Molina Clinical Policy
XEN Gel Stent for Glaucoma: Policy No. 389

Last Approval: 12/14/2022
Next Review Due By: December 2023

DISCLAIMER

This Molina Clinical Policy (MCP) is intended to facilitate the Utilization Management process. Policies are not a supplementation or recommendation for treatment; Providers are solely responsible for the diagnosis, treatment and clinical recommendations for the Member. It expresses Molina's determination as to whether certain services or supplies are medically necessary, experimental, investigational, or cosmetic for purposes of determining appropriFateness of payment. The conclusion that a particular service or supply is medically necessary does not constitute a representation or warranty that this service or supply is covered (e.g., will be paid for by Molina) for a particular Member. The Member's benefit plan determines coverage – each benefit plan defines which services are covered, which are excluded, and which are subject to dollar caps or other limits. Members and their Providers will need to consult the Member's benefit plan to determine if there are any exclusion(s) or other benefit limitations applicable to this service or supply. If there is a discrepancy between this policy and a Member's plan of benefits, the benefits plan will govern. In addition, coverage may be mandated by applicable legal requirements of a State, the Federal government or CMS for Medicare and Medicaid Members. CMS's Coverage Database can be found on the CMS website. The coverage directive(s) and criteria from an existing National Coverage Determination (NCD) or Local Coverage Determination (LCD) will supersede the contents of this MCP and provide the directive for all Medicare members. References included were accurate at the time of policy approval and publication.

OVERVIEW

Glaucoma is characterized by elevated intraocular pressure (IOP), which results in visual field loss and irreversible blindness if left untreated. Glaucoma is classified as open-or closed-angle, primary or secondary. Open angle glaucoma (OAG) is the most common form with nearly 80% specifically from OAG in the United States. OAG is a chronic, progressive, and irreversible multifactorial optic neuropathy that is characterized by open angle of the anterior chamber, typical optic nerve head changes, progressive loss of peripheral vision (typical visual field changes) followed by central visual field loss (blindness) for which IOP is an important risk factor. The disease is usually bilateral, but asymmetry is often seen depending on the etiology (Mahabadi, 2022). Treatment strategies for OAG, both pharmacologic and surgical or a combination thereof, are aimed at lowering IOP, the primary modifiable risk factor associated with disease progression (Sheybani, 2020).

Topical ophthalmic drops are often the first-line treatment for primary OAG. Available IOP-lowering pharmacologic options reduce IOP through reduction of aqueous humor production (alpha-adrenergic agonists, beta blockers, carbonic anhydrase inhibitors), or by facilitating aqueous humor drainage (prostaglandin analogs, alpha agonists, cholinergic agonists, Rho kinase inhibitors). Pharmacologic therapy can involve multiple medications with the potential for additive or systemic side effects, poor compliance to therapy, and ocular toxicity. If pharmacologic treatment is not sufficiently effective, surgical procedures may be required; these include laser surgery (trabeculoplasty or cycloablation), traditional surgery (trabeculectomy), or other procedures (e.g., shunts or canaloplasty) (Mahabadi, 2022).

Surgical intervention may be indicated in individuals with glaucoma when the target IOP cannot be reached pharmacologically. Current standard surgical treatments for glaucoma include trabeculectomy or trabeculoplasty (incisional or laser). Trabeculectomy, an incisional surgery, is a well-established procedure and considered the gold standard; however, carries the risk of potential vision-threatening complications and may also fail over time such as scar formation at the drainage site. A repeat trabeculectomy is associated with a higher complication rate and an increased risk of subsequent failure.

Microinvasive Glaucoma Surgery (MIGS) has been defined as any glaucoma surgical procedure that avoids conjunctival dissection and thus approaches via ab interno incision (clear cornea wound), aiming to provide a safer and less invasive means of lowering IOP than traditional surgery, with the goal of reducing dependency on topical medication (De Gregorio et al. 2018). Although MIGS are collectively categorized as a class of interventions, each MIGS is unique in its structure and/or mechanism of action. MIGS procedures use an ab interno approach and aim to lower IOP via four mechanisms:

1. Increasing trabecular outflow (Trabectome, iStent, Hydrus stent, gonioscopy-assisted transluminal trabeculotomy, excimer laser trabeculotomy);
2. Increasing outflow via suprachoroidal shunts (The CyPass micro-stent was voluntarily recalled by Alcon in October 2018 due to the potential to cause endothelial cell loss concluded by the COMPASS-XT study as data showed a statistically significant difference in endothelial cell loss at 5 years in patients who received the device with cataract surgery compared with those who underwent cataract surgery alone);
3. Reducing aqueous production (endocyclophotocoagulation); and
4. **Subconjunctival filtration (XEN Gel stent).** A type of MIGS is sub-conjunctival filtration, or XEN Gel Stent, manufactured by Allergan, implanted through an ab interno approach without conjunctival dissection.

