

Subject: XEN Gel Stent for Glaucoma		Original Effective Date: Q4 2020
Policy Number: MCP-389	Revision Date(s):	
MCPC Approval Date: Q4 2020	Review Date:	

Contents

Disclaimer	1
Recommendation	1
Description of Procedure/Service/Pharmaceutical	2
Summary of Medical Evidence	3
Definitions	8
Coding Information	9
References	9

DISCLAIMER

This Molina clinical policy is intended to facilitate the Utilization Management process. It expresses Molina's determination as to whether certain services or supplies are medically necessary, experimental, investigational, or cosmetic for purposes of determining appropriateness 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 (i.e., 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 Molina clinical policy document and provide the directive for all Medicare members.

RECOMMENDATION

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 Microinvasive Glaucoma Surgery (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).

DESCRIPTION OF PROCEDURE/SERVICE/PHARMACEUTICAL

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 et al.). 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 (Weinreb RN, et al.).

Topical ophthalmic drops are often the first-line treatment for primary open-angle glaucoma (POAG). 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). (Glaucoma Foundation 2020)

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 intraocular pressure (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 (Cypass micro-stent; NOTE: The CyPass micro-stent was voluntarily recalled from the market in 2018 by Alcon after data from the COMPASS-XT study 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)**

U.S. Food and Drug Administration (FDA)

The FDA approved the XEN Glaucoma Treatment System (K161457) on November 21, 2016, through the 510(k) Premarket Notification process as a Class II aqueous shunt. The XEN Glaucoma Treatment System consists of the XEN 45 Gel Stent preloaded into a XEN injector. XEN Gel Stent (Allergan PLC, Irvine, CA, USA) is the only filtering MIGS device that allows subconjunctival filtration. The XEN Gel Stent (Allergan, Parsippany, NJ, US) is implanted through an ab interno approach without conjunctival dissection either as a standalone procedure (Xen solo) or in combination with cataract surgery (XenPhaco). XEN Gel Stent is indicated for the treatment of patients with refractory glaucoma in whom previous surgical treatment failed and patients who have primary open-angle glaucoma or pseudoexfoliative or pigmentary glaucoma with open angles who are unresponsive to maximum tolerated medical therapy.

There are multiple clinical trials in progress relating to the XEN Glaucoma Treatment System. For more information, go to www.clinicaltrials.gov.

SUMMARY OF MEDICAL EVIDENCE

XEN® Glaucoma Treatment System

- The evaluation of the safety and effectiveness of the XEN45 system are mainly 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, et al., 2018; Grover et al., Nov 2017; Schlenker, et al., 2017; Hengerer, et al., 2017; Pérez-Torregrosa, et al., 2016; Widder, et al., 2018)] [Table 1]
- Studies have also been conducted investigating XEN used with mitomycin C (Galal, et al., 2017). In a prospective interventional study, 13 eyes with primary OAG underwent XEN implantation with subconjunctival mitomycin-C (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 $\geq 20\%$ from preoperative baseline at 1 year without any glaucoma medications, while partial success as IOP reduction of $\geq 20\%$ 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 POAG, 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]**
- Schlenker et al. (2017) conducted an international, multicenter, retrospective cohort study of consecutive eyes with uncontrolled glaucoma who underwent either standalone microstent insertion with mitomycin C (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. The study enrolled eligible participants (30 - 90 years old) with multiple types of glaucoma, with above-target IOP on maximum medical therapy. 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. In summary, the authors reported, “there was no detectable difference in risk of failure and safety profiles between standalone ab interno microstent with MMC and trabeculectomy with MMC.” The authors concluded that the ab interno gelatin microstent with MMC was noninferior to trabeculectomy plus MMC. [Table 1]

- 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]
- 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 subconjunctival 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 (XenPhaco) and without cataract surgery (Hohberger, et al., 2018; Fea, et al., 2017).

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, %
<p>Sheybani et al published a nonrandomized prospective pilot study on 37 eyes undergoing XEN140 and XEN63 placement concomitantly with cataract extraction and intraocular lens implantation (CE/IOL) without the use of a metabolite. Another nonrandomized prospective study by Sheybani et al evaluated 49 eyes with implantation of the XEN140 alone, where 45% of the cohort had prior glaucoma surgery. This study defined success similarly with 40% and 89% completed and qualified success rates, respectively. They also showed an 8.4mmHg reduction in IOP and a reduction in medications from 3.0 to 1.3 (P<0.001) with 42% of patients off medications completely at 12 months. However, these studies evaluate the use of XEN63 and XEN140, which are not currently recommended by the manufacturer.</p>								
Sheybani et al, 2015 ¹	Prospective	XEN140 and XEN63	37	None	32.25	50	64	32
Sheybani et al, 2016 ²	Prospective	XEN140	49	45	36.4	42	56.6	43
<p>Pérez-Torregrosa et al (2016) and De Gregorio et al (2017) published the first 2 clinical prospective studies on XEN45 gel stent implantation with adjunctive mitomycin C (MMC) combined with cataract surgery</p>								
Pérez-Torregrosa et al, 2016 ³	Prospective	XEN45 + MMC	30	None	29.34	90	94.57	None

