Medical Policy

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Title: Aqueous Shunts and Stents for Glaucoma

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Populations	Interventions	Comparators	Outcomes
Individuals: • With refractory open-angle glaucoma	Interventions of interest are: • Ab externo aqueous shunts	Comparators of interest are: • Ocular medication • Trabeculectomy	Relevant outcomes include: • Change in disease status • Functional outcomes • Medication use • Treatment-related morbidity
Individuals: • With refractory open-angle glaucoma	Interventions of interest are: • Ab interno aqueous stents	Comparators of interest are: • Ocular medication • Trabeculectomy	Relevant outcomes include: • Change in disease status • Function outcomes • Medication use

Populations	Interventions	Comparators	Outcomes
			• Treatment-related morbidity
Individuals: • With mild-to-moderate open-angle glaucoma who are undergoing cataract surgery	Interventions of interest are: • Aqueous microstents	Comparators of interest are: • Cataract surgery alone	Relevant outcomes include: • Change in disease status • Functional outcomes • Medication use • Treatment-related morbidity
Individuals: • With mild-to-moderate open-angle glaucoma who are not undergoing cataract surgery	Interventions of interest are: • Aqueous microstents as a stand-alone procedure	Comparators of interest are: • Standard care	Relevant outcomes include: • Change in disease status • Functional outcomes • Medication use • Treatment-related morbidity

DESCRIPTION

Glaucoma surgery is intended to reduce intraocular pressure (IOP) when the target IOP cannot be reached using medications. Due to complications with established surgical approaches such as trabeculectomy, a variety of shunts are being evaluated as alternative surgical treatments for patients with inadequately controlled glaucoma. Microstents are also being evaluated in patients with mild to moderate open-angle glaucoma (OAG) currently treated with ocular hypotensive medication.

OBJECTIVE

The objective of this evidence review is to determine whether aqueous shunts or microstents improve the net health outcome in individuals with open-angle glaucoma.

BACKGROUND

Glaucoma

Glaucoma is characterized by elevated intraocular pressure (IOP), which results in visual field loss and irreversible blindness if left untreated. In the primary (conventional) outflow pathway from the eye, aqueous humor passes through the trabecular meshwork, enters a space lined with endothelial cells (Schlemm canal), drains into collector channels, and then into the aqueous veins. Increases in resistance in the trabecular meshwork and/or the inner wall of the Schlemm canal can disrupt the balance of aqueous humor inflow and outflow, resulting in an increase in IOP and glaucoma risk.

Treatment

Ocular Medication

First-line treatment typically involves pharmacologic therapy. Topical medications either increase the aqueous outflow (prostaglandins, alpha-adrenergic agonists, cholinergic agonists, Rho kinase inhibitors) or decrease aqueous production (alpha-adrenergic agonists, beta-blockers, carbonic anhydrase inhibitors). Pharmacologic therapy may involve multiple medications, have potential side effects, and may be inconvenient for older adults or incapacitated patients.

Surgery

Surgical intervention may be indicated in patients with glaucoma when the target IOP cannot be reached pharmacologically. Surgical procedures for glaucoma aim to reduce IOP from impaired

aqueous humor drainage in the trabecular meshwork and/or Schlemm canal. Trabeculectomy (guarded filtration surgery) is the most established surgical procedure for glaucoma, which involves dissecting the conjunctiva, creating a scleral flap and scleral ostomy then suturing down the flap and closing the conjunctiva, allowing aqueous humor to directly enter the subconjunctival space. This procedure creates a subconjunctival reservoir, which can effectively reduce IOP, but commonly results in filtering "blebs" on the eye, and is associated with numerous complications (e.g., hemorrhage, scarring, hypotony, infection, leaks, bleb-related endophthalmitis) and long-term failure. Other surgical procedures (not addressed herein) include trabecular laser ablation, deep sclerectomy (which removes the outer wall of the Schlemm canal and excises deep sclera and peripheral cornea), and viscocanalostomy (which unroofs and dilates the Schlemm canal without penetrating the trabecular meshwork or anterior chamber). Canaloplasty involves dilation and tension of the Schlemm canal with a suture loop between the inner wall of the canal and the trabecular meshwork. This ab externo procedure uses the iTrack illuminated microcatheter (iScience Interventional) to access and dilate the entire length of the Schlemm canal and to pass the suture loop through the canal.

