Corneal Collagen Cross-Linking (for Louisiana Only)

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➲ Instructions for Use

Certain content mandated by Louisiana Department of Health

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Application

This Medical Policy only applies to the state of Louisiana. Portions of the coverage rationale contained in this policy represents Louisiana Medicaid coverage policy and is set forth below in accordance with state requirements.

Coverage Rationale

State-Specific Criteria

The Corneal Collagen Cross-Linking (CXL) procedure, including the riboflavin drops and administration of UV light, is approved for patients between 14-20 years of age with progressive Keratoconus.

Clinical Guidelines

Epithelium-Off photochemical CXL using riboflavin and ultraviolet A may be considered medically necessary for treatment of progressive Keratoconus when conservative treatments (e.g., spectacles and contact lens) have been tried without success and the individual does not have either of the following contraindications:

- A corneal thickness of fewer than 400 microns; or
- A prior herpetic ocular infection

(Louisiana Department of Health, Informational Bulletin 24-17)

Non State-Specific Criteria

Corneal Collagen Cross-Linking (C-CXL) using an Epithelium-Off approach, riboflavin (vitamin B2), and ultraviolet A is proven and medically necessary for the treatment of Corneal Ectasia resulting from refractive surgery in individuals who have failed conservative treatment (e.g., rigid contact lens, spectacle correction).

C-CXL is unproven and not medically necessary for all other indications or using any other methods due to insufficient evidence of efficacy.

Definitions

Accelerated Corneal Collagen Cross-Linking (CXL): A variation of Epithelium-Off Corneal Collagen Cross-Linking or Epithelium-On Corneal Collagen Cross-Linking in which the irradiance of ultraviolet A (UVA) light is increased and the procedure duration is decreased (American Academy of Ophthalmology, 2016).

Corneal Collagen Cross-Linking Plus (CXL-Plus): Performance of Epithelium-Off Corneal Collagen Cross-Linking or Epithelium-On Corneal Collagen Cross-Linking in combination with other refractive eye procedures such as intrastromal corneal ring segments, or topography-guided photorefractive keratectomy (PRK). (American Academy of Ophthalmology, 2021).

Corneal Ectasia: A forward bulging and thinning of the cornea. It may result from a disease of the cornea (e.g., Keratoconus), trauma, atrophy, raised intraocular pressure or as a complication of photorefractive surgery in which the corneal stroma has been left thinner than about 250µm. (American Academy of Ophthalmology, 2021).

Epithelium-Off Corneal Collagen Cross-Linking (CXL): The conventional method of performing the CXL procedure. After de-epithelializing the central (7-9mm) cornea, riboflavin activated by UVA light is used to generate reactive oxygen species that interact with collagen in the corneal stroma. Also referred to as the Dresden Protocol. (American Academy of Ophthalmology, 2017).

Epithelium-On Corneal Collagen Cross-Linking (CXL): A modification of Epithelium-Off Corneal Collagen Cross-Linking in which the corneal epithelium is left intact prior to instilling the eye with riboflavin followed by exposure to UVA light. Also referred to as transepithelial Corneal Collagen Cross-Linking. (American Academy of Ophthalmology, 2017).

Keratoconus: A progressive ocular disease that increases the curvature of the cornea, leading to decreased visual acuity. Ultraviolet (UV) light is combined with riboflavin eye drops to induce collagen crosslinks in the cornea, strengthening and stabilizing the cornea, and delaying progressive deformation (Louisiana Dept of Health, 2024).

Progressive keratoconus is defined as one or more of the following:
- An increase of 1 diopter (D) in the steepest keratometry value; or
- An increase of 1 D in regular astigmatism evaluated by subjective manifest refraction; or
- A myopic shift (decrease in the spherical equivalent) of 0.50 D on subjective manifest refraction; or
- A decrease > 0.1 mm in the back optical zone radius in rigid contact lens wearers where other information was not available.

(Louisiana Dept of Health, 2024)

Applicable Codes

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Listing of a code in this policy does not imply that the service described by the code is a covered or non-covered health service. Benefit coverage for health services is determined by federal, state, or contractual requirements and applicable laws that may require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment. Other Policies and Guidelines may apply.

