KAISER PERMANENTE® Mid-Atlantic States	**Corneal Collagen Cross-Linking for Progressive Keratoconus Medical Coverage Policy**

Utilization *ALERT*

- Prior to use of this MCP for evaluation of medical necessity, benefit coverage MUST be verified in the member's EOC or benefit document.
- For Medicare members, please refer to CMS guidelines through Medicare Coverage Database requirements.
- Medicare does not have a National Coverage Determination (NCD) for Corneal Collagen Crosslinking.
- Local Coverage Determinations (LCDs)/Local Coverage Articles (LCAs) do not exist at this time.
- Note: After searching the Medicare Coverage Database, if no NCD/LCD/LCA is found, then use the policy referenced above for coverage guidelines

I. Procedure: Corneal Collagen Cross-Linking for Progressive Keratoconus

II. Coverage Policy

A. Covered for progressive keratoconus and keratectasia.
Epithelium-off photochemical collagen cross-linkage using riboflavin and ultraviolet A is considered medically necessary for progressive keratoconus and keratectasia.

B. Photochemical collagen cross-linkage is considered experimental and investigational for all other indications because it's effectiveness for other indications has not been established.

C. **Epithelium-on** (transepithelial) collagen cross-linkage is considered experimental and investigational for keratoconus, keratectasia, and all other indications.

D. Performance of photochemical collagen cross-linkage 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.

References

1. Kojima, Takashi; Primack, Jonathan D.; Azar, Dimitri T__ Corneal Collagen Crosslinking (CXL) Intrastromal Corneal Ring Segments and Collagen Crosslinking› Surgical Technique. *Ophthalmology*. January 1, 2014. © 2014.
2. Greenstein, Steven A.; Hersh, Peter S Future of Corneal Collagen Crosslinking for Post-Refractive Ectasia.. *Cornea.* Published January 1, 2017. © 2017.
3. Kocak I, Aydin A, Kaya F, Koc H, Comparison of transepithelial corneal collagen crosslinking with epithelium-off crosslinking in progressive keratoconus. *J Fr Ophtalmol* May 1, 2014; 37 (5); 371-6.
4. Medeiros, Carla S.; Giacomin, Natalia T.; Bueno, Renata L.; Ghanem, Ramon C.; Moraes, Jr., Haroldo V.; Santhiago, Marcony R.. Review/Update: Accelerated corneal collagen **cr**osslinking**:** Technique, efficacy, safety, and applications Detail Only Available Academic Journal *Journal of Cataract & Refractive Surgery*. December 2016 42(12):1826-1835 Language: English. DOI: 10.1016/j.jcrs.2016.11.028.
5. Mohammadpour, Mehrdad; Masoumi, Ahmad; Mirghorbani, Masoud; Shahraki, Kianoosh; Hashemi, Hassan. Review: Updates on corneal collagen cross**-**linking**:** Indications, techniques and clinical outcomes *Journal of Current Ophthalmology*. December 2017 29(4):235-247 Language: English. DOI: 10.1016/j.joco.2017.07.003.
6. Subasinghe, Sandeepani K.; Ogbuehi, Kelechi C.; Dias, George J. *Graefe's* Current perspectives on corneal collagen crosslinking (CXL). *Archive of Clinical & Experimental Ophthalmology.* Aug2018, Vol. 256 Issue 8, p1363-1384. 22p. DOI: 10.1007/s00417-018-3966-0. ,
7. Peter S. Hersh MD, R. Doyle Stulting MD, PhD, David Muller PhD , Daniel S. Durrie MD and Rajesh K. Rajpal MD; U.S. Multicenter Clinical Trial of Corneal Collagen Crosslinking for Treatment of Corneal Ectasia after Refractive Surgery Ophthalmology, 2017-10-01, Volume 124, Issue 10, Pages 1475-1484, Copyright © 2017 American Academy of Ophthalmology
8. Apostolos, Lazaridis; Spiros, Tsamassiotis; Konstantinos, Droutsas; Volker, Besgen; Walter, Sekundo; Frank Michael, Schroeder; Yaroslava, Wenner. Revisiting the Safety of the Corneal Collagen Crosslinking Procedure: Evaluation of the Effect of Ultraviolet A Radiation on Retinal Function and Structure *Cornea.* Sep 30, 2019, Language: English,
9. Subasinghe, Sandeepani K.; Ogbuehi, Kelechi C.; Dias, George J. Graefe's Current perspectives on corneal collagen crosslinking (CXL). *Archive of Clinical & Experimental Ophthalmology,* Aug2018, Vol. 256 Issue 8, p1363-1384, 22p.
10. Al-Mohaimeed M. M. (2019). Combined corneal CXL and photorefractive keratectomy for treatment of keratoconus: a review. *International journal of ophthalmology*, *12*(12), 1929–1938. https://doi.org/10.18240/ijo.2019.12.16.
11. Shajari, M., Kolb, C. M., Agha, B., Steinwender, G., Müller, M., Herrmann, E., Schmack, I., Mayer, W. J., & Kohnen, T. (2019). Comparison of standard and accelerated corneal cross-linking for the treatment of keratoconus: a meta-analysis. *Acta ophthalmologica*, *97*(1), e22–e35. https://doi.org/10.1111/aos.13814
12. Celia Vimont, Devin A Harrison MD; Corneal Collagen Cross-linking Approved to Treat Keratoconus in

