Corneal Collagen Cross-Linking for Keratoconus

Policy Number:	**M20181212105**
Effective Date:	**2/1/2019**
Sponsoring Department:	**Health Care Services**
Impacted Department(s):	**Health Care Services**

Type of Policy: ☒ Internal ☒ External

Data Classification: ☐Confidential ☐Restricted ☒Public

Applies to (Line of Business):

☐ Corporate (All)
☒ State Products, if yes which plan(s): ☒MediSource; ☒ MediSource Connect; ☒Child Health Plus ☒Essential Plan
☒ Medicare, if yes, which plan(s): ☒MAPD; ☐PDP; ☒ISNP; ☒CSNP
☒ Commercial, if yes, which type: ☒Large Group; ☒Small Group; ☒Individual
☒ Self-Funded Services *(Refer to specific Summary Plan Descriptions (SPDs) to determine any pre-authorization or pre-certification requirements and coverage limitations. In the event of any conflict between this policy and the SPD of a Self-Funded Plan, the SPD shall supersede the policy.)*

Excluded Products within the Selected Lines of Business (LOB)

Applicable to Vendors? Yes ☐ No☒

Purpose and Applicability:

To set forth Independent Health's policy for corneal **collagen cross-linking** (CXL) for **keratoconus**.

Policy:

Commercial, Self-Funded and Medicare Advantage:

Epithelium-off CXL is considered medically necessary as a treatment for progressive keratoconus or corneal ectasia following refractive surgery when **all** of the following conditions are met:

I. Diagnosis of progressive keratoconus defined as one or more of the following over 24 consecutive months:
   A. increase of 1.00 diopters (D) or more in the steepest keratometry measurement; or
   B. increase of 1.00 D or more in manifest cylinder; or
   C. increase of 0.50 D or more in manifest refraction spherical equivalent (MRSE); and
II. Age 14 years or older; and
III. Maximum keratometry 47.0 D or more on corneal topography (Placido-based); and
IV. Inferior-to-superior ratio of more than 1.5 on topography mapping; and
V. Corrected distance visual acuity (CDVA) worse than 20/20 with properly fitted spectacles or contact lenses; and
VI. Corneal thickness 300 microns or more; and
VII. No history of corneal or systemic disease that would interfere with healing after the procedure such as chemical injury or delayed epithelial healing in the past.

Collagen cross-linking is not considered medically necessary for the following:

I. Epithelium-on (transepithelial) collagen cross-linking is considered investigational for keratoconus, keratectasia, and all other indications.
II. Any type of collagen cross-linking is considered investigational in all other situations, including but not limited to treatment of infectious keratitis and in combination with other procedures (e.g., intrastromal corneal ring segments, PRK or phakic intra-ocular lens implantation) (CXL-plus).

MediSource, MediSource Connect, Essential Plan, Child Health Plus:
MediSource, MediSource Connect, Essential Plan and Child Health Plus do not cover collagen cross-linking for keratoconus.

Background:
Keratoconus is a noninflammatory disorder of the cornea of unknown etiology. In keratoconus, collagen fibers within the cornea weaken and no longer maintain the normal round shape of the cornea. Consequently, the cornea bulges outward, steepens, and develops a progressive conical 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. Patients may present with blurry vision or a sudden decrease in visual acuity. Visual impairment is initially managed with corrective lenses but may require surgical correction as the disease progresses. Patients present at puberty or early adulthood. There are a wide range of occurrences reported in the general population, ranging from 50 to 230 per 100,000. There is no difference in incidence and prevalence between genders.

The CXL procedure is normally done as an outpatient procedure using topical anesthesia, and typically takes 60–90 minutes. In epithelium-off CXL, the epithelium is first abraded with a blunt spatula to allow

penetration of riboflavin into the corneal tissue. Riboflavin eye drops are applied to the corneal surface before the procedure and intermittently during the procedure. The corneal surface is exposed to UV: precise timings and treatment protocols vary. Postoperatively, topical antibiotics and anti-inflammatory drops are normally prescribed, with topical steroids if necessary. In some cases, a bandage contact lens may also be used for a few days. The procedure is done with 1 eye at a time and may also be repeated if needed. In epithelium-on (transepithelial) CXL, the corneal epithelial surface is left intact (or may be partially disrupted) and a longer riboflavin loading time is needed.

