Prior Authorization Review Panel
MCO Policy Submission

A separate copy of this form must accompany each policy submitted for review.
Policies submitted without this form will not be considered for review.

Plan: Keystone First	**Submission Date**: 4/1/2024
Policy Number: ccp.1510	**Effective Date:** 4/2022 **Revision Date:** March 1, 2024
Policy Name: Xen gel stent for glaucoma	

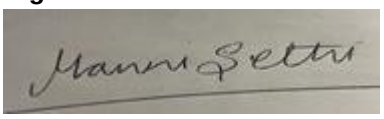
Type of Submission – Check all that apply:

- **New Policy**
- x **Revised Policy***
- **Annual Review – No Revisions**
- **Statewide PDL**

***All revisions to the policy must be highlighted using track changes throughout the document.**

Please provide any clarifying information for the policy below:

See tracked changes below.

Name of Authorized Individual (Please type or print): Manni Sethi, MD, MBA, CHCQM	**Signature of Authorized Individual:** 

Xen gel stent for glaucoma

Clinical Policy ID: CCP.1510

Recent review date: 3/2024

Next review date: 7/2025

Policy contains: Glaucoma, sub-conjunctival filtration, trabeculectomy, XEN gel stent

Keystone First- CHIP has developed clinical policies to assist with making coverage determinations. Keystone First- CHIP's clinical policies are based on guidelines from established industry sources, such as the Centers for Medicare & Medicaid Services (CMS), state regulatory agencies, the American Medical Association (AMA), medical specialty professional societies, and peer-reviewed professional literature. These clinical policies along with other sources, such as plan benefits and state and federal laws and regulatory requirements, including any state- or plan-specific definition of "medically necessary," and the specific facts of the particular situation are considered by Keystone First- CHIP, on a case by case basis, when making coverage determinations. In the event of conflict between this clinical policy and plan benefits and/or state or federal laws and/or regulatory requirements, the plan benefits and/or state and federal laws and/or regulatory requirements shall control. Keystone First- CHIP's clinical policies are for informational purposes only and not intended as medical advice or to direct treatment. Physicians and other health care providers are solely responsible for the treatment decisions for their patients. Keystone First- CHIP's clinical policies are reflective of evidence-based medicine at the time of review. As medical science evolves, Keystone First- CHIP will update its clinical policies as necessary. Keystone First- CHIP's clinical policies are not guarantees of payment.

Coverage policy

XEN gel stent is clinically proven and, therefore, may be medically necessary in cases of glaucoma with prior failure of filtering/cilioablative procedure and/or uncontrolled intraocular pressure (progressive damage and mean diurnal medicated intraocular pressure ≥ 20 mm Hg) on maximally tolerated medical therapy, i.e., ≥ 4 classes of topical intraocular pressure-lowering medications or fewer in the case of tolerability or efficacy issues (Buffault, 2019; Chen, 2022; Fea, 2020; Gillmann, 2020; Lim, 2021; Panarelli, 2023; Traverso, 2023; U.S. Food and Drug Administration, 2016; Yang, 2022).

XEN45 insertion is medically necessary only when performed by an ophthalmologist experienced with trabeculectomy and bleb management (U.S. Food and Drug Administration, 2016).

Limitations

Only one XEN45 device per eye is medically necessary.

Alternative covered services

- Trabeculoplasty.
- Trabeculectomy.

Background

Glaucoma is a painless, symptomless condition that can cause blindness. With one exception, narrow-angle glaucoma, it is associated with increased intraocular pressure within the eye. Inside the eye, fluid is constantly being manufactured and has to drain from inside the eye. High eye pressure is always related to some increased

resistance or obstruction of the normal outflow of the intraocular fluid. The chronic sustained high eye pressure leads to degenerative optic neuropathy, loss of retinal ganglion cells and axons, and ultimately to blindness if not treated.

A meta-analysis of 50 studies (n = 198,259) estimated the worldwide prevalence of primary open-angle glaucoma to be 2.4%, or over 68 million persons. Rates are 28% higher among males ($P < .01$), with the highest prevalence in Africa (Zhang, 2021). About half of worldwide glaucoma cases are undetected (Soh, 2021).