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

CPT® is a registered trademark of the American Medical Association

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

Description of Services

Keratoconus is a noninflammatory, degenerative eye condition characterized by progressive steepening and thinning of the normally round cornea into a cone shape. This abnormal shape prevents light entering the eye from focusing directly on the retina, resulting in irregular astigmatism and progressive myopia or visual loss. These changes lead to decreased visual acuity (distorted or blurred vision) and sensitivity to light or glare. The condition typically presents itself during adolescence or early adulthood. Although usually a bilateral disease, individuals may experience asymmetric symptoms with one eye more severely affected. Initial interventions generally include glasses or soft contact lenses, but as Keratoconus progresses, an individual may require fitting with rigid gas permeable or other types of contact lenses. (Mastropasqua, 2015)

Corneal Ectasia is a noninflammatory condition, the hallmark of which is progressive corneal steepening and thinning that has been associated with refractive surgery, especially laser-assisted in situ keratomileusis (LASIK). Ectasia is a form of Keratoconus, a progressive disorder in which the cornea thins and begins to bulge into a cone-like shape. It can significantly affect vision since the altered shape deflects light away from the retina. Types of Corneal Ectasia include Keratoconus, pellucid marginal degeneration, keratoglobus, post keratorefractive ectasia, and wound ectasia after penetrating keratoplasty (PK). Corneal Ectasias are associated with decreased uncorrected visual acuity (UCVA), an increase in ocular aberrations, and often a loss of best-corrected distance visual acuity (BCVA). 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. (Feder et al., 2013)

Refractive surgery refers to surgical procedures designed to correct refractive errors by reshaping the corneal surface, and to improve the focusing power of the eye, thus reducing or eliminating the need for corrective lenses. According to the AAO, refractive surgery is an elective procedure which may be considered by those who wish to become less dependent on spectacles or contact lenses or when there is an occupational or cosmetic reason to not wear spectacles. (AAO, 2017)

Refractive surgery, particularly laser-assisted in situ keratomileusis (LASIK), is a common cause of Corneal Ectasia. LASIK reshapes the surface of the cornea with an excimer laser to focus visual images directly onto the retina and improve visual acuity. Post-LASIK corneal ectasis is a serious side effect that involves progressive thinning and steepening of the central and inferior portions of the cornea. (Hayes, 2017, updated 2022)

The main objective of Corneal Collagen Cross-Linking (CXL) is to achieve strengthening of corneal tissue as a means to stop further progression of Keratoconus or Corneal Ectasia. In order to induce cross-links within and between collagen fibers of corneal stroma, long-wave ultraviolet A (UVA) radiation (370 nm) is used combined with a chromophore (riboflavin, vitamin B2). Riboflavin acts as photosensitizer that when exposed to UVA is activated, producing oxygen free radicals that initiate the creation of those new covalent bonds bridging the amino groups of collagen fibrils and possibly other corneal macromolecules such as proteoglycans and nucleic acids. This photopolymerization process results in the increased rigidity of corneal tissue. (Galvis et al., 2017)

As mentioned above 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.

- 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.
- 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. 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. (ECRI, 2018)

Clinical Evidence

Corneal Ectasia Following Refractive Surgery

In the pivotal prospective, multicenter, RCT, Hersh et al. (2017b) evaluated the safety and efficacy of CXL for the treatment of corneal ectasia after laser refractive surgery. The patient population was 179 subjects with corneal ectasia after previous refractive surgery. The treatment group underwent standard CXL, and the sham control group received riboflavin alone without removal of the epithelium. In the cross-linking treatment group, the maximum K value decreased by 0.7 diopters (D) from baseline to 1 year, whereas there was continued progression in the control group (1.3 D difference between treatment and control, $p < 0.0001$). In the treatment group, the maximum K value decreased by 2.0 D or more in 14 eyes (18%) and increased by 2.0 D or more in 3 eyes (4%). The CDVA improved by an average of 5.0 logarithm of the minimum angle of resolution (logMAR) letters. Twenty-three eyes (32%) gained and 3 eyes (4%) lost 10 or more logMAR letters. The UDVA improved 4.5 logMAR letters. Corneal haze was the most frequently reported cross-

linking-related adverse finding. The authors concluded that CXL was effective in improving the maximum K value, CDVA, and UDVA in eyes with corneal ectasia 1 year after treatment, with an excellent safety profile. Additional RCTs with longer-term outcomes are needed to evaluate the efficacy of CXL for this indication.