Insertion of shunts from outside the eye (ab externo) is another surgical option to lower IOP. Examples of ab externo devices cleared by the U.S. Food and Drug Administration (FDA) include the Ahmed, Baerveldt, Molteno, and EX-PRESS mini-shunt, which shunt aqueous humor between the anterior chamber and the suprachoroidal space. These devices differ by explant surface areas, shape, plate thickness, presence or absence of a valve, and details of surgical installation. Generally, the risk of hypotony (low pressure) is reduced with aqueous shunts compared with trabeculectomy, but IOP outcomes are worse than after standard guarded filtration surgery. Complications of anterior chamber shunts include corneal endothelial failure and erosion of the overlying conjunctiva. The risk of postoperative infection is lower with shunts than with trabeculectomy, and failure rates are similar (»10% of devices fail annually). The primary indication for aqueous shunts is for failed medical or surgical therapy, although some ophthalmologists have advocated their use as a primary surgical intervention, particularly for selected conditions such as congenital glaucoma, trauma, chemical burn, or pemphigoid.

Minimally Invasive Glaucoma Surgeries

MIGS are alternative, less invasive techniques that are being developed and evaluated. MIGS, which use microscopic-sized equipment and smaller incisions, involves less surgical manipulation of the sclera and the conjunctiva compared with other surgical techniques. There are several categories of MIGS: miniaturized trabeculectomy, trabecular bypass, milder laser photocoagulation, and totally internal or suprachoroidal stents (ab interno). This policy evaluates the placement of ab interno stents.

Examples of ab interno devices either approved or given marketing clearance by the FDA include the iStent, which is a 1-mm long stent inserted into the end of the Schlemm canal through the cornea and anterior chamber; the CyPass suprachoroidal stent; and XEN gelatin stent.

Because aqueous humor outflow is pressure-dependent, the pressure in the reservoir and venous system is critical for reaching the target IOP. Therefore, some devices may be unable to reduce IOP below the pressure of the distal outflow system used (e.g., <15 mm Hg) and are not indicated for patients for whom very low IOP is desired (e.g., those with advanced glaucoma). It has been proposed that stents such as the iStent, CyPass, and Hydrus Microstent may be useful in patients with early-stage glaucoma to reduce the burden of medications and problems with compliance. One area of investigation are patients with glaucoma who require cataract surgery.

An advantage of ab interno stents is that they may be inserted into the same incision and at the same time as cataract surgery. Also, most devices do not preclude subsequent trabeculectomy if needed. It may also be possible to insert more than 1 stent to achieve desired IOP. Therefore, health outcomes of interest are the IOP achieved, reduction in medication use, ability to convert to trabeculectomy, complications, and device durability.

REGULATORY STATUS

The regulatory status of the various ab externo and ab interno aqueous shunts and microstents is summarized in Table 1. The first-generation Ahmed™ (New World Medical), Baerveldt® (Advanced Medical Optics), Krupin (Eagle Vision), and Molteno® (Molteno Ophthalmic) ab externo aqueous shunts were cleared for marketing by the FDA through the 510(k) process between 1989 and 1993; modified Ahmed and Molteno devices were cleared in 2006. They are indicated for use "in patients with intractable glaucoma to reduce IOP where medical and conventional surgical treatments have failed." The AquaFlow™ Collagen Glaucoma Drainage Device (STAAR Surgical) was approved by the FDA through the premarket approval process for the maintenance of the subscleral space following nonpenetrating deep sclerectomy. In 2003, the ab externo EX-PRESS® Mini Glaucoma Shunt was cleared for marketing by the FDA through the 510(k) process. In 2016, the XEN® Glaucoma Treatment System (Allergan), which consists of the XEN45 Gel Stent preloaded into the XEN Injector, was cleared for marketing by the FDA through the 510(k) process as an ab interno aqueous stent for management of refractory glaucoma. The approval was for patients with refractory glaucoma who failed previous surgical treatment or for patients with primary open-angle glaucoma unresponsive to maximum tolerated medical therapy. The FDA determined that this device was substantially equivalent to existing devices, specifically the Ahmed™ Glaucoma Valve and the EX-PRESS® Glaucoma Filtration Device.

In 2018, the first microstent, the iStent® Trabecular Micro-Bypass Stent preloaded into the iStent *inject* device (Glaukos) was approved by the FDA through the 515(d) process for use in conjunction with cataract surgery for the reduction of IOP in adults with mild-to-moderate open-angle glaucoma currently treated with ocular hypotensive medication. The regulatory status of additional glaucoma devices is shown in Table 1.

In August 2018, Alcon announced an immediate voluntary recall of the CyPass microstent, which had been approved by the FDA in 2016 for use in conjunction with cataract surgery in adults with mild-to-moderate open-angle glaucoma. The recall was based on 5 year postsurgery data from the COMPASS-XT long-term safety study. Results showed a statistically significant increase in endothelial cell loss among patients receiving the CyPass microstent compared with patients receiving cataract surgery alone.