Glaucoma is an incurable disease, and all humans are at risk. Open-angle glaucoma, its most common form, has no symptoms, increasing the importance of early detection. An estimated three million Americans have the disease, but only half are aware of it. About 120,000 Americans are blind from glaucoma. African Americans are 15 times more likely to be visually impaired, and six to eight times more likely to be blind from glaucoma than American whites (Glaucoma Research Foundation, 2022a). A family history of glaucoma increases risk of the disorder by four to nine times (Glaucoma Research Foundation, 2022b).

First-line treatments for glaucoma are typically topical ophthalmic drops to reduce intra-ocular pressure, along with various medications. In cases refractory to these treatment, surgery can be considered, including laser surgery (often trabeculoplasty), traditional surgery (often trabeculectomy, the preferred surgery for glaucoma), or other procedures such as shunts or canaloplasty (Glaucoma Foundation, 2020).

Trabeculectomy and traditional glaucoma surgeries are not always effective, and often result in complications (Chaudhary, 2018). Researchers have developed minimally invasive surgery techniques for lowering intra-ocular pressure; the number of these surgeries increased by about 400% in the most recent eight years, including 203,146 eyes in the United States in the period 2013-2018 (Birnbaum, 2021; Yang, 2021). Large increases have also been reported in Germany (Luebke, 2021).

One type of minimally invasive surgery is sub-conjunctival filtration, or XEN Gel Stent (Allergan, Dublin, Ireland). XEN is implanted through an ab interno approach without conjunctival dissection. The U.S. Food and Drug Administration gave 510(k) Premarket Notification approval to the XEN Glaucoma Treatment System on November 21, 2016. The system consists of an injector, a single piece tube of porcine collagen/gelatin inserted permanently. An outflow pathway is created from the anterior chamber to the sub-conjunctival space through which aqueous humor can flow (U.S. Food and Drug Administration, 2016).

Findings

The American Academy of Ophthalmology practice guideline stated that trabeculectomy is the preferred treatment for open angle glaucoma cases not controlled by medicine. It also noted micro-invasive glaucoma surgeries are less effective in lowering intra-ocular pressure than trabeculectomy, but may have fewer short-term complications. The Academy's summary benchmarks for managing open angle glaucoma did not refer to any type of microinvasive surgery (American Academy of Ophthalmology, 2020; 2022).

A systematic literature review of 59 studies (n = 4,208) of Xen Gel Stent recipients documented median declines of intraocular pressure after surgery was 22.0 to 14.6 mmHg, and 2.8 to 0.7 for median medications. These patterns were consistent by follow-up (up to three years); by pre-operative level; by patient age; and by whether the procedure was standalone or part of a combination (Panarelli, 2023).

A systematic literature review of 96 studies found significant declines in intraocular pressure after Xen Gel Stent implant at 12, 24, and 36 months, each ending under 15 mmHg. In addition, 15 papers demonstrated similar

reductions whether phacoemulsification was or was not included; and significant declines in 11 papers that directly compared Xen Gel Stent with trabeculectomy (Traverso, 2023).

A systematic review/meta-analysis of eight studies showed the XEN45 Gel Stent alone or with phacoemulsification produced a statistically significant difference in intraocular pressure reduction and medication reduction one day, one week, and six months after the procedure (Lim, 2021).

A meta-analysis of 19 studies (n = 2,215) included glaucoma patients who underwent XEN surgery with and without cataract extraction. Reductions in intraocular pressure and medications were significant after two years. Four of the 19 studies (n = 221 eyes) compared improvements between the groups, which were not significantly different (Poelman, 2021).

A review of 77 studies evaluated performance of 10 types of minimally invasive glaucoma surgery, including XEN (five studies). XEN had the second highest weighted reduction of intraocular pressure at 38.5% at 12 to 24 months post-operative; the only type of surgery with a superior improvement included just one study. XEN also had an average 59.9% reduction in medications, superior to most other approaches (Gillmann, 2020).

A comprehensive review of 14 studies (n = 1,575) of XEN procedures for refractory glaucoma analyzed improvements, most after 12 months follow up. Intraocular pressure declines ranged from 27% to 54%, while medication reductions ranged from 38% to 96%, of which nine were over 69% (Fea, 2020).