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

Author, year	Study design	XEN model \pm MMC	Eye number	Previous glaucoma surgery, %	% IOP reduction	Patients off medications after XEN, %	% medication classes reduction	Needling rate, %
De Gregorio et al, 2017 ⁴	Prospective	XEN45 + MMC	41	2.4	41.82	80.4	84	2.4
Schlenker et al, 2017 ⁵	Retrospective	XEN45 + MMC	185	None	45.83	74.9	Not specified	43.2
Grover et al, 2017 ⁶	Prospective	XEN45 + MMC	65	84.6	35.6	38.5	51.42	32.3
Galal et al, 2017 ⁷	Prospective	XEN45 + MMC	13	None	29.4	42	94.57	30.7

Schlenker et al. (2017) conducted an international multicenter retrospective study compared the efficacy, safety, and risk factors for failure of standalone XEN45 gel stent implantation versus trabeculectomy, both with adjunctive mitomycin C (MMC). In this study, 354 eyes with uncontrolled glaucoma and no prior incisional filtering surgery underwent microstent implantation (n=185) or trabeculectomy (n=169) in 4 academic ophthalmology centers, providing a large database. The results demonstrated that there was no difference in efficacy, risk of failure, and safety profile between the 2 surgical procedures. 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. **The authors concluded that there was no detectable difference in risk of failure and safety between standalone microstent with MMC and trabeculectomy with MMC. However, further research is recommended to further investigate these procedures.**

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.**

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 the authors noted that although the data on newer techniques from recent randomized clinical trials include titratability of intraocular pressure with multiple trabecular microbypass stents (iStent; Glaukos) and greater reduction in intraocular pressure 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.**

Systematic Review/Meta-Analysis

Buffault et al. (2019) conducted a systematic review to analyze the change in intraocular pressure (IOP) and glaucoma medications using the XEN Gel Stent as a solo procedure or in association with phacoemulsification in patients with chronic open angle glaucoma (OAG). Using predetermined search terms, a systematic review was performed using PubMed.

- A total of 8 case series or cohort studies (6 prospective and 2 retrospective) that were published between 2016 and 2018 were included. There were no randomized controlled trials included.
- Data was analyzed for 777 patients or 958 eyes.
- The various studies showed a mean IOP at 12 months between 13 and 16 mmHg, which represented an IOP reduction between 25 and 56% (mean: 42%). This decrease was associated with a reduction in glaucoma medications in all studies. The decrease in IOP was significantly greater in XEN® implantation as a stand-alone procedure (44%) than in combined surgery (32%) ($p < 0.05$). Transient hypotony (< 1 month) (3%), choroidal detachment or choroidal folds (1.5%), hyphema (1.9%), bleb leak (1.1%) and shallow anterior chamber (1.1%) were the most frequent complications.
- As for severe complications, four cases of malignant glaucoma (0.4%) and one case of retinal detachment have been reported. In the follow-up period, needling was been required in 32% of cases, and a total of 55 eyes (5.7%) required repeat filtering surgery or cyclodestructive procedure.

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. While these results appear promising, randomized controlled trials are needed to confirm the XEN Gel Stent's safety and efficacy.

King et al. (2018) conducted a **Cochrane review** of randomized controlled trials (RCTs) that compared the Xen gelatin implant or InnFocus MicroShunt to other minimally-invasive glaucoma (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 open angle glaucoma and ocular hypertension

that were inadequately controlled with drops. The primary outcome was mean change in IOP. Secondary outcomes included subjects who were drop-free following the intervention; achieved an IOP of 21 mmHg or less, 17 mmHg or less or 14 mmHg or less; and the occurrence of intraoperative and postoperative complications. **The authors did not find any completed studies that could be included in this review. The review concluded that there is currently no high-quality evidence for the effects of subconjunctival draining MIG devices for medically uncontrolled open angle glaucoma. Properly designed RCTs are needed to assess the medium- and long-term efficacy and safety of this technique.**