The XEN45 Gel Stent is currently the only FDA-approved sub-conjunctival MIGS procedure. The Stent is composed of porcine-derived gelatin that has been formed into a tube and cross-linked with glutaraldehyde to retain its shape. Dry, the stent measures 6 millimeters in length and has inner and outer diameters of 45 and 150 microns, respectively. Hydration causes the stent to expand and become more flexible. Implantation of the XEN stent is performed as an outpatient procedure using standard ophthalmologic surgery techniques. The system consists of an injector, a single piece tube of porcine collagen/gelatin inserted permanently. The XEN45 Gel Stent creates a permanent channel through the sclera allowing aqueous flow from the anterior chamber to the subconjunctival space (Allergan, 2021).

XEN Gel Stent is contraindicated in angle-closure glaucoma where angle has not been surgically opened, previous glaucoma shunt/valve or conjunctival scarring/pathologies in the target quadrant, active inflammation, active iris neovascularization, anterior chamber intraocular lens, intraocular silicone oil, and vitreous in the anterior chamber. Complications may include choroidal effusion, hyphema, hypotony, implant migration, implant exposure, wound leak, need for secondary surgical intervention, and intraocular surgery complications. Safety and effectiveness in neovascular, congenital, and infantile glaucoma has not been established.

Medical management of glaucoma, trabeculotomy, trabeculoplasty, endoscoping cyclophotocoagulation, and several surgical drainage devices and shunts (e.g., CyPass Micro Stent; iStent Inject) are clinical alternatives to the XEN Gel Stent (Schuman et al., 2008; Francis et al., 2011; Schmidt et al., 2013; Zhang et al., 2015).

Regulatory
This section is intended solely for informative purposes. Coverage is not based solely on FDA approval.

The XEN Glaucoma Treatment System, which includes the XEN45 Gel Stent and a preloaded XEN Injector (Allergan, Inc.), was cleared for marketing by the FDA through the 510(k) process as an ab interno aqueous stent for management of refractory glaucoma. The system was indicated for "the management of refractory glaucomas, including cases where previous surgical treatment has failed, cases of primary open angle glaucoma, and pseudoexfoliative or pigmentary glaucoma with open angles that are unresponsive to maximum tolerated medical therapy." (FDA; K161457)

COVERAGE POLICY

The XEN Glaucoma Treatment System **is considered experimental, investigational, or unproven** for any indication. There is insufficient reliable evidence in the form of high-quality peer-reviewed medical literature to establish the efficacy or effects on health care outcomes.

While safer and predictable surgery is a priority for patients with glaucoma, the body of evidence for MIGS efficacy remains limited. The XEN Gel Implant is one of several approaches to MIGS currently being investigated as discussed in this policy. There is no established treatment algorithm to identify patients most likely to benefit from the XEN Gel Implant. Studies with larger patient populations comparing XEN with established treatment options for glaucoma are required. Larger, randomized trials with extended follow-up periods are also required to better evaluate long-term safety and comparative effectiveness and safety of MIGS, specifically XEN Gel Implant (Lavia et al., 2017; Buffault et al., 2019; Schlenker et al., 2017).

SUMMARY OF MEDICAL EVIDENCE

The evaluation of the safety and effectiveness of the XEN45 system is primarily based on retrospective reviews, prospective reviews, and case series with small patient populations (n=30-65) and short-term follow-ups (12 months) (Fea et al. 2020) [De Gregorio, 2018; Grover, Nov 2017; Schlenker, 2017; Hengerer, et al., 2017; Pérez-Torregrosa, 2016; Widder, 2018].