Wan et al. (2017) conducted a systematic review and meta-analysis to review the safety and stability of CXL for the treatment of keratectasia after Excimer Laser Refractive Surgery. Seven studies involving 118 patients treated with CXL for progressive ectasia after laser-assisted in situ keratomileusis (LASIK) or photorefractive keratectomy (PRK) (140 eyes; the follow-up time range from 12 to 62 months) were included in the meta-analysis. The primary outcome parameters included the changes of corrected distant visual acuity (CDVA), uncorrected visual acuity (UCVA), the maximum keratometry value (KMax) and minimum keratometry value (Kmin), the surface regularity index (SRI), the surface asymmetry index (SAI), the keratoconus prediction index (KPI), corneal thickness, and endothelial cell count. Efficacy estimates were evaluated by weighted mean difference (WMD) and 95% confidence interval (CI) for absolute changes of the interested outcomes. The authors concluded that CXL is a promising treatment to stabilize the keratectasia after Excimer Laser Refractive Surgery. Further long-term follow-up studies are necessary to assess the persistence of the effect of the CXL. Study limitations include variation in patient population, follow-up periods, clinical measurement, and quality, as well as lack of comparison to a different treatment.

Clinical Practice Guidelines

American Academy of Ophthalmology (AAO)

The AAO's 2017 Preferred Practice Pattern on external diseases of the cornea includes corneal collagen cross-linking as a potential surgical treatment for cornea ectasia, noting that the procedure can improve corneal rigidity by increasing bonds between fibers. AAO stated that options for the treatment of corneal ectasia after LASIK include corneal cross-linking. Studies have shown that CXL induced by topical riboflavin and ultraviolet irradiation may arrest keratectasia, as demonstrated by preoperative and postoperative corneal topography/tomography and a reduction in maximum keratometric readings. Long-term stability after CXL therapy for treatment of post-refractive corneal ectasia has been reported.

Accelerated Corneal Collagen Cross-Linking (A-CXL)

Because of lack of precision, frequent indeterminate risk of bias due to inadequate reporting, and inconsistency in outcomes measured and reported among studies, it remains unknown whether A-CXL confers an advantage over conventional epithelium-off CXL for patients with progressive keratoconus with respect to further progression of keratoconus, visual acuity outcomes, and patient-reported outcomes (PROs). Furthermore, methods of assessing and defining progressive keratoconus should be standardized. Trials with longer follow-up are required in order to assure that outcomes are measured after corneal wound-healing and stabilization of keratoconus.

Shajari et al. (2019) conducted a systematic review and meta-analysis to compare the results of conventional corneal crosslinking (C-CXL) and accelerated corneal crosslinking (A-CXL) for the treatment of keratoconus. Twenty two studies including fourteen prospective randomized controlled trials, four prospective nonrandomized comparative studies and four retrospective reviews met the inclusion criteria. The primary outcomes were measured changes in uncorrected distance visual acuity (UDVA), corrected distance visual acuity (CDVA), spherical equivalent (SE), spherical and cylindrical error, central and minimum corneal resistance factor (CRF), anterior stromal keratocyte density, sub-basal nerve density, endothelial cell density (ECD), percentage of hexagonal endothelial cells, as well as average, maximal and minimal keratometry values. There was no statistically significant difference in uncorrected distance visual acuity, corrected distance visual acuity, spherical equivalent, spherical error, cylindrical error, maximal keratometry, average keratometry, central corneal thickness, corneal biomechanical properties, time of re-epithelialization, sub-basal nerve density, endothelial cell density and morphology. Study limitations included the use of heterogeneous A-CXL protocols (e.g., various duration, composition, and frequency of riboflavin exposure) and all trials were weighed similarly regardless of study type. The authors concluded that C-CXL and A-CXL seem to provide comparable results in halting keratoconus. However, larger studies with longer follow up times are necessary to evaluate the long-term results of different A-CXL protocols compared to C-CXL.

Artola et al. (2017) conducted a prospective case series to evaluate accelerated transepithelial CXL in a total of 19 keratoconus eyes of 12 patients between 26 and 69 years of age. One month after surgery, a non-statistically significant change was noted in sphere and in spherical equivalent, whereas a significant improvement was observed in corrected distance visual acuity. A significant change was observed in topographic astigmatism and posterior corneal a sphericity. In the authors' opinion, accelerated transepithelial CXL may be a useful technique for the management of progressive keratoconus. CXL maintained the topographic and aberrometric profile of the cornea without significant changes for a period of 12 months after the procedure. The authors recommend future studies to show the corneal biomechanical changes that occur in-vivo with the use of this technique. The findings are limited by lack of comparison group.

