

FEP 9.03.28 Corneal Collagen Cross-Linking

Effective Date: July 15, 2017

Related Policies:

9.03.05 Corneal Topography/Computer-Assisted Corneal Topography/Photokeratoscopy

Corneal Collagen Cross-Linking

Description

Corneal collagen cross-linking (CXL) is a photochemical procedure approved by the Food and Drug Administration for the treatment of progressive keratoconus and corneal ectasia. Keratoconus is a dystrophy of the cornea characterized by progressive deformation (steepening) of the cornea while corneal ectasia is keratoconus that occurs after refractive surgery. Both lead to functional loss of vision and need for corneal transplantation.

FDA REGULATORY STATUS

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.

POLICY STATEMENT

Corneal collagen cross-linking using riboflavin and ultraviolet A may be considered **medically necessary** as a treatment of progressive keratoconus or corneal ectasia after refractive surgery in patients who have failed conservative treatment (eg spectacle correction, rigid contact lens).

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

POLICY GUIDELINES

Progressive keratoconus or corneal ectasia is defined as 1 or more of the following:

- An increase of 1 D in the steepest keratometry value
- An increase of 1 D in regular astigmatism evaluated by subjective manifest refraction
- A myopic shift (decrease in the spherical equivalent) of 0.50 D on subjective manifest refraction
- A decrease ≥ 0.1 mm in the back optical zone radius in rigid contact lens wearers where other information was not available.

BENEFIT APPLICATION

Experimental or investigational procedures, treatments, drugs, or devices are not covered (See General Exclusion Section of brochure).

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RATIONALE

Summary of Evidence

For individuals who have progressive keratoconus who receive collagen cross-linking (CXL) using riboflavin and ultraviolet A, the evidence includes multiple randomized controlled trials (RCTs), systematic reviews, and nonrandomized studies. Relevant outcomes are change in disease status, functional outcomes, and treatment-related morbidity. In both pivotal RCTs, the primary end point (an intermediate outcome) of reducing maximum corneal curvature (Kmax) by 1 diopter (D) was achieved at month 3 and maintained at months 6 and 12 in CXL-treated patients, compared to sham controls. In the 2 RCTs, the difference in mean change in Kmax from baseline to 12 months was 1.9 and 2.3 D, respectively, favoring the CXL-treated patients. Long-term follow-up for visual acuity outcomes are needed. The adverse events associated with CXL include corneal opacity (haze), corneal epithelial defects, and other ocular findings. Most adverse events resolved in the first month but, in a few (1%-6%) patients, continued for 6 to 12 months. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals who have corneal ectasia after refractive surgery who receive CXL using riboflavin and ultraviolet A, the evidence includes multiple RCTs, systematic reviews, and nonrandomized studies. Relevant outcomes are change in disease status, functional outcomes, and treatment-related morbidity. In both pivotal RCTs, the primary end point (an intermediate outcome) of reducing Kmax by 1 D was achieved at month 3 and maintained at months 6 and 12 in the CXL-treated patients compared to sham controls. In the 2 RCTs, the difference in mean change in Kmax from baseline to 12 months was 2.0 and 1.1 D, respectively, favoring CXL-treated patients. Long-term follow-up for visual acuity outcomes are needed. The adverse events associated with CXL include corneal opacity (haze), corneal epithelial defects, and other ocular findings. Most adverse events resolved in the first month, but, in a few (1%-6%) patients, continued for 6 to 12 months. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

SUPPLEMENTAL INFORMATION

Practice Guidelines and Position Statements

National Institute for Health and Care Excellence

In 2013 the National Institute for Health and Care Excellence (NICE) issued guidance on corneal collagen cross-linking (CXL) using riboflavin and ultraviolet A updated and replaced its 2009 guidance. The 2013 guidance stratified NICE recommendations for corneal CXL as follows:

“Most of the published evidence on photochemical corneal collagen cross-linkage (CXL) using riboflavin and ultraviolet A (UVA) for keratoconus and keratectasia relates to the technique known as 'epithelium-off' CXL. 'Epithelium-on (transepithelial) CXL' is a more recent technique and less evidence is available on its safety and efficacy. Either procedure (epithelium-off or epithelium-on CXL) can be combined with other interventions, and the evidence base for these combination procedures (known as 'CXL-plus') is also limited. Therefore, different recommendations apply to the variants of this procedure, as follows.

1.1 Current evidence on the safety and efficacy of epithelium-off CXL for keratoconus and keratectasia is adequate in quality and quantity. Therefore, this procedure can be used provided that normal arrangements are in place for clinical governance, consent and audit.

1.2 Current evidence on the safety and efficacy of epithelium-on (transepithelial) CXL, and the combination (CXL-plus) procedures for keratoconus and keratectasia is inadequate in quantity and

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quality. Therefore, these procedures should only be used with special arrangements for clinical governance, consent and audit or research.”

U.S. Preventive Services Task Force Recommendations

Not applicable.

Medicare National Coverage

There is no national coverage determination (NCD). In the absence of an NCD, coverage decisions are left to the discretion of local Medicare carriers.

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POLICY HISTORY

Date	Action	Description
September 2012	New Policy	
June 2013	Update Policy	Policy updated with literature review. References 5, 6, 11 added. Policy statement unchanged.
June 2014	Update Policy	Policy updated with literature review, adding reference 4. The policy statement is unchanged.
June 2015	Update Policy	Policy updated with literature review through February 25, 2015; references 3-4 and 11 added; policy statement unchanged.
September 2016	Update Policy	Policy updated with literature review, references 4-5 added. Regulatory status updated with FDA approval information. Policy statement changed to medically necessary.
June 2017	Update Policy	Policy updated with literature review through January 25, 2017; references 3, 6-8, and 15-17 added. The Policy section was changed to (1) corneal collagen cross-linking using riboflavin and ultraviolet A may be considered medically necessary as a treatment of progressive keratoconus or corneal ectasia after refractive surgery in patients who have failed conservative treatment (eg spectacle correction, rigid contact lens), and (2) corneal collagen cross-linking using riboflavin and ultraviolet A is considered investigational for all other indications. A specific definition of progressive keratoconus or corneal ectasia was added to the Policy Guidelines section.

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