- Some studies evaluate the use of XEN140 and/or XEN63 which are no longer recommended by the manufacturer (Sheybani, et al., 2016; Sheybani, et al., 2015) [Table 1].
- Schlenker et al. (2017) conducted an international, multicenter, retrospective cohort study of consecutive eyes with uncontrolled glaucoma who underwent either standalone microstent insertion with MMC or

trabeculectomy with MMC. The study enrolled a total of 354 eyes of 293 participants, 185 eyes of 159 participants received the microstent and 169 eyes of 139 participants received the trabeculectomy. Eligibility criteria included patients with multiple types of glaucoma and above-target IOP on maximum medical therapy. Participants were between the ages of 30-90 years with no history of previous incisional surgery for their eye disease. Participants were excluded if they had prior incisional filtering glaucoma surgery or a history of neovascular glaucoma, uveitic glaucoma, iridocorneal endothelial syndrome, and Axenfeld-Rieger syndrome. The results demonstrated that there was no difference in efficacy, risk of failure, and safety profile between the 2 surgical procedures. The authors concluded that there was no detectable difference in risk of failure and safety between standalone microstent with MMC and trabeculectomy with MMC and that the ab interno gelatin microstent with MMC was noninferior to trabeculectomy plus MMC. However, further research is recommended to further investigate these procedures. [Table 1]

- Grover et al. (2017) evaluated the performance and safety of the XEN 45 Gel Stent for the treatment of refractory glaucoma in a prospective, single-arm, open-label, multicenter clinical study sponsored by the manufacturer. Selection criteria included individuals with refractory glaucoma, defined as prior failure of a filtering or cilioablative procedure and/or uncontrolled IOP on maximally tolerated medical therapy. A total of 65 eyes in patients 45 years of age and older were implanted. No intraoperative complications or unexpected postoperative AEs were reported. During the 1 year of follow up, most AEs were considered mild/moderate and resolved with no sequelae. The authors concluded that the XEN 45 Gel Stent safely reduced both IOP and medication use and offer a less invasive surgical option for this subset of patients. Potential study limitations include the absence of comparator and open-label study design, which could have impacted the outcomes.

- Chaudhary et al. (2018) noted XEN devices are not directly comparable to the currently commercialized devices and techniques. Furthermore, the study noted that a potentially greater degree of postoperative management is needed with the XEN due to formation of a subconjuctival bleb requiring close follow-up. It is not yet been established if this additional workload is made worthwhile by its efficacy and whether the greater simplicity and safety profile outbalance the established efficacy of traditional filtering surgery. Studies with larger patient populations and long-term follow-ups comparing XEN with established treatment options for glaucoma are required.

- Case series (n=12 -111) reported the six- to 12-month outcomes of XEN implant with XEN-phacoemulsification and without cataract surgery (Hohberger, et al., 2018; Fea, et al., 2017).

- Studies have also been conducted investigating XEN used with mitomycin-C (MMC) (Galal, et al., 2017). In a prospective interventional study, 13 eyes with primary OAG underwent XEN implantation with subconjunctival MMC. Of those eyes, 3 were pseudophakic and 10 underwent simultaneous phacoemulsification and XEN. One year of follow-up documentation of IOP, number of medications, visual acuity, and complications. Complete success was defined as IOP reduction ≥ 20% from preoperative baseline at 1 year without any glaucoma medications, while partial success as IOP reduction of ≥ 20% with medications. 42% of eyes achieved complete success and 66% qualified success. Complications included choroidal detachment in 2 eyes, implant extrusion in 1 eye, and 2 eyes underwent trabeculectomy. The authors concluded that the XEN implant is an effective surgical treatment for primary OAG, with significant reduction in IOP and glaucoma medications at 1 year, and state that longer follow-up is needed (Galal et al., 2017). [Table 1]

- Kerr et al. (2017) published a literature review concluding that an increasing body of evidence suggests that primary MIGS (including but not limited to the XEN Glaucoma Treatment System) may be a viable initial treatment option to non-surgical intervention. However, further investigator-initiated randomized trials of sufficient size and duration are necessary to better evaluate efficacy.

- Vinod and Gedde (2017) reviewed published literature from 2015 through 2016 and noted that although the data on newer techniques from recent randomized clinical trials include titratability of IOP with multiple trabecular microbypass stents (iStent; Glaukos) and greater reduction in IOP and medication usage following intracanalicular scaffolding (Hydrus Microstent; Ivantis Inc.) combined with phacoemulsification versus phacoemulsification alone. It was concluded that the early studies of investigational subconjunctival filtering devices (XEN Gel Stent; AqueSys, Inc., and InnFocus MicroShunt; InnFocus Inc.) presents promising evidence; however, well-designed randomized clinical trials with extended follow-up are necessary to determine the long-term efficacy and late complications of these procedures.