In a comparative, retrospective, consecutive case series of 78 eyes in 58 pediatric patients with keratoconus, Baenninger et al. (2017) evaluated visual and topographic outcomes 1 year after conventional (C-CXL) vs accelerated corneal cross-linking (A-CXL). In this single-center analysis, 39 eyes underwent C-CXL and 39 eyes A-CXL. No subjects were lost to follow-up after 12 months. No significant difference between changes in 12 months after as compared to the time before CXL for UCVA (0.01 log MAR; 95% confidence interval -0.14 to 0.15, p = .944), BCVA (0.05 log MAR; 95% confidence interval -0.05 to 0.15, p = .310), and KMax (-0.77 diopters; 95% confidence interval -2.20 to 0.65, p = .282) between the C-CXL and A-CXL group were observed. Treatment failure rate was observed in 9 of 39 eyes (23.1%) in C-CXL and in 6 of 39 eyes (15.4%) in A-CXL (p = .389). Adverse events were seen only in 1 eye in the C-CXL group. In this retrospective comparison, the authors concluded that the accelerated approach was equally as effective as the conventional protocol to treat pediatric keratoconus. However, the study was not designed and may not have been powered to demonstrate non-inferiority. Furthermore, lack of randomization may have led to biases. Randomized controlled trials with larger patient populations and longer follow-ups are needed to validate these findings.

Woo et al. (2017) compared the visual, refractive, topographic, and biomechanical outcomes of conventional (CXL 3mW/cm^2 for 30 minutes) or accelerated cross linking (KXL; 30mW/cm^2 for 4 minutes) in a prospective, non-randomized interventional study of 76 patients with progressive keratoconus. At the 1-year follow-up, both groups showed no significant increase in K1, K2 and Kmean from baseline. There was also no difference between the CXL and KXL group for postoperative corneal topography as well as central and minimal pachymetry up to 12 months. There was a significant increase in both corneal hysteresis (0.62mm Hg, p = 0.04) and corneal resistance factor (0.91mm Hg, p = 0.003) in the KXL group at 12 months but not in the CXL group. There was no significant endothelial cell loss throughout follow up in both the groups. Although the authors' concluded that accelerated CXL provided a biochemical advantage, the study was not designed and may not have been powered to demonstrate non-inferiority. Lack of randomization may have led to biases.

Wang et al. (2017) conducted a comparative evaluation of progression rate in keratoconus with accelerated CXL. One hundred forty-five eyes were followed without CXL (no-CXL group) for a median duration of 31 months whereas 45 eyes were followed up for 41 months before (pre-CXL) and after (post-CXL) accelerated, epithelium-off CXL. Progression was defined based on significant slope found in linear mixed effect models against time. Swept-source optical coherence tomography was used for measurement of anterior steep keratometry, anterior flat keratometry (Ant Kf), anterior average keratometry (Ant Avg K); posterior steep keratometry, posterior flat keratometry (Post Kf), posterior average keratometry (Post Avg K) and corneal thickness. The patients in the pre-CXL group were significantly younger (26.3 ±5.48 years) compared with the patients in no-CXL group (32.7 ±10.24 years) (p = 0.004). Significant differences were observed during baseline examination for all parameters (p ≤ 0.035) between pre-CXL and no-CXL groups except Ant Cyl and Post Cyl. During the observation period, statistically significant differences were noted between pre-CXL and no-CXL groups in the progression rate of Ant Kf, Ant Avg K, Post Kf and Post Avg K (p ≤ 0.045). After CXL, the progression rate in the post-CXL group was comparable to that in no-CXL group. All corneal parameters remained stable in the no-CXL group throughout the follow-up period. The authors observed a decrease in progression rate of corneal parameters after CXL. In cases with stable corneal parameters over time, careful monitoring can be considered instead of collagen cross-linking. The findings are limited by lack of randomization, which could have introduced biases and lack of comparison with proven therapies.

In a prospective non-randomized study, Badawi (2016) evaluated the effects of accelerated CXL on corneal endothelium in keratoconus (n = 40 eyes) and post-laser-assisted in situ keratomileusis (LASIK) ectasia (n = 10 eyes). Over the course of 12 months (at 3-month intervals), qualitative and quantitative analyses of the corneal endothelial cells were conducted. There was a significant reduction in endothelial cell count particularly at 3 and 6 months post-CXL. In addition, the coefficient of variance was also statistically significantly higher at 3 and 6 months postoperatively than the pre-CXL value. There was a slight change in the percentage of hexagonal cells. In this patient population, the author concluded that the use of accelerated CXL (10 mW/cm2 for 9 minutes) has a transient negative impact on endothelial cell density and/or endothelial morphology. The study is limited bay lack of comparison group. Well-designed RCTs with larger patient populations and longer follow-up periods are needed to compare accelerated CXL to conventional CXL in terms of safety and efficacy.