U.S.; © American Academy of Ophthalmology 2018; Aug.01, 2016; https://www.aao.org/eye-health/news/cross-linking-approved-keratoconus-united-states
13. American Academy of Ophthalmology (AAO). Corneal Ectasia PPP – 2018. For additional information visit the AAO website: https://www.aao.org/preferred-practice-pattern/corneal-ectasia-ppp-2018. Accessed on October 26, 2021
14. Davis SA, Bovelle R, Han G, Kwagyan J. Corneal collagen cross-linking for bacterial infectious keratitis. *Cochrane Database Syst Rev.* 2020 Jun17;6(6):CD013001. Accessed on October 26, 2021. https://pubmed.ncbi.nlm.nih.gov/32557558/
15. Highlights of prescribing information. Photrexa Viscous and Photrexa Photrexa [Product Information], Waltham, MA. Avedro Inc. Last updated July 2016. Accessed on October 26, 2021. https://www.accessdata.fda.gov/drugsatfda_docs/label/2016/203324s000lbl.pdf.
16. Sykakis, E., Karim, R., Evans, J. R., Bunce, C., Amissah-Arthur, K. N., Patwary, S., McDonnell, P. J., & Hamada, S. (2015). Corneal collagen cross-linking for treating keratoconus. *The Cochrane database of systematic reviews*, (3), CD010621. Accessed on October 26, 2021. https://doi.org/10.1002/14651858.CD010621.pub2.
17. American Academy of Ophthalmology (AAO). Cornea/external disease summary benchmarks for preferred practice pattern® guidelines. December 2020. Available at: Cornea/External Disease Summary Benchmarks - 2020 - American Academy of Ophthalmology (aao.org).https://www.aao.org/summary-benchmark-detail/cornea-external-disease-summary-benchmarks-2020
18. Centers for Medicare & Medicaid Services (CMS), Healthcare Common Procedure Coding System, (HCPCS), Public Meeting Agenda, Drugs, Biologicals and Radiopharmaceuticals, Wednesday, May 17, 2017, 9:00 am – 5:00 pm, CMS Auditorium, 7500 Security Boulevard, Baltimore (Woodlawn), Maryland 21244-1850
19. Gaster RN; Margines JB; Li X; Canedo AC; Rabinowitz YS, Results of corneal crosslinking in adolescents with progressive keratoconus: prospective study. *Journal of cataract and refractive surgery [J Cataract Refract Surg,* ISSN: 1873-4502, 2021 Oct 01; Vol. 47 (10), pp. 1333-1337; Publisher: Wolters Kluwer on behalf of ASCRS and ESCRS; PMID: 33769766, Database: MEDLINE
20. Wajnsztajn, D., Shmueli, O., Zur, K., Frucht-Pery, J., & Solomon, A. (2022). Predicting factors for the efficacy of cross-linking for keratoconus. *PloS one*, *17*(2), e0263528. https://doi.org/10.1371/journal.pone.0263528
21. Agarwal, R., Jain, P., & Arora, R. (2022). Complications of corneal collagen cross-linking. *Indian journal of ophthalmology*, *70*(5), 1466–1474. https://doi.org/10.4103/ijo.IJO_1595_21
22. Chang, L., Zhang, L., Cheng, Z., Zhang, N., Wang, C., Wang, Y., & Liu, W. (2022). Effectiveness of collagen cross-linking induced by two-photon absorption properties of a femtosecond laser in *ex vivo* human corneal stroma. *Biomedical optics express*, *13*(9), 5067–5081. https://doi.org/10.1364/BOE.468593
23. Greenstein, S. A., & Hersh, P. S. (2021). Corneal Crosslinking for Progressive Keratoconus and Corneal Ectasia: Summary of US Multicenter and Subgroup Clinical Trials. *Translational vision science & technology*, *10*(5), 13. https://doi.org/10.1167/tvst.10.5.13
24. Badawi A. E. (2022). Corneal Haze and Densitometry in Keratoconus after Collagen Cross-Linking by