Table 1: Outcomes of Published Studies at 12-month Follow-Up

Author, year	Study design	XEN model ± MMC	Eye number	Previous glaucoma surgery, %	% IOP reduction	Patients off medications after XEN, %	% medication classes reduction	Needling rate, %
Sheybani et al, 2015	Prospective	XEN140 + XEN63	37	None	32.25	50	64	32
Sheybani et al, 2016	Prospective	XEN140	49	45	36.4	42	56.6	43
Pérez-Torregrosa et al, 2016	Prospective	XEN45 + MMC	30	None	29.34	90	94.57	None
De Gregorio et al, 2018	Prospective	XEN45 + MMC	41	2.4	41.82	80.4	84	2.4
Schlenker et al, 2017	Retrospective	XEN45 + MMC	185	None	45.83	74.9	Not specified	43.2
Grover et al, 2017	Prospective	XEN45 + MMC	65	84.6	35.6	38.5	51.42	32.3
Galal et al, 2017	Prospective	XEN45 + MMC	13	None	29.4	42	94.57	30.7

Systematic Review/Meta-Analysis

Chen et al. (2022) published a systematic review on XEN gel stents used in the treatment of OAG that included 56 studies (n=4,410 eyes) published between September 2015 and December 2021, but none were RCTs. Some of the studies mentioned above were also included in this systematic review: De Gregorio (2018), Grover (2017), Galal (2017), and Pérez-Torregrosa (2018). According to the authors, the XEN gel stent reduced IOP by approximately 35%, resulting in a final average of 15 mmHg. Furthermore, the number of antiglaucoma drugs has significantly decreased. After two years, the overall complete success rate ranged from 21.0-70.8% using strict criteria originally designed to record success rates in filtration surgery. The analysis is limited in that it only reports findings from before and after measurements without comparing treatment groups. The authors concluded that the XEN gel stent was safe and effective; however, more research is needed to determine the effect of ethnicity on the success and failure rate after XEN implantation, as the majority of patients in the study were Caucasian.

Lim et al. (2021) conducted a systematic review and meta-analysis of 10 studies to compare the efficacy of standalone XEN45 Gel Sent implantation ("Standalone XEN45") and combined XEN-phacoemulsification surgery ("XEN45-Phaco"). At post-operative day 1, week 1, month 1, 3, and 6, there was a statistically significant difference in IOP reduction and decrease in IOP-lowering medications favoring Standalone XEN45. The review concluded that Standalone XEN45 has superior IOP-lowering outcomes compared to XEN45-Phaco in the early post-operative period, up to 6 months after surgery.

Poelman et al. (2021) conducted a meta-analysis of 19 studies (n = 2,215) with glaucoma patients who had XEN surgery with or without cataract removal and concluded that after two years, there were significant reductions in IOP and the number of IOP-lowering medications. There were no differences between standalone and combined procedures. Only 4 of the 19 studies evaluated differences in IOP and IOP-lowering medication between XEN-implant as a standalone procedure and as a combined procedure. Differences were not statistically significant at follow-up. The authors concluded that the XEN-implant is effective in lowering IOP in glaucoma and its performance in terms of IOP and IOP-lowering medications seems less than that of conventional glaucoma surgery; however, the risk profile of complications due to XEN-implant surgery seems to be better than that of conventional glaucoma surgery. Unfortunately, studies with longer follow-up are currently lacking. Future prospective RCTs on XEN-implant surgery are required to verify the current results and to establish a place in current therapy.

Wang et al. (2020) compared XEN Gel implant with trabeculectomy (5 studies) and XEN plus phacoemulsification (8 studies) in a systematic review and meta-analysis of 12 studies (n = 1,602 eyes). XEN added to trabeculectomy groups failed to lower IOP but reduced the number of drugs. XEN alone significantly lowered IOP reduced medications after 3 months The authors concluded that larger, better-designed, strictly blinded, multicenter randomized clinical trials are needed to confirm our findings.

