



Medical Policy

2.01.064 Corneal Cross Linking for Treatment of Keratoconus and Corneal Ectasia

Original MPC Approval: 03/09/2011

Last Review: 07/17/2017

Last Revision: 07/17/2017

▼ Description

Keratoconus and corneal ectasia are conditions involving steepening, thinning, and protrusion of the cornea of the eye. Although the conditions exhibit similar characteristics, they arise from different origins. The cause of keratoconus has not been determined, and research into the disorder is ongoing. Corneal ectasia, on the other hand, is usually a complication associated with surgery to correct a refractive error such as laser in-situ keratomileusis (LASIK). Progression of the disorders with advancing corneal distortion leads to loss of visual acuity, which can be treated with specially fitted, gas permeable rigid contact lenses. In many cases this will provide a lasting remedy. For patients with severe disease or those who cannot tolerate a rigid contact lens, a corneal transplant procedure such as penetrating keratoplasty may be performed. Corneal inserts such as Intacs®, have been used in selected patients where contact lenses are no longer suitable in an attempt to stabilize the cornea and avoid or delay a corneal transplant. Approximately 15-20% of patients with keratoconus will eventually require a corneal transplant.

Corneal collagen cross-linking (CXL) using riboflavin (vitamin B2) and ultraviolet light is a treatment option that has been in use in Europe and Asia and is being investigated in the United States for treatment of both keratoconus and corneal ectasia associated with refractive surgery. The procedure is performed using local anesthesia, often preceded by removal of a thin layer of corneal epithelium to allow for better penetration of the riboflavin solution. The riboflavin is applied for 15 to 20 minutes, then the eye is exposed to ultraviolet (UV) light at a wavelength of 365 nm for 30 minutes as additional drops of riboflavin are applied every 2 to 5 minutes. At the end of the treatment the eyes are rinsed with saline and treated with a topical antibiotic and a bandaging soft contact lens. Patients later receive a week of treatment with a topical ophthalmic corticosteroid medication. The rationale is that the interaction of UV with the riboflavin induces the formation of chemical bonds within and between collagen fibrils present in the cornea causing strengthening and stiffening, so to retard or halt the progression of keratoconus or corneal ectasia.

▼ Policy

Corneal collagen cross-linking (CXL) using riboflavin and ultraviolet A may be considered medically necessary for the treatment of progressive keratoconus and corneal ectasia following refractive surgery in patients who have failed conservative treatment (e. g. rigid contact lens).

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

▼ Policy Guidelines

Rationale (2011):

1. The technology must have final approval from the appropriate government regulatory bodies:

At the present time the FDA has not yet approved any UV lamps for corneal collagen cross-linking treatment. Three clinical trials have been approved, however, which are designed to evaluate the safety and effectiveness of CXL in

patients with progressive keratoconus or corneal ectasia after previous refractive surgery. Two multicenter studies are expected to enroll 160 patients each, to study progressive keratoconus and ectasia respectively, comparing results of CXL with UV to riboflavin solution alone as a control.

2. The scientific evidence must permit conclusions concerning the effect on health outcomes:

There have been no U.S. studies published to date. A randomized controlled trial of CXL for keratoconus was reported in 2008 by Wittig-Silva et al, which randomized 66 eyes to either CXL or no cross-linking. At 6 months follow-up there was a statistically significant difference between the groups in primary outcome measures of best spectacle-corrected visual acuity and maximum keratometry. The largest uncontrolled study was that of Wolf-Raiskup et al (2008) which followed 241 eyes treated with CXL for a mean of 27 months. Visual acuity was significantly improved and astigmatism was decreased. Four other small, uncontrolled studies report benefits of CXL in terms of stabilization of progression of keratoconus, improvements in visual acuity and astigmatism. However, small study size, lack of controls and short follow-up periods hinders the ability to draw conclusions regarding the effects of CXL on health outcomes.

3. The technology must improve the net health outcome:

Although generally felt to be a safe procedure, case reports have identified various forms of bacterial and viral keratitis after CXL, and occasional delays of corneal healing are known. The available studies provide some preliminary evidence that corneal cross-linking slows or stops progression of keratoconus and may actually reverse existing damage. However, most of the studies are small and uncontrolled with short follow-up periods.

4. The technology must be as effective as any established alternatives:

Initially keratoconus is treated with rigid gas permeable contact lenses that preserve visual acuity. Intacs corneal inserts and corneal transplantation are alternative surgical treatments although the latter is felt to be a last-resort. There have been no comparative studies between CXL and existing alternatives.

5. The improvement must be attainable outside the investigational settings:

Although CXL has been used in Europe and Asia for over a decade it has been seldom performed in the United States, and there are no U.S. investigative data available. The available information is preliminary in nature and so it is not known if a net improvement can be expected outside of the investigational settings.

Update 2013:

A search of the peer reviewed literature was performed from April 2011 through March 2013. Findings in the literature do not change the conclusion that corneal cross linking for the treatment of keratoconus and corneal ectasia is experimental / investigational. No corneal cross-linking devices have received FDA approval for these indications. Clinical trials are ongoing.

Update 2015:

A search of the peer reviewed literature was performed from April 2013 through March 2015. A search of the available studies found there are no randomized controlled studies with outcome measures greater than one year published U.S. studies to date. In addition, there are no corneal cross-linking devices that have received FDA approval for these indications. Clinical trials remain ongoing however according to ClinicalTrials.gov there are none completed with results. Therefore, the policy statement remains unchanged.

Update 2017:

A search of the peer-reviewed literature was performed from April 2015 through May 2017. In April of 2016, The Food and Drug Administration had determined approval for corneal collagen cross-linking using riboflavin and ultraviolet A in the treatment of progressive keratoconus and corneal ectasia following refractive surgery. The safety and effectiveness of corneal collagen cross-linking (CXL) was evaluated in 3 randomized, parallel-group, open-label, sham-controlled trials. Patients were monitored up to 12 months. In each study, only one eye of each patient was designated as the study eye/experimental eye. Experimental eyes were randomized to receive one of the two study treatments (CXL or sham) at the baseline visit and were assessed at Day 1, Week 1, and Months 1, 3, 6, and 12. At month 3 or later, sham study eyes and non-study eyes had the option of receiving CXL treatment, and were monitored for 12 months from the time of receiving CXL treatment. Each CXL treated eye received a single course of CXL treatment only. Safety data were obtained from: 193 randomized CXL study eyes (102 keratoconus, 91

corneal ectasia), 191 control eyes, and 319 nonrandomized CXL non-study eyes (191 keratoconus, 128 corneal ectasia). Overall, 512 eyes (293 keratoconus, 219 corneal ectasia) in 364 patients received CXL treatment. In concluding, adverse events such as corneal opacity (haze), eye pain, dry eye, reduced visual acuity, corneal epithelium defect and blurred vision were reported. However, these events resolved within 12 months of treatment. No deaths were reported and patients experienced positive changes in visual function including visual acuity.

The safety and effectiveness for CXL have not been established in pediatric (< 14) and geriatric (> 65) patients.

▼ Provider Guidelines

This procedure should be reported with the Category III CPT® code for Collagen cross-linking of cornea (including removal of the corneal epithelium and intraoperative pachymetry when performed)

▼ References

The following were among the resources reviewed and considered in developing this policy. By reviewing and considering the resources, CareFirst does not in any way endorse the contents thereof nor assume any liability or responsibility in connection therewith. The opinions and conclusions of the authors of these resources are their own, and may or may not be in agreement with those of CareFirst.

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