

Riboflavin 5'-phosphate ophthalmic solution (EPIOXA)

National Drug Monograph

July 2026

VA Pharmacy Benefits Management Services and National Formulary Committee

The purpose of VA National Formulary Committee drug monographs is to provide a focused drug review for making formulary decisions. The Product Information or other resources should be consulted for detailed and most current drug information.

FDA PRESCRIBING INFORMATION¹

Description / MOA	Photo enhancer
Indication Under Review	Use in epithelium-on corneal collagen cross-linking (CXL) for the treatment of keratoconus in adults and pediatric patients aged 13 years and older, in conjunction with the O2n System and the Boost Goggles
Dosage Forms Under Review	0.177% ophthalmic solution in a single-dose glass syringe (EPIOXA) 0.239% ophthalmic solution in a single-dose glass syringe (EPIOXA HD)

EFFICACY CONSIDERATIONS

Trials	Study 1 [NCT03442751]	Study 2 [NCT05759559]
Design	Prospective, randomized, parallel-group, sham procedure/vehicle-controlled trials; R randomized in a 2:1 treatment allocation to receive epithelium-on corneal collagen cross-linking (CXL) or sham control	
Population	280 eyes of 201 patients with keratoconus	312 eyes of 208 patients with keratoconus
Intervention	189 eyes (67.5%) received CXL treatment using riboflavin 5'-phosphate ophthalmic solutions (0.239% and 0.177%)	200 eyes (64.1%) received CXL treatment using riboflavin 5'-phosphate ophthalmic solutions
Comparator	90 eyes (32.1%) received sham control	112 eyes (35.9%) received sham control
Results	Primary Endpoint (Month 6): LS Mean change from baseline in maximum corneal curvature (Kmax) EPIOXA CXL -0.3 D, Control +0.6 D Treatment difference (TD) : -1.0 D (95% CI: -1.5, -0.4); P < 0.01 Secondary Endpoint (Month 12): LS Mean change from baseline in Kmax. EPIOXA CXL: -0.4 D, Control: +0.7 D, TD: -1.1 D (95% CI: -1.6, -0.6); P < 0.01	Primary Endpoint (Month 12): LS Mean change from baseline in Kmax. EPIOXA CXL: -0.5 D, Sham Control: +0.4 D, TD: -1.0 D (95% CI: -1.3, -0.6); P < 0.01 Secondary Endpoint (Month 6): LS Mean change from baseline in Kmax EPIOXA CXL:-0.4 D, Sham Control: +0.1 D, TD: -0.6 D (95% CI: -0.9, -0.2); P < 0.01

SAFETY CONSIDERATIONS

Boxed Warnings	none
Contraindications	Hypersensitivity, aphakic and pseudophakic patients without a UV-blocking intraocular lens
Other Warnings	Herpetic keratitis
Adverse Events	Conjunctival hyperaemia (31%), corneal opacity (haze) (5%-25%), photophobia (5%-25%), punctate keratitis (5%-25%), eye pain (5%-25%)

THERAPEUTIC ALTERNATIVES AND THEIR PLACE IN THERAPY

DRUG	VANF	Comment
Riboflavin 5'-phosphate ophthalmic solution (EPIOXA)	TBD	
Riboflavin (PHOTREXA) cross-linking kit	NF	Product anticipated to be discontinued and replaced with EPIOXA

POTENTIAL PLACE IN THERAPY

- Keratoconus is a progressive eye condition characterized by the thinning and bulging of the cornea. It causes the cornea to protrude into a cone shape, leading to blurred vision and increased sensitivity to light.
- The treatment options for keratoconus include corneal collagen cross-linking, eyeglasses, contact lenses, other lenses, and surgery
- The agent currently being used to perform the crosslinking procedure is riboflavin (PHOTREXA) in combination with the iLink CXL system. The downside of this procedure is that it requires removal of the epithelium which can cause postoperative pain and prolonged healing time. Epioxa is the newest version from Glaukos which is designed for epithelium-on crosslinking and requires a new machine (O2n) that does not work with the iLink device. The benefit to epithelium-on crosslinking is that it does not require the removal of corneal epithelium which is preferred in terms of pain and infection risk.
- The results of Study 1 and Study 2 support the use of riboflavin 5'-phosphate ophthalmic solution in epithelium-on corneal collagen cross-linking in individuals with keratoconus

References

1. PHOTREXA (riboflavin 5'-phosphate in 20% dextran ophthalmic solution) 0.146% and PHOTREXA (riboflavin 5'-phosphate ophthalmic solution) 0.146% Prescribing Information.. Glaukos. February 2025. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2025/203324s010lbl.pdf. Accessed December 3 , 2025
2. EPIOXA HD (riboflavin 5'-phosphate ophthalmic solution) 0.239% and EPIOXA (riboflavin 5'-phosphate ophthalmic solution) 0.177% Prescribing Information. Avedro, a Glaukos company. October 2025. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2025/219910s000lbl.pdf
3. Beckman KA. Epithelium-on Corneal Collagen Cross-Linking with Hypotonic Riboflavin Solution in Progressive Keratoconus. Clin Ophthalmol. 2021;15:2921-2932. Published 2021 Jul 7. doi:10.2147/OPTH.S318317
4. Beckman KA, Parkhurst GD, Lee JH, et al. Randomized, Controlled Study to Evaluate the Safety and Efficacy of Oxygen-Enriched Epithelium-On Corneal Cross-Linking for the Treatment of Keratoconus. Ophthalmol Ther. 2026;15(4):1463-1484. doi:10.1007/s40123-026-01364-7

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