Buffault et al. (2019) conducted a systematic review to analyze the change in IOP and glaucoma medications using the XEN Gel Stent as a solo procedure or in association with phacoemulsification in patients with chronic OAG. The systematic review included 8 studies (n = 777 patients, 958 eyes) and reported that the decrease in mean IOP at 12 months following surgery with XEN Gel Stents ranged between 25% to 56% (mean: 42%). In each study, the use of glaucoma medications decreased. The decrease in IOP was significantly greater in XEN implantation as a stand-alone procedure (44%) than in combined surgery (32%). The most common complication was transient hypotony within one month (3%), and only five cases of severe complications were recorded. The authors concluded that the XEN Gel Stent appears effective for reducing IOP and the number of medications in OAG patients within 1 year postoperatively, and with an acceptable safety profile. However, its use required vigilant postoperative follow-up and frequent postoperative interventions. RCTs are required to confirm the safety and effectiveness of the XEN Gel Stent, although these results appear beneficial.

King et al. (2018) conducted a Cochrane review of RCTs that compared the Xen gelatin implant or InnFocus MicroShunt to other MIG device techniques, trabeculectomy, laser treatment or medical treatment. The objective of the review was to evaluate the efficacy and safety of subconjunctival draining MIG devices in patients with OAG and ocular hypertension that were inadequately controlled with drops. The primary outcome was mean change in IOP. The review concluded that there is no randomized trials or high-quality evidence of subconjunctival draining MIG devices to prevent glaucoma progression, including the XEN gelatin implant and InnFocus stent. Properly designed RCTs are needed to assess the medium- and long-term efficacy and safety of this technique.

A Health Technology Assessment (HTA) (published in December 2019, updated December 2021) rated the use of the XEN Glaucoma Treatment System in patients with OAG as potential but unproven benefit based on published evidence suggesting that safety and impact on health outcomes are at least comparable to standard treatment. However, substantial uncertainty remains about safety and/or impact on health outcomes because of poor-quality studies, sparse data, conflicting study results, and/or other concerns. The HTA included 7 observational studies which compared XEN treatment system with standard care, trabeculectomy, and the individual study quality ratings. The low-quality body of evidence base consisted of 6 poor-quality studies and 1 very-poor-quality study. Although the results generally demonstrated a reduction in IOP and medication use from baseline, reduction rates varied greatly between studies suggesting that that XEN implantation led to a variable rate of treatment success across studies. In general, evidence comparing XEN implantation with trabeculectomy is insufficient to determine whether XEN implantation is equivalent or superior to trabeculectomy as there were only 2 studies evaluating this comparison, impairing any determination of consistency (Hayes, 2021).

National and Specialty Organizations

The **American Academy of Ophthalmology (AAO)** practice guideline indicates that trabeculectomy is the preferred treatment for OAG that cannot be controlled by medication. It is also noted that MIGS are less effective than trabeculectomy in reducing IOP but may have fewer short-term complications. The summary benchmarks established by the Academy for the management of OAG did not mention any type of MIGS (American Academy of Ophthalmology, 2020a; 2020b).

The 2020 AAO Preferred Practice Patterns on Primary OAG state that while several other glaucoma surgeries exist as alternatives to trabeculectomy and aqueous shunt implantation (e.g., nonpenetrating procedures, MIGS), the precise role of these procedures in the surgical management of glaucoma remains to be determined.

- iStent, iStent inject and XEN gel stent studies were of insufficient quality (i.e., the estimate of the effect is very uncertain) and therefore, the use of these devices should be left to the discretion of the treating ophthalmologist, in consultation with the individual patient. The guideline also states that Hydrus microstent studies were of moderate quality and that the desirable effects of this device clearly outweigh the undesirable effects.
- Regarding the topic of combining glaucoma and cataract surgery:
  - The decision of which procedure(s) to perform first or whether to combine cataract and glaucoma

surgery is determined by the ophthalmologist and patient.
- Generally, combined cataract and glaucoma surgery is not as effective as glaucoma surgery alone in lowering IOP, so patients who require filtration surgery who also have mild cataract may be better served by filtration surgery alone and cataract surgery later.