Conventional corneal cross-linking (C-CXL) is a procedure and therefore not subject to FDA regulation. However, any medical devices, drugs, or tests used as part of the procedure may be subject to FDA regulation. Avedro Inc. received FDA approval for the combination product Photrexa (riboflavin 5-phosphate ophthalmic solution) and Photrexa Viscous (riboflavin 5-phosphate in 20% dextran solution) for use with the KXL UVA Light system for treatment of progressive keratoconus.

An evaluation of the peer-reviewed scientific literature, including but not limited to subscription materials, has provided Independent Health the basis for its medical necessity coverage outlined above.

Pre-Authorization Required? Yes ☒ No☐

Pre-authorization is required for this service.

Definitions

Corneal collagen cross-linking is a procedure using a combination of riboflavin (vitamin B2) eye drops to be absorbed throughout the cornea stroma and UV-A radiation which triggers photochemical reaction to change the cross links between and within collagen fibers to increase the biomechanical stiffness of the corneal stroma.

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

Placido-based topography involves projecting series of concentric rings of light onto the anterior surface of the cornea and using placido disc reflection systems to capture the reflected light. Using data captured by the reflection systems, computer algorithms can measure corneal curvature, irregularities and other characteristics of the cornea. Corneal curvature is measured in diopters of curvature along thousands of points on the concentric rings.

References

Related Policies, Processes and Other Documents
N/A

Non-Regulatory references
Hayes, Inc. Comparative Effectiveness Review Corneal Cross-Linking for Treatment of Keratoconus. Lansdale, PA; February 2018.

Hayes, Inc. Annual Review Comparative Effectiveness Review Corneal Cross-Linking for Treatment of Keratoconus. Lansdale, PA; January 2022.

Hersh PS, Stulting RD, Muller D, et al.; United States Crosslinking Study Group. United States Multicenter Clinical Trial of Corneal Collagen Crosslinking for Keratoconus Treatment. Ophthalmology. 2017 Sep;124(9):1259-1270.

National Institute for Health and Care Excellence (NICE) [web site]. Photochemical corneal collagen cross-linkage using riboflavin and ultraviolet A for keratoconus and keratectasia. Available at: https://www.nice.org.uk/guidance/ipg466/resources/photochemical-corneal-collagen-crosslinkage-using-riboflavin-and-ultravioleta-for-keratoconus-and-keratectasia-pdf-1899869874302149 Accessed September 20, 2023.

Raiskup F, Theuring A, Pillunat LE, Spoerl E. Corneal collagen crosslinking with riboflavin and ultraviolet-A light in progressive keratoconus: ten-year results. J Cataract Refract Surg. 2015 Jan;41(1):41-6.

Sorkin N, Varssano D. Corneal collagen crosslinking: a systematic review. Ophthalmologica. 2014;232(1):10-27.

Wayman, LL. Keratoconus. In: UpToDate, Post TW (Ed), UpToDate, Waltham, MA. (Accessed on September 20, 2023)

Wittig-Silva C, Chan E, Islam FM, Wu T, Whiting M, Snibson GR. A randomized, controlled trial of corneal collagen cross-linking in progressive keratoconus: three-year results. Ophthalmology. 2014 Apr;121(4):812-21.

Regulatory References

New York State Department of Health, Division of Managed Care Response to Coverage Question (CovQuest). Email response 10/30/2018.

United States Food and Drug Administration (FDA) [web site]. Approval Letter. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2016/203324s000lbl.pdf September 20, 2023.

This policy contains medical necessity criteria that apply for this service. Please note that payment for covered services is subject to eligibility criteria, contract exclusions and the limitations noted in the member's contract at the time the services are rendered.

Version Control

Signature / Approval on File? Yes ☒ No☐

Revision Date	Owner	Notes
12/1/2023	Health Care Services	Reviewed
12/1/2022	Health Care Services	Reviewed
1/1/2022	Health Care Services	Reviewed
2/1/2021	Health Care Services	Revised

2/1/2020	Medical Management	Revised