Clinical Policy: Ophthalmic Riboflavin (Photrexa, Photrexa Viscous, Epioxa HD, Epioxa)

Reference Number: CP.PHAR.536
Effective Date: 06.01.21
Last Review Date: 11.26
Line of Business: Commercial, HIM/ICHRA, Medicaid

Coding Implications
Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description

Photrexa®, Photrexa® Viscous, Epioxa, and Epioxa HD are topical ophthalmic photoenhancers.

FDA Approved Indication(s)

Photrexa and Photrexa Viscous are indicated for use in corneal collagen cross-linking in combination with the KXL™ System for the treatment of:

- Progressive keratoconus
- Corneal ectasia following refractive surgery

Epioxa and Epioxa HD are indicated for use in epithelium-on corneal collagen cross-linking for the treatment of keratoconus in adults and pediatric patients aged 13 years and older, in conjunction with O_2n System and the Boost Goggles.

Policy/Criteria

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with Centene Corporation® that Photrexa, Photrexa Viscous, Epioxa, and Epioxa HD are **medically necessary** when the following criteria are met:

I. Initial Approval Criteria*

**Approval of the drug does not translate to an approval of the corneal cross-linking procedure*

A. Progressive Keratoconus (must meet all)**:**

1. Diagnosis of progressive keratoconus;
2. Prescribed by or in consultation with an ophthalmologist;
3. Member meets one of the following (a or b):
   a. Photrexa or Photrexa Viscous: Age ≥ 14 years;
   b. Epioxa or Epioxa HD: Age ≥ 13 years;
4. Dose does not exceed one kit per eye.

Approval duration: 6 months (up to one kit per eye)

B. Corneal Ectasia (must meet all)**:**

1. Request is for Photrexa or Photrexa HD;
2. Diagnosis of corneal ectasia following refractive surgery;
3. Prescribed by or in consultation with an ophthalmologist;
4. Age ≥ 14 years;

5. Dose does not exceed one kit per eye.

Approval duration: 6 months (up to one kit per eye)

C. Other diagnoses/indications (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace/ICHRA) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace/ICHRA, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace/ICHRA) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace/ICHRA, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace/ICHRA, and CP.PMN.53 for Medicaid.

II. Continued Therapy*

**Approval of the drug does not translate to an approval of the corneal cross-linking procedure*

A. All Indications in Section I (must meet all)**:**

1. Member meets one of the following (a or b):
   a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
   b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B);*
2. At least 6 months have passed since member's last collagen cross-linking procedure;
3. Member is responding positively to therapy as evidenced by a reduction in diopters in the treated eye(s);
4. If request is for a dose increase, new dose does not exceed one kit per eye.

Approval duration: 6 months (up to one kit per eye)

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace/ICHRA) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace/ICHRA, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace/ICHRA) or PDL (Medicaid), the non-formulary policy for the

relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace/ICHRA, and CP.PMN.16 for Medicaid; or

2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace/ICHRA, and CP.PMN.53 for Medicaid.

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace/ICHRA, and CP.PMN.53 for Medicaid or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key
FDA: Food and Drug Administration

Appendix B: Therapeutic Alternatives
Not applicable

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s): known hypersensitivity to benzalkonium chloride or any ingredients in Epioxa HD and Epioxa, aphakic and pseudophakic patients (*Epioxa and Epioxa HD only*)
- Boxed warning(s): none reported

V. Dosage and Administration

Drug Name	Dosing Regimen	Maximum Dose
Riboflavin 5'-phosphate in 20% dextran ophthalmic solution 0.146% for topical ophthalmic use (Photrexa Viscous) Riboflavin 5'-phosphate ophthalmic solution 0.146% for topical ophthalmic use (Photrexa)	Dosage and Administration, Section 2: Prescribing Information: • Debride the epithelium using standard aseptic technique using topical anesthesia. • Then instill 1 drop of ***Photrexa Viscous*** topically on the eye every 2 minutes for 30 minutes. • After 30 minutes, examine the eye under slit lamp for presence of a yellow flare in the anterior chamber. If flare is not detected, instill 1 drop of ***Photrexa Viscous*** every 2 minutes for an additional 2 to 3 drops and recheck for yellow flare. Repeat as necessary. • Once flare is observed, perform ultrasound pachymetry. If corneal thickness is less than 400 microns, instill 2 drops of ***Photrexa*** every 5 to 10	See dosing regimen