The AAO (2020) Glaucoma Summary Benchmarks for the management of primary OAG stated that medical therapy is the most common intervention initial intervention to lower IOP.
- Laser trabeculoplasty may be used as initial or adjunctive therapy in patients with primary OAG.
- Trabeculectomy is generally indicated when medications and appropriate laser therapy are insufficient to control disease and can be considered in selected cases as initial therapy. No reference is made in the guidelines to the XEN Gel Stent.

The **National Institute for Health and Care Excellence (NICE)** (2017) updated its recommendations for trabecular stent bypass microsurgery for OAG. According to the guidelines, "Current evidence on trabecular stent bypass microsurgery for OAG raises no major safety concerns." Evidence of efficacy is sufficient in both quality and quantity."

An Interventional procedures guidance [IPG612] provided evidence-based recommendations on microinvasive subconjunctival insertion of a trans-scleral gelatin stent for primary open-angle glaucoma in adults. This procedure was described as '*involves putting a tiny gelatin tube (stent) under the skin at the base of the eye to create a new drainage channel for excess fluid*.' The guidance noted that the '*evidence on the safety and efficacy of microinvasive subconjunctival insertion of a trans-scleral gelatin stent for primary open-angle glaucoma is limited in quantity and quality. Therefore, this procedure should only be used with special arrangements for clinical governance, consent, and audit or research*.' NICE encourages '*further research into microinvasive subconjunctival insertion of a trans-scleral gelatin stent for primary open-angle glaucoma, including randomized studies. Further research should include details of patient selection and long-term outcomes.*' The next scheduled review of this guidance is April 2021 (no updates published as of December 2022).

SUPPLEMENTAL INFORMATION

Intraocular pressure (IOP): IOP refers to the pressure of the fluid inside the eye; regulated by the balance of aqueous humour synthesis and secretion into the eye and outflow from the eye; therefore, most therapies for glaucoma aim to lower IOP to avoid disease progression. Elevated IOP is the crucial modifiable risk factor in the development of primary OAG.

Hypotony: Low IOP; or an IOP below which the eye does not maintain its normal shape and may subsequently lose vision. Hypotony is usually defined as an IOP of 5 mm Hg or less. Low IOP is associated with a number of complications, including corneal decompensation, accelerated cataract formation, maculopathy, and discomfort.

Trabeculectomy: Referred to as filtration surgery; A surgical procedure used in the treatment of glaucoma to relieve IOP by removing part of the eye's trabecular meshwork and adjacent structures. It is the most common glaucoma surgery and allows drainage of aqueous humor from within the eye to beneath the conjunctiva, where it is absorbed. This is currently considered the gold standard treatment for glaucoma that is resistant to medical management; however, it is a technically complex procedure that can result in a range of adverse outcomes.

CODING & BILLING INFORMATION

CPT	Description
0449T	Insertion of aqueous drainage device, without extraocular reservoir, internal approach, into the subconjunctival space; initial device
66183	Insertion of anterior segment aqueous drainage device, without extraocular reservoir, external approach
0450T	Insertion of aqueous drainage device, without extraocular reservoir, internal approach, into the subconjunctival space; each additional device (List separately in addition to code for primary procedure)

HCPCS	Description
C1783	Ocular implant, aqueous drainage assist device
L8612	Aqueous shunt

CODING DISCLAIMER. Codes listed in this policy are for reference purposes only and may not be all-inclusive. Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement. Listing of a service or device code in this policy does not guarantee coverage. Coverage is determined by the benefit document. Molina adheres to Current Procedural Terminology (CPT®), a registered trademark of the American Medical Association (AMA). All CPT codes and descriptions are copyrighted by the AMA; this information is included for informational purposes only. Providers and facilities are expected to utilize industry standard coding practices for all submissions. When improper billing and coding is not followed, Molina has the right to reject/deny the claim and recover claim payment(s). Due to changing industry practices, Molina reserves the right to revise this policy as needed.

APPROVAL HISTORY

12/14/2022	Policy reviewed and updated. No changes in coverage criteria. Updated references.
12/8/2021	Policy reviewed and updated. No changes in coverage criteria. Updated references. Converted to new format.
12/9/2020	New policy. IRO Peer Review. 10/16/20. Practicing Physician. Board certified in Ophthalmology.