Three Different Protocols. *Journal of current ophthalmology*, *33*(4), 422–430. https://doi.org/10.4103/joco.joco_145_21

25. MCG 28th edition. Copyright 2024 MCG Health, LLC ACG: A-1040 (AC) Corneal Cross-linking. Accessed 12/25/2023
26. Larkin, D. F. P., Chowdhury, K., Burr, J. M., Raynor, M., Edwards, M., Tuft, S. J., Bunce, C., Caverly, E., Doré, C., & KERALINK Trial Study Group (2021). Effect of Corneal Cross-linking versus Standard Care on Keratoconus Progression in Young Patients: The KERALINK Randomized Controlled Trial. *Ophthalmology*, *128*(11), 1516–1526. https://doi.org/10.1016/j.ophtha.2021.04.019
27. Hersh, P. S., Stulting, R. D., Muller, D., Durrie, D. S., Rajpal, R. K., & United States Crosslinking Study Group (2017). United States Multicenter Clinical Trial of Corneal Collagen Crosslinking for Keratoconus Treatment. *Ophthalmology*, *124*(9), 1259–1270. https://doi.org/10.1016/j.ophtha.2017.03.052
28. American Academy of Ophthalmology (AAO). Preferred Practice Pattern. (2018). *Corneal ectasia.* Accessed 12/07/2023. https://www.aao.org/education/preferred-practice-pattern/corneal-ectasia-ppp-2018

Approval History

Effective June 01, 2016, state filing is no longer required per Maryland House Bill HB 798 – Health Insurance – Reporting

Date approved by RUMC	Date of Implementation
03/30/2017	03/30/2017
03/29/2018	03/29/2018
02/20/2019	02/20/2019
02/25/2020	02/25/2020
01/20/2021	01/20/2021
01/24/2022	01/24/2022
01/26/2023	01/26/2023
01/24/2024	01/24/2024

*The Regional Utilization Management Committee received **delegated authority** to review and approve designated Utilization Management and Medical Coverage Policies by the Regional Quality Improvement Committee in 2011.

Note: Kaiser Permanente Mid-Atlantic States (KPMAS) include referral and authorization criteria to support primary care and specialty care practitioners, as appropriate, in caring for members with selected conditions. Whenever possible, Medical Coverage Policies are evidence-based and may also include expert opinion. Medical Coverage Policies are not intended or designed as a substitute for the reasonable exercise of independent clinical judgment by a practitioner in any particular set of circumstances for an individual member.