Table 1. Regulatory Status of Aqueous Shunts and Stents

Device	Manufacturer	Type	FDA Status	Date
AquaFlow™	STAAR Surgical	Drainage device	PMA	2001
Ahmed™	New World Medical	Aqueous glaucoma shunt, ab externo	510(k)	<1993
Baerveldt®	Advanced Medical Optics	Aqueous glaucoma shunt, ab externo	510(k)	<1993

Device	Manufacturer	Type	FDA Status	Date
Krupin	Eagle Vision	Aqueous glaucoma shunt, ab externo	510(k)	<1993
Molteno®	Molteno Ophthalmic	Aqueous glaucoma shunt, ab externo	510(k)	<1993
EX-PRESS®	Alcon	Mini-glaucoma shunt, ab externo	510(k)	2003
XEN® Gel Stent; XEN injector	AqueSys/Allergan	Aqueous glaucoma stent, ab interno	510(k)	2016
iStent®; iStent inject®	Glaukos	Microstent, ab interno	515(d) in conjunction with cataract surgery	2018
iStent *supra*®	Glaukos	Suprachoroidal stent	Not approved; in clinical trial	
CyPass®	Alcon	Suprachoroidal stent, ab interno	Company voluntarily recalled	2018
Hydrus™	Ivantis	Microstent, ab interno	PMA approval	2018
SOLX® Gold	SOLX	Micro-Shunt, ab externo	Not approved; in clinical trial	
Beacon Aqueous Microshunt	MicroOptx	Micro-Shunt, ab externo	Not approved; in clinical trial	
PRESERFLO® MicroShunt	Santan	Micro-Shunt, ab externo	Not approved; in clinical trial	

FDA: U.S. Food and Drug Administration; PMA: premarket approval.
FDA product codes: OGO, KYF.

POLICY

A. In conjunction with cataract surgery, the implantation of 1 or 2 FDA approved ab interno stents may be considered **medically necessary** in patients with mild to moderate open-angle glaucoma

B. As a standalone surgery, the insertion of FDA approved ab externo / ab interno aqueous shunts, including the Xen gel Stents, may be considered **medically necessary** as a method to reduce the intraocular pressure in patients with glaucoma where medical therapy has failed to adequately control intraocular pressure

C. Use of the ab external / ab interno aqueous shunts or stents for any other condition not listed above, is considered **experimental/ investigational**

POLICY GUIDELINES

Shunts and stents are only able to reduce intraocular pressure (IOP) to the mid-teens and may be inadequate when very low IOP is needed to reduce glaucoma damage.

RATIONALE

This evidence review has been updated regularly with searches of the PubMed database. The most recent literature update was performed through July 27, 2020.

Evidence reviews assess the clinical evidence to determine whether the use of technology improves the net health outcome. Broadly defined, health outcomes are the length of life, quality of life, and ability to function-including benefits and harms. Every clinical condition has specific outcomes that are important to patients and managing the course of that condition. Validated outcome measures are necessary to ascertain whether a condition improves or worsens; and whether the magnitude of that change is clinically significant. The net health outcome is a balance of benefits and harms.

To assess whether the evidence is sufficient to draw conclusions about the net health outcome of technology, 2 domains are examined: the relevance, and quality and credibility. To be relevant, studies must represent one or more intended clinical use of the technology in the intended population and compare an effective and appropriate alternative at a comparable intensity. For some conditions, the alternative will be supportive care or surveillance. The quality and credibility of the evidence depend on study design and conduct, minimizing bias and confounding that can generate incorrect findings. The randomized controlled trial (RCT) is preferred to assess efficacy; however, in some circumstances, nonrandomized studies may be adequate. RCTs are rarely large enough or long enough to capture less common adverse events and long-term effects. Other types of studies can be used for these purposes and to assess generalizability to broader clinical populations and settings of clinical practice.

AQUEOUS SHUNTS AND STENTS FOR GLAUCOMA

Clinical Context and Therapy Purpose

The purpose of aqueous shunts and stents in patients who have glaucoma is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The question addressed in this evidence review is: Does the use of aqueous shunts and stents improve the net health outcomes of patients with glaucoma compared to standard of care (including medical therapy or trabeculectomy)?

The following PICO was used to select literature to inform this review.