REFERENCES

Government Agencies

1. Centers for Medicare and Medicaid Services (CMS). Medicare coverage database (search: Xen, Xen gel stent). Available from CMS.
   - No NCD Identified. Local Coverage Determination (LCD) Micro-Invasive Glaucoma Surgery L37578 (also L37244, L37531, L38223, L38233, L38299, L38301 is available) Available from CMS. Accessed October 2022.
2. United States Food and Drug Administration (FDA) Center for Devices and Radiological Health. 510K notification database (K161457): Xen glaucoma treatment system). Published October 2016. Available from FDA. Accessed October 2022.

Manufacturer

1. Allergan. Directions for use for the XEN glaucoma treatment system. Accessed October 2022.

Peer Reviewed Publications

1. Buffault J, Baudouin C, Labbé A. XEN® Gel Stent for management of chronic open angle glaucoma: A review of the literature. J Fr Ophtalmol. 2019 Feb;42(2):e37-e46.
2. Chaudhary A, Salinas L, Guidotti J, Mermoud A, Mansouri K. XEN Gel Implant: A new surgical approach in glaucoma. Expert Rev Med Devices. 2018 Jan;15(1):47-59.
3. Chen XZ, Liang ZQ, Yang KY, et al. The outcomes of XEN Gel stent implantation: A systematic review and meta-analysis. Front Med (Lausanne). 2022 Feb 4;9:804847.
4. De Gregorio A, Pedrotti E, Stevan G, et al. XEN glaucoma treatment system in the management of refractory glaucomas: a short review on trial data and potential role in clinical practice. Clin Ophthalmol. 2018;12:773-782. Published 2018 Apr 30. doi:10.2147/OPTH.S146919.
5. De Gregorio A, Pedrotti E, Russo L, Morselli S. Minimally invasive combined glaucoma and cataract surgery: Clinical results of the smallest ab interno gel stent. Int Ophthalmol. 2018 Jun;38(3):1129-1134. doi: 10.1007/s10792-017-0571-x. Epub 2017 May 29. PMID: 28555256.
6. Fea AM, Durr GM, Marolo P, Malinverni L, Economou MA, Ahmed I. XEN Gel Stent: A comprehensive review on its use as a treatment option for refractory glaucoma. Clin Ophthalmol. 2020 Jun 30;14:1805-1832. doi: 10.2147/OPTH.S178348. PMID: 32636610; PMCID: PMC7335291.
7. Fea AM, Spinetta R, Cannizzo PML, et al. Evaluation of Bleb morphology and reduction in IOP and glaucoma medication following implantation of a novel gel stent. J Ophthalmol. 2017;2017:9364910. doi: 10.1155/2017/9364910. Epub 2017 Jun 20. PMID: 28751986; PMCID: PMC5511657.
8. Galal A, Bilgic A, Eltanamly R, Osman A. XEN glaucoma implant with mitomycin C 1-year follow-up: result and complications. J Ophthalmol. 2017;2017:5457246. doi: 10.1155/2017/5457246. Epub 2017 Mar 1. PMID: 28348884; PMCID: PMC5350531.
9. Grover DS, Flynn WJ, Bashford KP, et al. Performance and safety of a new ab interno gelatin stent in refractory glaucoma at 12 months. Am J Ophthalmol. 2017 Nov;183:25-36. doi: 10.1016/j.ajo.2017.07.023. Epub 2017 Aug 5. PMID: 28784554.
10. Hengerer FH, Kohnen T, Mueller M, Ab Interno C-HI. Gel implant for the treatment of glaucoma patients with or without prior glaucoma surgery: 1-year results. *J Glaucoma*. 2017;26(12):1130–1136. doi:10.1097/IJG.0000000000000803. PMID: 29035911.
11. Hohberger B, Welge-Lussen UC, Lammer R. MIGS: Therapeutic success of combined Xen Gel Stent implantation with cataract surgery. Graefes Arch Clin Exp Ophthalmol. 2018;256(3):621–625. doi:10.1007/s00417-017-3895-3.
12. Kerr NM, Wang J, Barton K. Minimally invasive glaucoma surgery as primary stand-alone surgery for glaucoma. Clin Exp Ophthalmol. 2017 May;45(4):393-400. doi: 10.1111/ceo.12888. Epub 2017 Jan 29. PMID: 27928879.
13. King AJ, Shah A, et al. Subconjunctival draining minimally-invasive glaucoma devices for medically uncontrolled glaucoma. Cochrane Database of Systematic Reviews 2018, Issue 12. Art. No.: CD012742. DOI: 10.1002/14651858.CD012742.pub2.
14. Lim SY, Betzler BK, Yip LWL, et al. 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.
15. Mahabadi N, Foris LA, Tripathy K. Open angle glaucoma. [Updated 2022 Aug 22]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK441887/