A systematic review of 87 studies of minimally invasive glaucoma surgery found 74% had no control group. Of the 11 studies of XEN, all were prospective, and none were randomized; these also had the lowest “quality score” calculated by authors, of 13 types of surgery (Rosdahl, 2020).

A systematic review/meta-analysis of 12 studies (n = 1,602 eyes) compared XEN Gel with trabeculectomy (five studies) and with XEN plus phacoemulsification (eight studies). Adding XEN to trabeculectomy groups failed to lower intraocular pressure but reduced the number of drugs. XEN alone significantly lowered intraocular pressure reduced medications after three months (Wang, 2020).

A systematic review of eight studies (n = 777 patients, 958 eyes), showed the decrease in mean intraocular pressure at 12 months after surgery with XEN Gel Stents ranged from 25% to 56%. Glaucoma medications declined in each study. The most common complication was transient hypotony within one month (3%), and only five cases of severe complications occurred. Needling was required in 32% of cases, and 5.7% of eyes required repeat filtering surgery or cyclodestructive procedure (Buffault, 2019).

A systematic review/meta-analysis of 56 studies (n = 4,410) found ab-interno XEN implant, alone or combined with cataract surgery, reduced intra-ocular pressure by 35%, and reduced the number of anti-glaucoma medications. Vision-threatening complications occurred in 1% of subjects (Chen, 2022).

A systematic review/meta-analysis of 78 studies found XEN gel stent implants to be effective in lowering intra-ocular pressure ($P < .01$) and the number of glaucoma medications ($P < .001$) (Yang, 2022). Reductions in intra-ocular pressure for XEN implants and trabeculectomy were similar, but XEN had a higher bleb needling rate ($P < .004$) (Yang, 2022).

References

On December 15, 2023, we searched PubMed and the databases of the Cochrane Library, the U.K. National Health Services Centre for Reviews and Dissemination, the Agency for Healthcare Research and Quality, and the Centers for Medicare & Medicaid Services. Search terms were “glaucoma,” “sub-conjunctival filtration’” “trabeculectomy,” and “XEN gel stent,”. We included the best available evidence according to established evidence hierarchies (typically systematic reviews, meta-analyses, and full economic analyses, where available) and professional guidelines based on such evidence and clinical expertise.

American Academy of Ophthalmology. Preferred Practice Pattern Guidelines. Primary open-angle glaucoma. https://www.aao.org/preferred-practice-pattern/primary-open-angle-glaucoma-ppp. Published November, 2020.

American Academy of Ophthalmology. Preferred Practice Pattern Guidelines. Glaucoma summary benchmarks. https://www.aao.org/summary-benchmark-detail/glaucoma-summary-benchmarks-2020. Published December, 2022.

Birnbaum FA, Neeson C, Del Valle DS. Microinvasive glaucoma surgery: An evidence-based review. *Semin Ophthalmol*. 2021;36(8):772-786. Doi: 10.1080/08820538.2021.1903513.

Buffault J, Baudouin C, Labbe A. XEN® Gel Stent for management of chronic open angle glaucoma: A review of the literature. *J Fr Ophtalmol*. 2019;42(2):e37-e46. Doi: 10.1016/j.jfo.2018.12.002.

Chaudhary A, Salinas L, Guidotti J, Mermoud A, Mansouri K. XEN gel implant: A new surgical approach in glaucoma. *Expert Rev Med Devices*. 2018;15(1):47-59. Doi: 10.1080/17434440.2018.1419060.

Chen X-Z, Liang Z-Q, Yang K-Y, et al. The outcomes of XEN gel stent implantation: A systematic review and meta-analysis. *Front Med (Lausanne)*. 2022;9:804847. Doi: 10.3389/fmed.2022.804847.

Fea AM, Durr GM, Marolo P. XEN® gel stent: A comprehensive review on its use as a treatment option for refractory glaucoma. *Clin Ophthalmol*. 2020;14:1805-1832. Doi: 10.2147/OPTH.S178348.