Drug Name	Dosing Regimen	Maximum Dose
	seconds until the corneal thickness increases to at least 400 microns. • Irradiation should not be performed unless this 400 micron threshold is met and the yellow flare is seen.	
Riboflavin 5'-phosphate ophthalmic solution 0.239% for topical ophthalmic use (Epioxa HD) Riboflavin 5'-phosphate ophthalmic solution 0.177% for topical ophthalmic use (Epioxa)	Dosage and Administration, Section 2: Prescribing Information: • Debride the corneal epithelium (epithelium-on) using topical anesthesia. • Then apply 2 drops of ***Epioxa HD*** topically on the eye every 60 seconds for 4 minutes, followed by 2 drops of ***Epioxa*** topically on the eye every 30 seconds for 6 minutes. • Gently rinse the corneal surface with approximately 5mL of balanced salt solution. • Perform ultrasound parchymetry. If corneal thickness is less than 325 microns, irradiation should not be performed. • Apply the Boost Goggles and turn on the oxygen flow as per the instructions in the Boost Goggles User Guide.	

VI. Product Availability

Drug Name	Availability
Riboflavin 5'-phosphate in 20% dextran ophthalmic solution 0.146% (Photrexa Viscous) Riboflavin 5'-phosphate ophthalmic solution 0.146% (Photrexa)	Cross-linking kit: containing the following components for use with the KXL System: • Riboflavin 5'-phosphate ophthalmic solution 0.146% for topical ophthalmic use (Photrexa) • Riboflavin 5'-phosphate in 20% dextran ophthalmic solution 0.146% for topical ophthalmic use (Photrexa Viscous)
Riboflavin 5'-phosphate ophthalmic solution 0.239% (Epioxa HD) Riboflavin 5'-phosphate ophthalmic solution 0.177% (Epioxa)	Epithelium-on cross-linking kit: containing the following components for use with the O2n System and Boost Goggles: • Riboflavin 5'-phosphate ophthalmic solution 0.239% for topical ophthalmic use (Epioxa HD) • Riboflavin 5'-phosphate ophthalmic solution 0.177% for topical ophthalmic use (Epioxa)

VII. References

1. Photrexa Viscous and Photrexa Prescribing Information. Burlington, MA: Avedro; February 2025. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2025/203324s010lbl.pdf. Accessed February 11, 2026.
2. Avedro Inc., KXL System: Operator's Manual. Burlington, MA: Avedro, Inc. Copyright 2019. ML-00006 Rev R. Available at: https://www.glaukos.com/int/cornea/kxl-system/. Accessed February 11, 2026.
3. Epioxa HD and Epioxa Prescribing Information. Burlington, MA: Avedro; October 2025. Available at: https://www.epioxa.com. Accessed August 27, 2026.

Coding Implications

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
J2787	Riboflavin 5'-phosphate, ophthalmic solution (photrexa viscous/photrexa), up to 3 ml
J2789	Riboflavin 5'-phosphate, ophthalmic solution (epioxa hd/epioxa), up to 2 ml

Reviews, Revisions, and Approvals	Date	P&T Approval Date
2Q 2022 annual review: no significant changes; references reviewed and updated.	01.27.22	05.22
Template changes applied to other diagnoses/indications and continued therapy section.	10.05.22	
2Q 2023 annual review: no significant changes; references reviewed and updated.	02.02.23	05.23
2Q 2024 annual review: updated HCPCS code description for J2787; references reviewed and updated.	01.12.24	05.24
2Q 2025 annual review: no significant changes; references reviewed and updated.	02.07.25	05.25
2Q 2026 annual review: no significant changes; references reviewed and updated. Added ICHRA line of business.	03.31.26	05.26
HCPCS J2787: Revised the description language to align with updated coding verbiage.	06.02.26	
Added Epioxa HD and Epioxa to criteria per local market request.	08.27.26	11.26

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program

approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions, and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment, or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

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Note:
For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

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