uncorrected distance visual acuity (UCVA), and maximum keratometry (Kmax), assessed at 6 and 12 months postoperatively. At 12 months, mean CDVA improved from 20/41 to 20/35 Snellen ($p < 0.001$), and mean UCVA improved from 20/150 to 20/120 Snellen ($p <$

0.001). Kmax decreased by an average of −0.45 D ($p < 0.05$). CDVA remained stable or improved in 80% of patients, increasing to 89% in those ≤21 years. No significant differences in outcomes were found between treatment groups. While Kmax reduction did not correlate directly with visual acuity gains, improved surface regularity was associated with better vision. Corneal thickness remained stable, indicating preserved structural integrity. The treatment was well tolerated, with a low rate of adverse events (8.8%). Epithelial defects occurred in only 1.4% of patients—mostly from one site—and resolved within a week. No serious complications such as corneal striae, infection, or significant haze were observed, offering a safer profile compared to traditional epi-off CXL. Study limitations included the absence of sham control and incomplete 12-month follow-up due to the original 6-month design. The findings support epithelium-on CXL as a safe, noninvasive, and effective treatment for keratoconus.

Hersh et al. (2017) completed a phase 3, prospective RCT involving 205 participants with keratoconus treated with CXL (n=102) or a sham procedure (n=103). Inclusion criteria included age ≥ 14 years, axial topography pattern consistent with corneal ectasia (including relative inferior steepening with inferior:superior difference ≥ 1.5 D), corrected distance visual acuity worse than 20/20, and corneal thickness of ≥ 300 microns as measured on Pentacam. Participants that had a history of corneal surgery other than laser refractive surgery were excluded. This included a corneal pachymetry < 300 microns, and a history of corneal disease that would interfere with healing, At 1 year, those in the treatment group had a significant decrease in maximum corneal curvature score (1.6) compared with baseline, while the control group saw an increase in maximum corneal curvature (1.0); the between-group difference in maximum corneal curvature change was 2.6 D. Mean corrected distance visual acuity improved significantly more in the treatment group (5.7 logMAR) than in the control group (2.2 logMAR; between-group difference, 3.5 logMAR). A similar finding, though statistically insignificant, was observed for mean uncorrected distance visual acuity, with the treatment group improving by 4.4 logMAR, compared with the control group (2.6 logMAR; between-group difference, 1.8 logMAR). Endothelial cell count did not change significantly from baseline to 1 year in either group. The trial was limited in that patients in the control group were allowed to switch to corneal CXL treatment after 3 months; thus, their data were imputed based on the last observation carried forward method. Also, patients in the control group did not undergo removal of their epithelium.

Systematic Reviews and Meta-Analyses
Shajari et al. (2018) completed a meta-analysis of 22 studies comparing conventional CXL (C-CXL) and accelerated CXL (A-CXL) for the treatment of progressive keratoconus. The analysis included 1,158 eyes (577 in the C-CXL group and 581 in the A-CXL group). Primary outcomes included visual acuity, refractive error, corneal thickness, biomechanical properties keratocyte and nerve density, demarcation line depth, and time to re-epithelialization. Both techniques showed similar improvements in uncorrected distance visual acuity (UDVA) through 12 months, after which C-CXL showed greater improvement. C-CXL also showed better correction in spherical error at 3 and 6 months, though A-CXL was superior beyond 6 months. Spherical equivalent and cylindrical error were significantly better with C-CXL at final follow-up. Keratometric changes (Kmax and Kmin) were similar until the final visit, where C-CXL was more effective in flattening the cornea. C-CXL showed greater early reduction in central and minimum corneal thickness, as well as anterior stromal keratocyte density and demarcation line depth. Biomechanical metrics (corneal hysteresis, resistance factor) and nerve density changes were similar between groups. Endothelial cell loss was slightly higher in A-CXL at 1 month, but greater in C-CXL at 6 and 12 months. Minimal complications were noted with 2 cases of delayed epithelial healing in the C-CXL group and 4 cases in the A-CXL group. Anterior stromal scarring was noted in 2 eyes in the A-CXL group. Trace or mild haze was reported in 10 eyes in the C-CXL group and 10 eyes in the A-CXL group. There was only one case of severe central haze in the C-CXL group. Overall, both C-CXL and A-CXL were effective, but C-CXL showed superior long-term outcomes in visual acuity and corneal flattening.

Non-Randomized Studies, Retrospective Reviews, and Other Evidence
Moghadam et al. (2019) conducted a prospective interventional study to evaluate the safety and efficacy of corneal collagen cross-linking (CXL) in patients with advanced progressive keratoconus, defined by a maximum keratometry (Kmax) value greater than 58 diopters. The study included 30 eyes from 27 participants, all of whom had a definitive diagnosis warranting CXL. Inclusion criteria included age over 12 years and clinical indication for treatment. Exclusion criteria included pregnancy or lactation, corneal scarring due to advanced keratoconus, and any history of systemic disease, prior corneal or intraocular surgery, chemical ocular injury, delayed epithelial healing, or neurological or retinal disorders affecting vision. Of the 27 participants, 3 underwent bilateral CXL, and 24 received unilateral treatment. Follow-up evaluations were conducted at 1 week, 1, 3-, 6-, 12-, and 24-months post-procedure with Pentacam imaging repeated at 12 and 24 months. The mean UCVA improved from 0.73 ± 0.36 logMAR at baseline to 0.47 ± 0.31 at 12 months and 0.48 ± 0.30 at 24 months. The mean BCVA improved from 0.59 ± 0.34 logMAR to 0.44 ± 0.33 at 12 months