Epithelium-On Corneal Collagen Cross-Linking

Current evidence on the safety and efficacy of epithelium-on (transepithelial) CXL procedures for keratoconus and corneal ectasia is inadequate in quantity and quality. Further long-term follow-up studies are necessary to assess the persistence of the effect of the CXL using epithelium-on procedure. Study limitations include variation in patient population, follow-up periods, clinical measurement, and quality.

In an RCT, Rush and Rush (2017) compared the outcomes of CXL for the treatment of progressive corneal ectasia using a standard epithelium-off technique versus a transepithelial technique with enhanced riboflavin solution. One hundred forty-four eyes with progressive corneal ectasia were prospectively randomized into a transepithelial CXL study arm or an

epithelium-off CXL control arm. Follow-up examinations were set at 3, 6, 12 and 24 months. The primary outcome measure was change in the maximum simulated keratometry value (Ksteep) after 24 months of follow-up. The secondary outcome measure was change in the best spectacle-corrected visual acuity (BSCVA) after 24 months follow-up. One hundred and thirty-one eyes completed the 24-month follow-up interval. Change in Ksteep was -1.52 ±0.66 dioptres (D) for the control group versus -0.54±0.58 D for the study group at 24 months of follow-up (p = 0.0320). Change in BSCVA was -0.18 ±0.09 logMAR for the control group versus -0.14 ±0.08 logMAR for the study group at 24 months of follow-up (p = 0.4978). Two eyes in the control group had minor postoperative complications that did not affect the final visual acuity, and one eye in the control group underwent keratoplasty during the study interval. At 24 months of follow-up, subjects in the epithelium-off CXL group demonstrated a greater improvement in Ksteep compared with subjects in the transepithelial CXL group, but no statistically significant difference in BSCVA was found between groups.

In a systematic review and meta-analysis, Li and Wang (2017) evaluated the efficacy and safety of transepithelial CXL versus standard CXL on keratoconus. Three trials involving 244 eyes were evaluated, with 111 eyes in the standard CXL group and 133 eyes in the transepithelial CXL group. The pooled results showed that there were significant differences between the two groups in maximum keratometry (mean difference = 1.05D, 95% CI 0.19 to 1.92, p = 0.02)), with the standard CXL is more effective in decreasing the maximum keratometry at least 12 months after operation; the transepithelial CXL group gained more improvement in CDVA (mean difference = -0.07, 95% CI -0.12 to -0.02, p = 0.007);there were no significant differences in uncorrected distant visual acuity (UDVA) between the two groups (mean difference = -0.03, 95% CI -0.20 to 0.15, p = 0.75). A similar change was found in corneal thickness (mean difference = 4.35, 95% CI -0.43 to 9.13, p = 0.07)). The authors concluded that standard CXL is more effective in decreasing the maximum keratometry than the transepithelial CXL; the transepithelial CXL provided favorable visual outcomes; they both exhibit similar safety.

Bikbova and Bikbov (2016, included in the systematic review by Li and Wang) conducted an RCT of 149 eyes of 119 patients with keratoconus I-II of Amsler classification. Patients were divided into two groups: (1) 73 eyes with standard cross-linking (CXL) and (2) 76 eyes with transepithelial iontophoresis-assisted CXL. Depending on the group, epithelium removal or administration of riboflavin solution by iontophoresis for 10 min was performed, after which standard surface UVA irradiation (370 nm, 3 mW/cm2) was performed at a 5-cm distance for 30 min. The authors concluded that transepithelial iontophoresis-assisted collagen cross-linking was less effective than standard CXL after 24 months of follow-up, possibly due to a more superficial formation of corneal collagen crosslinks; however, the stopping of disease progression was achieved 24 months after procedure.

Corneal Collagen Cross-Linking Plus (CXL-Plus)

Current evidence on the safety and efficacy of the combination (CXL-plus) procedures for keratoconus and keratectasia is inadequate in quantity and quality.