Professional Society Guidelines and Position Statements

American Academy of Ophthalmology (AAO)

The (2015) preferred practice patterns on primary OAG indicated that the AAO considered laser trabeculoplasty as initial therapy in select patients or an alternative for patients who cannot or will not use medications reliably due to cost, memory problems, difficulty with installation, or intolerance to the medication. The AAO stated that aqueous shunts have traditionally been used to manage refractory glaucoma when trabeculectomy has failed to control IOP or is unlikely to succeed, but these devices are being increasingly used in other indications for the surgical management of glaucoma. The AAO also stated that micro-invasive glaucoma surgeries that are frequently combined with phacoemulsification have **limited long-term data but seem to result in modest IOP reduction with postoperative pressures** in the mid to upper teens. Although they are less effective in lowering IOP than trabeculectomy and aqueous shunt surgery, micro-invasive glaucoma surgeries may have a more favorable safety profile in the short-term.

The AAO (2018) 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 can be considered as initial therapy in selected patients or an alternative for patients at high risk for nonadherence to medical therapy who cannot or will not use medications reliably. **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.** The AAO suggests that laser trabeculoplasty can be an initial or alternative therapy for patients at risk of nonadherence to medication therapy for primary OAG. The guidelines suggest trabeculectomy as a treatment alternative when medication or laser trabeculoplasty have failed to adequately control the disease. **No reference is made in the guidelines to MIGS or specifically, the XEN Gel Stent.**

National Institute for Health and Care Excellence (NICE)

The 2017 guideline [NG81] ‘Glaucoma: Diagnosis and Management’ did not mention XEN or other minimally invasive glaucoma (MIG) surgeries. The guideline recommended that patients with chronic open-angle glaucoma (OAG) that are not responding to pharmacologic therapy should be offered additional glaucoma medications, ‘a drug from another therapeutic class (a beta-blocker, carbonic anhydrase inhibitor or sympathomimetic)’ or surgery (e.g., laser trabeculoplasty or cyclodiode laser treatment) with or without pharmacologic augmentation (mitomycin-C; MMC) as indicated.

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 randomised studies. Further research should include details of patient selection and long-term outcomes.’** The next scheduled review of this guidance is April 2021.

Hayes

A ‘Health Technology Assessment’ was published in December 2019 addressing the XEN Glaucoma Treatment System (Allergan) for Treatment of Open-Angle Glaucoma.

Hayes rated the use of the XEN Glaucoma Treatment System in patients with open-angle glaucoma (OAG) as potential but unproven benefit. This rating is reflective of the 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.

Hayes noted the low-quality body of evidence from 7 studies which results primarily from a limited evidence base evaluating XEN implantation compared with standard care, trabeculectomy, and the individual study quality ratings. The evidence base consisted of 6 poor-quality studies and 1 very-poor-quality study. Overall quality was based on the balance of benefits and harms and was assessed taking into consideration the quality of individual studies and the applicability, precision, and consistency of data. Although the results generally demonstrated a reduction in IOP and medication use from baseline, reduction rates varied greatly between studies. Results suggest 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.

DEFINITIONS

Intraocular pressure (IOP): The fluid pressure of the eye. Intraocular pressure is regulated by the balance of aqueous humour synthesis and secretion into the eye and outflow from the eye; therefore, most therapies for glaucoma seek lowering intraocular pressure to avoid disease progression. IOP is the cardinal modifiable risk factor for glaucoma.

Hypotony: Low intraocular pressure; or an IOP below which the eye does not maintain its normal shape and may subsequently lose vision. Hypotony is usually defined as an intraocular pressure (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: Sometimes referred to as filtration surgery; a surgical procedure used in the treatment of glaucoma to relieve intraocular pressure (IOP) by removing part of the eye's trabecular meshwork and adjacent structures. It is the most common glaucoma surgery performed and allows drainage of aqueous humor from within the eye to underneath the conjunctiva where it is absorbed. This is currently considered the gold standard treatment for glaucoma that is refractory to medical management; however, it is a technically complex procedure that may result in a range of adverse outcomes.

CODING INFORMATION: THE CODES LISTED IN THIS POLICY ARE FOR REFERENCE PURPOSES ONLY. LISTING OF A SERVICE OR DEVICE CODE IN THIS POLICY DOES NOT IMPLY THAT THE SERVICE DESCRIBED BY THIS CODE IS COVERED OR NON-COVERED. COVERAGE IS DETERMINED BY THE BENEFIT DOCUMENT. THIS LIST OF CODES MAY NOT BE ALL INCLUSIVE.