Patients
The relevant populations of interest are:
- Patients with refractory open-angle glaucoma (OAG)
- Patients with mild-to-moderate primary open-angle glaucoma (POAG) who are undergoing cataract surgery
- Patients with indications for glaucoma treatment other than cataract surgery or refractory OAG

Interventions
The therapies being considered are:
- For patients with refractory OAG
  - Ab externo aqueous shunts
  - Ab interno aqueous stents
- For patients with mild-to-moderate OAG undergoing cataract surgery: ab interno aqueous stents
- For patients with indications for glaucoma treatment other than cataract surgery or refractory OAG: ab externo aqueous shunts or ab interno aqueous stents

Comparators
Comparators include medical therapies and trabeculectomy.

Outcomes
The general outcomes of interest are a change in intraocular pressure (IOP) and change in medication use. Changes in IOP and medication use are measured for at least 12 months. Safety measures involve longer follow-up, for several years.

Study Selection Criteria
Methodologically credible studies were selected using the following principles:
- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.
- To assess long-term outcomes and adverse effects, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.
- Studies with duplicative or overlapping populations were excluded.

This section reviews the evidence for aqueous shunts and stents with the U.S. Food and Drug Administration (FDA) approval. Evidence on nonapproved devices and indications are discussed in the Appendix.

AB EXTERNO AQUEOUS SHUNTS

Review of Evidence
Systematic Reviews
A Cochrane review by Minckler et al (2006) included 15 randomized or pseudo-RCTs (total n=1153 participants) evaluating the Ahmed, Baerveldt, Molteno, and Schocket shunts.[1,] Trabeculectomy was found to lower mean IOP by 3.8 mm Hg more than the Ahmed shunt at 1 year. This systematic review did not compare complications, because reviewers considered them to be too variably reported to permit comparative tabulation. There was no evidence of the superiority of 1 shunt over another.

A technology assessment on commercially available aqueous shunts, including the Ahmed, Baerveldt, Krupin, and Molteno devices, from the American Academy of Ophthalmology was published by Minckler et al (2008).[2,] It indicated that IOP would generally settle at higher levels (»18 mm Hg) with aqueous shunts than with standard trabeculectomy (14-16 mm Hg) or trabeculectomy with antifibrotic agents 5-fluorouracil or mitomycin C (8-10 mm Hg). In 1 study, mean IOPs with the Baerveldt shunt and adjunct medications were equivalent to trabeculectomy with mitomycin C (13 mm Hg). Five-year success rates for the 2 procedures were similar (50%). The assessment concluded that, based on level 1 evidence, aqueous shunts were comparable to trabeculectomy for IOP control and duration of benefit. The risk of postoperative infection was lower with aqueous shunts than with trabeculectomy. Complications of aqueous shunts included: immediate hypotony after surgery, excessive capsule fibrosis and clinical failure, erosion of the tube or plate edge, strabismus, and, very rarely, infection. The most problematic long-term consequence of anterior chamber tube placement was accelerated damage to the corneal endothelium.

BAERVELDT GLAUCOMA SHUNT
Randomized Controlled Trials
Results from the open-label, multicenter, randomized Tube vs Trabeculectomy study were reviewed in the 2008 American Academy of Ophthalmology technology assessment and by Gedde et al (2012) who reported on the 5-year follow-up.[2,3,4,] That study included 212 eyes of 212 patients (age range, 18-85 years) from 17 study centers, who had trabeculectomy and/or cataract extraction with intraocular lens implantation and uncontrolled glaucoma with IOP of 18 mm Hg or greater and 40 mm Hg or lower on maximally tolerated medical therapy, randomized to tube (Baerveldt shunt) or trabeculectomy. Excluding patients who had died, the study had an 82% follow-up rate at 5 years, with a similar proportion of patients in the tube and trabeculectomy groups. At 5 years, neither IOP (14.3 mm Hg in the shunt group vs 13.6 mm Hg in the trabeculectomy group) nor the number of glaucoma medications (1.4 in the shunt group vs 1.2 in the trabeculectomy group) differed significantly based on intention-to-treat analysis. The cumulative probability of failure over the 5 years was lower in the shunt group (29.8%) than in the trabeculectomy group (46.9%), and the rates of reoperation were lower (9% vs 29%, respectively). The rates of loss of 2 or more lines of visual acuity were similar (46% in the shunt group vs 43% in the trabeculectomy group).

Kotecha et al (2017) assessed the vision-related quality of life outcomes in the Tube vs Trabeculectomy study.[5,] Quality of life was measured using the National Eye Institute Visual Functioning Questionnaire-25, administered at baseline and annual follow-ups over 5 years. A comparison of composite quality of life scores and change in scores over time among the 2 groups revealed no significant differences at any of the follow-up measurements.