Al-Amri (2018) reported 5-year results from a prospective, interventional, non-randomized, and non-controlled case series in which 60 eyes with mild, non-progressive keratoconus were treated with combined non-topography guided (TG) photorefractive keratectomy (PRK) and CXL. Refraction, uncorrected distance visual acuity (UDVA) and corrected distance visual acuity (CDVA), flat and steep keratometry readings, and adverse events were evaluated preoperatively and postoperatively. All study parameters showed a statistically significant improvement at 5y over baseline values. The author concluded that combined non-TG-PRK+CXL demonstrates positive 5-year outcomes in patients with mild, stable keratoconus. The findings are limited by lack of comparison groups. Based on these findings, the author recommends conducting future large scale, comparative, randomized trials with extended duration of follow-up to establish the long-term stability of this procedure in keratoconus.

Kontadakis et al. (2016) compared the results of CXL alone with combined simultaneous topography-guided photorefractive keratectomy plus CXL (tPRK-CXL) for progressive keratoconus for a 3-year interval (n = 60 eyes). Thirty eyes underwent combined tPRK with a solid-state laser (maximum ablation depth, 50 µm) followed by CXL, and 30 eyes underwent CXL alone. Groups were matched in terms of age and keratoconus stage. Corrected distance visual acuity (CDVA), uncorrected distance visual acuity (UDVA), keratometry, and corneal confocal microscopy were measured. In the authors' opinion, simultaneous tPRK followed by CXL in this series of keratoconus patients offered significantly improved vision to treated patients in comparison with CXL alone, and similar results regarding postoperative stability. The findings are however limited by lack of randomization, which could have introduced biases in the comparisons. Well-designed RCTs are needed to fully evaluate CXL-plus in the treatment of keratoconus.

U.S. Food and Drug Administration (FDA)

This section is to be used for informational purposes only. FDA approval alone is not a basis for coverage.

Corneal collagen cross-linking is a procedure and not subject to FDA regulations.

In 2016, riboflavin 5-phosphate in 20% dextran ophthalmic solution (Photrexa Viscous®; Avedro) and riboflavin 5-phosphate ophthalmic solution (Photrexa®; Avedro) were approved by the U.S. Food and Drug Administration for use with KXL System in corneal collagen cross-linking for the treatment of progressive keratoconus and corneal ectasia after refractive surgery.

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Policy History/Revision Information

Date	Summary of Changes
07/18/2024	**Application** • Added language to indicate portions of the *Coverage Rationale* contained in this policy represents Louisiana Medicaid coverage policy and is set forth [in the policy] in accordance with state requirements **Coverage Rationale** • Revised language to indicate: ***State-Specific Criteria*** ○ The Corneal Collagen Cross-Linking (CXL) procedure, including the riboflavin drops and administration of UV light, is approved for patients between 14-20 years of age with progressive Keratoconus Clinical Guidelines ○ Epithelium-Off photochemical CXL using riboflavin and ultraviolet A may be considered medically necessary for treatment of progressive Keratoconus when conservative treatments (e.g., spectacles and contact lens) have been tried without success and the individual does not have either of the following contraindications: ▪ A corneal thickness of fewer than 400 microns ▪ A prior herpetic ocular infection ***Non State-Specific Criteria*** ○ Corneal Collagen Cross-Linking (C-CXL) using an Epithelium-Off approach, riboflavin (vitamin B2), and ultraviolet A is proven and medically necessary for the treatment Corneal Ectasia resulting from refractive surgery in individuals who have failed conservative treatment (e.g., rigid contact lens, spectacle correction) ○ C-CXL is unproven and not medically necessary for all other indications or using any other methods due to insufficient evidence of efficacy **Definition** • Updated definition of “Keratoconus” **Applicable Codes** • Removed notation indicating CPT/HCPCS codes 0402T and J2787 are not on the State of Louisiana Medicaid Fee Schedule and therefore may not be covered by the State of Louisiana Medicaid Program **Supporting Information** • Updated *Clinical Evidence* and *References* sections to reflect the most current information • Archived previous policy version CS367LA.B

Instructions for Use

This Medical Policy provides assistance in interpreting UnitedHealthcare standard benefit plans. When deciding coverage, the federal, state or contractual requirements for benefit plan coverage must be referenced as the terms of the federal, state or contractual requirements for benefit plan coverage may differ from the standard benefit plan. In the event of a conflict, the federal, state or contractual requirements for benefit plan coverage govern. Before using this policy, please check the federal, state or contractual requirements for benefit plan coverage. UnitedHealthcare reserves the right to

modify its Policies and Guidelines as necessary. This Medical Policy is provided for informational purposes. It does not constitute medical advice.

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