and 0.45 ± 0.32 at 24 months. Mean Kmax decreased from 62.19 ± 4.56 D to 60.91 ± 4.36 D at 12 months and 60.95 ± 4.42 D at 24 months. The thinnest point corneal thickness showed only modest changes, from 438.65 ± 40.11 microns at baseline to 430.46 ± 41.05 at 12 months and 431.43 ± 61.92 at 24 months. Results demonstrated meaningful improvements in visual acuity and corneal parameters. Only one eye was classified as a treatment failure, due to a Kmax increase greater than 2.0 D. No intraoperative or postoperative complications were reported. The authors concluded that standard CXL was both safe and effective in stabilizing vision and corneal structure in patients with advanced keratoconus. Limitations of the study included its small sample size, lack of a control group, and nonrandomized design, which may affect generalizability.

National and Specialty Organizations

The **American Academy of Ophthalmology (AAO)** published a Preferred Practice Pattern pertaining to corneal ectasia in 2024 ([2]AAO 2024). The AAO noted that CXL reduces the risk of progressive ectasia (particularly in its early stages) and stabilizes the corneal contour, particularly in mild to moderate keratoconus. Evidence also supports CXL for patients with corneal ectasia after keratorefractive surgery. Prior to keratorefractive surgery, topography and tomography should be performed. A recommendation was also made for corneal topography and tomography following a period of contact lens abstinence when there is evidence of irregular astigmatism or any abnormalities that may indicate keratoconus or any type of corneal ectasia. Current CXL protocols require either the removal of the epithelium or exposure of the intact epithelium to agents that increase the permeability of the cell layer, followed by the application of topical riboflavin and UV-A treatment.

SUPPLEMENTAL INFORMATION

Cornea: The outermost layer of the eye; dome shaped and covers the front of the eye.

Ectasia: A condition that occurs when the cornea is so thin that pressure within the eye leads to bulging of the cornea.

Keratoconus: Cone-shaped cornea with the apex of the cone being forward; also called conical cornea.

Keratometry (K): Measurement of the curvature of the cornea.

Manifest cylinder: A subjective measure of a change in the cylinder (astigmatism). For example, an increase of 1.00 D or more in manifest cylinder indicates that the glasses prescription astigmatism has changed by 1 or more.

Manifest refraction spherical equivalent (MRSE): A subjective measure of a change in the cylinder (astigmatism). It is calculated arithmetically by adding the sphere power and half of the cylinder power. MRSE is used in the calculation of spherical equivalent.

CODING & BILLING INFORMATION

CPT (Current Procedural Terminology)

Code	Description
0402T	Collagen cross-linking of cornea, including removal of the corneal epithelium, when performed, and intraoperative pachymetry, when performed

HCPCS (Healthcare Common Procedure Coding System)

Code	Description
J2787	Riboflavin 5'-phosphate, ophthalmic solution, up to 3 mL [Photrexa, Photrexa Viscous]

AVAILABLE DOSAGE FORMS: Photrexa-Photrexa Viscous Kit: Photrexa 0.146%; Photrexa Viscous 0.146% in Dextran 20% (6 mL) [contains dextran]

CODING DISCLAIMER. Codes listed in this policy are for reference purposes only and may not be all-inclusive. Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement. Listing of a service or device code in this policy does not guarantee coverage. Coverage is determined by the benefit document. Molina adheres to Current Procedural Terminology (CPT®), a registered trademark of the American Medical Association (AMA). All CPT codes and descriptions are copyrighted by the AMA; this information is included for

informational purposes only. Providers and facilities are expected to utilize industry standard coding practices for all submissions. When improper billing and coding is not followed, Molina has the right to reject/deny the claim and recover claim payment(s). Due to changing industry practices, Molina reserves the right to revise this policy as needed.

APPROVAL HISTORY

08/13/2025	Policy revised. Removed prescriber requirements. Updated Summary of Medical Evidence and References. IRO Peer Review on July 11, 2025, by a practicing physician board-certified in Ophthalmology.
08/14/2024	Policy reviewed, no changes to criteria. Updated References.
08/09/2023	Policy reviewed, no changes to criteria. Updated Overview, Summary of Medical Evidence, and References. Grammatical edits to Disclaimer section and Documentation Requirements disclaimer. IRO Peer Review on July 19, 2023, by practicing, board-certified physician with a specialty in Ophthalmology.
08/10/2022	Policy reviewed and updated. No changes to coverage criteria. Updated references. Removed references to Photrexa Viscous in policy due to discontinuation of product.
08/11/2021	Policy reviewed. No changes to coverage criteria. Updated references.
07/2020	Policy re-instated. IRO Peer Review. 7/7/2020. Practicing Physician. Board certified in Ophthalmology. Added Photrexa Viscous (riboflavin 5'-phosphate in 20% dextran ophthalmic solution) 0.146%, and Photrexa (riboflavin 5'phosphate ophthalmic solution) 0.146%, to be used with the KXL System for the FDA approved indications. All content, clinical evidence, coverage criteria, practice guidelines, appendices and reference sections were revised with the most recent medical literature and available evidence.
06/19/2019	Policy retired. IRO Peer Review: 10/29/18. Policy reviewed by practicing MD board certified in Ophthalmology.
12/19/2018	New policy. IRO Peer Review. Policy reviewed by practicing MD board certified in Ophthalmology.

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