16. Perez-Torregrosa VT, Olate-Perez A, Cerda-Ibanez M, et al. Combined phacoemulsification and XEN45 surgery from a temporal approach and 2 incisions. Arch Soc Esp Oftalmol. 2016 Sep;91(9):415-21. English, Spanish. doi: 10.1016/j.oftal.2016.02.006. Epub 2016 Mar 16. PMID: 26995503.
17. Poelman HJ, Pals J, Rostamzad P, et al. 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.
18. Schlenker MB, Gulamhusein H, Conrad-Hengerer I, et al. Efficacy, safety, and risk factors for failure of standalone ab interno gelatin microstent implantation versus standalone trabeculectomy. Ophthalmology. 2017;124(11):1579–1588. doi: 10.1016/j.ophtha.2017.05.004. Epub 2017 Jun 7. Erratum in: Ophthalmology. 2018 Mar;125(3):463. PMID: 28601250.
19. Sheybani A, Lenzhofer M, Hohensinn M, Reitsamer H, Ahmed II. Phacoemulsification combined with a new ab interno gel stent to treat open-angle glaucoma: Pilot study. J Cataract Refract Surg. 2015;41(9):1905–1909. doi: 10.1016/j.jcrs.2015.01.019.
20. Sheybani A, Dick B, Ahmed II. Early clinical results of a novel Ab interno gel stent for the surgical treatment of open-angle glaucoma. J Glaucoma. 2016;25(7):e691–e696. doi: 10.1097/IJG.0000000000000352.
21. Sheybani A, Scott R, Samuelson TW, et al. Open-angle glaucoma: Burden of illness, current therapies, and the management of nocturnal IOP variation. Ophthalmol Ther. 2020 Mar;9(1):1-14. doi: 10.1007/s40123-019-00222-z. Epub 2019 Nov 15. PMID: 31732872; PMCID: PMC7054505.
22. Vinod K, Gedde SJ. Clinical investigation of new glaucoma procedures. Curr Opin Ophthalmol. 2017 Mar;28(2):187-193. doi: 10.1097/ICU.0000000000000336. PMID: 27764024.
23. 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. PMID: 33209889; PMCID: PMC7661862.
24. Widder RA, Dietlein TS, Dinslage S, et al. The XEN45 Gel Stent as a minimally invasive procedure in glaucoma surgery: success rates, risk profile, and rates of re-surgery after 261 surgeries. Graefes Arch Clin Exp Ophthalmol. 2018;256(4):765–771. doi: 10.1007/s00417-018-3899-7. Epub 2018 Jan 22. PMID: 29356886.

National and Specialty Organizations

1. American Academy of Ophthalmology (AAO).
   - Preferred practice pattern guidelines. Primary open-angle glaucoma. doi: 10.1016/j.ophtha.2020.10.022. Published November, 2020. PMID: 34933745. Published 2021 Jan;128(1):P71-P150. Accessed October 2022.
   - Preferred practice pattern guidelines: Glaucoma summary benchmarks. Dec 2021. Available from AAO. Accessed October 2022.
2. National Institute for Health and Care Excellence (NICE).
   - Glaucoma: Diagnosis and management [NG81]. Published April 2009. Updated: January 2022. Available from NICE. Accessed October 2022.
   - Microinvasive subconjunctival insertion of a trans-scleral gelatin stent for primary open-angle glaucoma. Interventional procedures guidance [IPG612]. Published April 25, 2018. Available from NICE. Accessed October 2022.

Other Peer Reviewed and National Organization Publications (used in the development of this policy)

1. Hayes, Inc. Health technology assessment: XEN glaucoma treatment (Allergan) for treatment of open-angle o. Available from Hayes. Published December 19, 2019. Annual Review December 19, 2021. Accessed October 2022.Registration and login required.
2. Schehlein EM, Kaleem MA, Swamy R, Saeedi OJ. Microinvasive glaucoma surgery: An evidence-based assessment. Expert Rev Ophthalmol. 2017;12(4):331-343. doi:10.1080/17469899.2017.1335597.