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Kaiser Foundation Health Plan of Washington

Clinical Review Criteria
Collagen Cross-Linking for the Treatment of Keratoconus

Criteria

For Medicare Members

Source	Policy
CMS Coverage Manuals	None
National Coverage Determinations (NCD)	None
Local Coverage Determinations (LCD)	Non-Covered Services (L35008).
Local Coverage Article	None

For Non-Medicare Members

A. To qualify for photochemical cross-linkage using riboflavin and Ultraviolet A light **ALL** of the following must be met:
   1. Has a diagnosis of keratoconus
   2. Patient is not older than 40 years old
   3. Treatment is limited to a once in a lifetime

Notes:
KPWA considers epithelium-off photochemical collagen cross-linkage using riboflavin and ultraviolet A medically necessary for keratoconus. All other diagnosis such as keratectasia is considered experimental and investigational, as the effectiveness has not been established. Epithelium-on (transepithelial) collagen cross-linkage and performance of photochemical collagen cross-llinkage in combination with other procedures (CXL-plus) (e.g., intrastromal corneal ring segments, PRK or phakic intra-ocular lens implantation) is considered experimental and investigational.

The following information was used in the development of this document and is provided as background only. It is not to be used as coverage criteria. Please only refer to the criteria listed above for coverage determinations.

Background

Keratoconus is a disease of the cornea that is characterized by a gradual thinning and protuberance of the cornea resulting in visual damage. The cause of keratoconus is not known; its prevalence varies from 50 to 230 per 100,000 (Kennedy, Bourne et al. 1986, Heidecke, Burkert et al. 2008) and the association between African Americans and Latinos and keratoconus has been described (Woodward, Blachley et al. 2016). Several risk factors have been identified; these include eye-rubbing, contact lens use, systemic disorders (Down syndrome, Ehlers-Danlos syndrome, and osteogenesis imperfecta), family history, and environment (asthma, atopic disease) (Gasset, Houde et al. 1978, Rabinowitz 1998, Sugar and Macsai 2012, Woodward, Blachley et al. 2016).

Clinical characteristics include bilateral or unilateral visual impairment, sudden decrease in visual acuity, and/or astigmatism. Patient may also present with difficulty with visual correction and protrusion of the cornea with an indentation of the lower eyelid on downgaze. Disease progression is marked by corneal hydrops. Diagnosis can be done by slit lamp examination when the disease progresses. The mainstay of treatment is the correction of the vision which can be performed with spectacle correction, contact lens, surgical treatments or intrastromal corneal ring, keratectomy, keratoplasty (corneal implantation) and collagen crosslinking (CXL).

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Corneal collagen crosslinking aims to slow the progression of keratoconus by increasing covalent bonds in the cornea. During the corneal crosslinking treatment, riboflavin drops saturate the cornea, which is then activated by ultraviolet light. In laboratory and clinical studies this procedure has been shown to strengthen the cornea. CXL is not a cure for keratoconus. The goal of this treatment is to stop the progression of keratoconus, and prevent further deterioration in vision. The procedure consists of applying riboflavin every 3-5 minutes for 25-30 minutes and irradiating the cornea with UVA light after removal of the corneal epithelium. Then bandage lens are applied and assessment of re-epithelialization is performed about one week after the treatment. The intervention lasts one hour to 90 minutes. Although no approval statement was found on the Food and Drug Administration website, Avedro, the manufacturer of Photrexa® Viscous, Photrexa® and KXL® System indicated that in 2016, the US Food and Drug Administration approved corneal collagen cross-linking using riboflavin and UV for progressive keratoconus (Avedro 2016). Collagen crosslinking is believed to flatten the cornea and improve vision.

Medical Technology Assessment Committee (MTAC)

Collagen Cross-Linking for the treatment of Keratoconus

09/19/2016: MTAC REVIEW

Evidence Conclusion: Two randomized trials were critically appraised. These studies assessed the efficacy and effectiveness of CXL. Comparison was made between CXL and no treatment or between CXL and riboflavin only. Baseline characteristics were similar between the groups and patients were followed up for one year. The results showed that CXL led to positive outcomes by reducing corneal steepness and asphericity. Adverse events were reported and these include corneal opacity, eye pain, punctate keratitis, blurry vision, corneal striae and corneal epithelial defect. However, the open label nature of the design, the lack of clarification on how the sequence generation was performed, the lack of information of allocation concealment, the short follow-up (1 year), the small sample size, and the fact that the sponsor of one of the trials was the manufacturer compromise the validity of the studies. The body of evidence is also constituted of prospective and observational studies. The sample size in these studies varied from 13 to 97 and a reduction in keratoconus progression was globally observed. It is worth noted that the follow-up period varied from 6 to 24 months. No meaningful conclusion can be reached because these studies are non-comparative studies.

Conclusion:

The body of evidence is of low quality and there is insufficient evidence to determine whether CXL is effective and safe in stopping the progression of keratoconus as compared to the use of alternative treatments.

Articles:

The literature revealed a number of articles; the following articles were selected for critical appraisal:
Safety and Effectiveness of the UV-X System for Corneal Collagen Cross-Linking in Eyes with Progressive Keratoconus (NCT00647699)
https://clinicaltrials.gov/ct2/show/results/NCT00647699?term=corneal+collagen+crosslinking&rank=19&sect=X016 See Evidence Table 1 (not peer reviewed). Corneal collagen crosslinking for progressive keratoconus in Saudi Arabia: One-year controlled clinical trial analysis (Khattak, Nakhli et al. 2015) See Evidence Table 2.

The use of Collagen Cross-Linking for the treatment of Keratoconus does not meet the *Kaiser Permanente Medical Technology Assessment Criteria.*

Date Created	Date Reviewed	Date Last Revised
10/04/2016	10/04/2016[MPC], 08/01/2017[MPC], 07/10/2018[MPC]	11/01/2016

[MPC] Medical Policy Committee

Revision History	Description
10/04/2016	Created document & added MTAC review
11/01/2016	MPC approved criteria of medical necessity for collagen cross linking for the treatment of keratoconus

Codes

CPT code – 0402T

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