Gillmann K, Mansouri K. Minimally invasive glaucoma surgery: Where is the evidence? *Asia Pac J Ophthalmol (Phila)*. 2020;9(3):203-214. Doi: 10.1097/APO.0000000000000294.

Glaucoma Research Foundation. Glaucoma Facts and Stats. https://www.glaucoma.org/glaucoma/glaucoma-facts-and-stats.php. Last reviewed February 28, 2022 (a)

Glaucoma Research Foundation. Are You at Risk for Glaucoma? https://www.glaucoma.org/glaucoma/are-you-at-risk-for-glaucoma.php. Published May 13, 2022. (b)

Glaucoma Foundation. Treating Glaucoma. Glaucoma Foundation website. https://glaucomafoundation.org/aboutglaucoma/treating-glaucoma/. Published 2020.

Lim SY, Betzler BK, Yip LWL, Dorairai S, Ang BCH. Standalone XEN45 Gel Stent implantation versus combined XEN45-phacoemulsification in the treatment of openangle glaucoma – A systematic review and meta-analysis. *Graefes Arch Clin Exp Ophthalmoll*. 2021;259(11):3209-3219. Doi: 10.1007/s00417-021-05189-x.

Luebke J, Boehringer D, Anton A, Daniel M, Reinhard T, Lang S. Trends in surgical glaucoma treatment in Germany between 2006 and 2018. *Clin Epidemiol*. 2021;13:581-592. Doi: 10.2147/CLEP.S310542.

Panarelli JF, Vera V, Sheybani A, et al. Intraocular pressure and medication changes associated with Xen gel stent: A systematic review of the literature. *Clin Ophthalmol*. 2023;17:25-46. Doi: 10.2147/OPTH.S390955.

Poelman HJ, Pals J, Rostamzad P, Bramer WM, Wolfs RCW, Ramdas WD. Efficacy of the XEN-implant in glaucoma and a meta-analysis of the literature. *J Clin Med*. 2021;10(5):1118. Doi: 10.3390/jcm10051118.

Rosdahl JA, Gupta D. Prospective studies of minimally invasive glaucoma surgeries: Systematic review and quality assessment. *Clin Ophthalmol*. 2020;14:231-243. Doi: 10.2147/OPTH.S239772.

Soh Z, Yu M, Betzler BK, Majithia S. The global extent of undetected glaucoma in adults: A systematic review and meta-analysis. *Ophthalmology*. 2021;128(10):1393-1404. Doi: 10.1016/j.ophtha.2021.04.009.

Traverso CE, Carassa RG, Fea AM, et al. Effectiveness and safety of Xen Gel Stent in glaucoma surgery: A systematic review of the literature. *J Clin Med*. 2023;12(16):5339. Doi: 10.3390/jcm12165339.

U.S. Food and Drug Administration. Letter from Malvina Eydelman to Allergan, Inc. https://www.accessdata.fda.gov/cdrh_docs/pdf16/k161457.pdf. Published November 21, 2016.

Wang B, Leng X, An X, Zhang X, Liu X, Lu X. XEN gel implant with or without pharmacoemulsification for glaucoma: A systematic review and meta-analysis. *Ann Transl Med*. 2020;8(20):1309. Doi: 10.21037/atm-20-6354.

Yang S-A, Mitchell WG, Hall N, et al. Usage patterns of minimally invasive glaucoma surgery (MIGS) differ by glaucoma type: IRIS registry analysis 2013-2018. *Ophthalmic Epidemiol*. 2021;1-9. Doi: 10.1080/09286586.2021.1955391.

Yang X, Zhao Y, Zhong Y, Duan X. The efficacy of XEN gel stent implantation in glaucoma: A systematic review and meta-analysis. *BMC Ophthalmol*. 2022;22(1):305. Doi: 10.1186/s12886-022-02502-y.

Zhang N, Wang J, Li Y, Jiang B. Prevalence of primary open angle glaucoma in the last 20 years: A meta-analysis and systematic review. *Sci Rep*. 2021;11(1):13762. Doi: 10.1038/s41598-021-92971-w.

Policy updates

3/2022: initial review date and clinical policy effective date: 4/2022

3/2023: Policy references updated.

3/2024: Policy references updated.