CPT	Description
0449T	Insertion of aqueous drainage device, without extraocular reservoir, internal approach, into the subconjunctival space; initial device
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
L8612	Aqueous shunt

ICD-10	Description: [For dates of service on or after 10/01/2015]

REFERENCES

Government Agency

FDA

- Center for Devices and Radiological Health. 510K Notification Database (2016, October). K161457. (Xen Glaucoma Treatment System). Available at: <https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm>. Accessed on October 2020

Centers for Medicare & Medicaid Services (CMS). Medicare Coverage Database. National coverage determination (NCD) Search. Available at: <http://www.cms.gov/medicare-coverage-database/>

*Please reference CMS Database for applicable reviews to locate current NCDs/LCDs

Peer Reviewed Publications

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.

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.

De Gregorio A, Pedrotti E, Stevan G, Bertoncello A, Morselli S. 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 Available at: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5933334/> Accessed on October 2020

De Gregorio A, Pedrotti E, Russo L, et al. Minimally invasive combined glaucoma and cataract surgery: clinical results of the smallest ab interno gel stent. *Int Ophthalmol*. 2017 May 29.

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;14:1805-1832. Published 2020 Jun 30. doi:10.2147/OPTH.S178348 Available at: [Link](#) Accessed on October 2020

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 Available at: [Link](#) Accessed October 2020

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. Available at: [PMC PubMed](#)

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* 183:25–36. pii: S0002-9394(17)30324-0. Available at: [Link](#) Accessed October 2020

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 Available at: [Link](#) Accessed October 2020

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 Available at: [Link](#) Accessed October 2020

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.

Mahabadi N, Foris LA, Tripathy K. Open Angle Glaucoma. [Updated 2020 Jul 4]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2020 Jan-. Available at: [Link](#) Accessed October 2020

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;91(9):415–421. doi:10.1016/j.oftal.2016.02.006 Available at: [Link](#) Accessed October 2020

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. Available at: [PubMed](#). Accessed October 2020

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. Available at: [PubMed](#) Accessed October 2020

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. Available at: [PubMed](#) Accessed October 2020

Vinod K, Gedde SJ. Clinical investigation of new glaucoma procedures. *Curr Opin Ophthalmol*. 2017 Mar;28(2):187-193.

Widder RA, Dietlein TS, Dinslage S, Kuhnrich P, Rennings C, Rossler G. 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 Available at: [Link](#) Accessed October 2020

Systematic Review and Meta-Analysis

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. Available at: [Cochrane](#)

Lavia C, Dallorto L, Maule M, et al. Minimally-invasive glaucoma surgeries (MIGS) for open angle glaucoma: a systematic review and meta-analysis. *PLoS One* 2017; 12: e0183142.

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

Professional Society Guidelines

American Academy of Ophthalmology (AAO)

- Preferred Practice Pattern Guidelines. Primary Open-Angle Glaucoma. Available at: [AAO](#) Published November 2015. Updated March 2018. Accessed October 2020
- Preferred Practice Pattern Guidelines. Glaucoma Summary Benchmarks. October 2019. Available at: [AAO](#) Accessed October 2020.

ECRI Institute

- Product Brief (ARCHIVED). XEN glaucoma treatment system (Allergan, plc) for treating open-angle glaucoma. <https://www.ecri.org>. Published June 1, 2017. Accessed October 2020.

National Institute for Health and Care Excellence (NICE)

- NICE guideline [NG81]. Glaucoma: Diagnosis and Management. Published Apr 2009. Updated November 2017.
This guideline is an update of NICE guideline CG85 (published April 2009) and replaces it. New recommendations have been added for case-finding, diagnosis, reassessment and treatment.
- Microinvasive subconjunctival insertion of a trans-scleral gelatin stent for primary open-angle glaucoma. Interventional procedures guidance [IPG612] Published date: 25 April 2018. Available at: [NICE](#) Accessed October 2020.

Other Resources

Glaucoma Foundation. Treating Glaucoma. Glaucoma Foundation website. Available at: <https://glaucomafoundation.org/aboutglaucoma/treating-glaucoma/>. Accessed October 2020.

Hayes, Inc. Health Technology Assessment. XEN glaucoma treatment (Allergan) for treatment of open-angle glaucoma. <https://evidence.hayesinc.com>. Published December 19, 2019. Accessed October 2020.

Review/Revision History:

10/2020: New Policy. Advanced Medical Review (AMR): Policy reviewed by practicing MD Board-Certified in ophthalmology. 10/16/20