EX-PRESS MINI SHUNT

Systematic Reviews

A Cochrane review by Wang et al (2015) evaluated the efficacy of adjunctive procedures for trabeculectomy.[6] Three RCTs were included which compared trabeculectomy alone with trabeculectomy plus EX-PRESS Mini Shunt. These trials were rated as having a high or unclear risk of bias using the Cochrane criteria. None of the RCTs reported a significant improvement for the EX-PRESS group. However, in the pooled analysis, IOP was lower in the combination group than in the trabeculectomy alone group (weighted mean difference, -1.58; 95% confidence interval [CI], -2.74 to -0.42). The pooled analysis also showed that subsequent cataract surgery was less frequent in the combination group than in trabeculectomy alone (relative risk, 0.34; 95% CI, 0.14 to 0.74). The combination group had a lower rate of some complications (e.g., hyphema, needling).

Randomized Controlled Trials

De Jong et al (2009) reported on a randomized study that compared the EX-PRESS Mini Shunt with standard trabeculectomy in 78 patients (80 eyes) diagnosed with OAG uncontrolled using maximally tolerated medical therapy (Table 2).[7] Five year follow-up was reported by de Jong et al (2011).[8] The 2 groups were similar after randomization, except mean age (62 years for the EX-PRESS group vs 69 years for the trabeculectomy group). At 12-month follow-up, mean IOP and antiglaucoma medications use decreased in both groups (see Table 2). Twelve-month Kaplan-Meier success rates (defined as an IOP >4 mm Hg with medication and ≤18 mm Hg without medication) were 82% for the EX-PRESS shunt and 48% for trabeculectomy. At 5 years, success rates did not differ significantly between groups. In the EX-PRESS group, IOP remained stable from year 1 (12.0 mm Hg) to year 5 (11.5 mm Hg), while, in the trabeculectomy group, IOP decreased from year 3 (13.5 mm Hg) to year 5 (11.3 mm Hg) (see Table 3). More complications occurred after trabeculectomy than after EX-PRESS implantation.

A U.S. multicenter randomized trial by Netland et al (2014), compared trabeculectomy with EX-PRESS implantation in 120 patients (120 eyes) (Table 2).[9] Comparator groups were similar at baseline. Throughout a 2 year postsurgical follow-up, average IOP and number of medications were similar between groups (see Table 3). Surgical success was 90% and 87% at 1 year and 83% and 79% at 3 years in the EX-PRESS and trabeculectomy groups, respectively. Visual acuity returned to near baseline levels at 1 month after EX-PRESS implantation (median, 0.7 months) and at 3 months after trabeculectomy (median, 2.2 months; p=0.041). Postoperative complications were higher after trabeculectomy (41%) than after EX-PRESS implantation (18.6%).

One additional small RCT was published by Wagschal et al (2015),[10] presenting 1-year results, and by Gonzalez-Rodriguez et al (2016), presenting 3-year results (Table 2).[11] The trial corroborated the results of the earlier RCTs, reporting no differences between trabeculectomy and EX-PRESS shunt groups on outcomes for mean IOP, success rates, number of medications used, or complication rates (Table 3).

Table 2. Summary of Key RCT Characteristics for EX-PRESS

Study	Countries	Sites	Dates	Participants	Interventions	
					Active	*Comparator*
de Jong et al (2009)[7,];de Jong et al (2011)[8,]	Netherlands	1	2003-2004	Patients with primary OAG not controlled by IOP medication	EX-PRESS (n=39)	Trabeculectomy (n=39)
Netland et al (2014)[9,]	U.S., Canada	7	NR	Patients with OAG treated with IOP medications who were candidates for glaucoma surgery	EX-PRESS (n=59)	Trabeculectomy (n=61)
Wagschal et al (2015)[10,]; Gonzalez-Rodriguez et al (2016)[11,]	Canada	1	2011-2012	Patients with OAG not controlled by IOP medication	EX-PRESS (n=33)	Trabeculectomy (n=31)

IOP: intraocular pressure; NR: not reported; OAG: open-angle glaucoma; RCT: randomized controlled trial.

Table 3. Summary of Key RCT Results for EX-PRESS

Study	Mean IOP (SD), mm Hg		p	Mean Medication Use (SD)	
	EX-PRESS	*Trabeculectomy*		*EX-PRESS*	*Trabeculectomy*
de Jong et al (2009)[7,]; de Jong et al (2011)[8,]					
Baseline	23.6 (7.0)	20.7 (7.0)	0.09	NR	NR
Year 1	12.2 (3.8)	13.9 (3.8)	0.05	0.31	0.74
Year 2	12.0 (3.3)	13.8 (3.2)	0.01	0.49	1.05
Year 3	12.1 (3.4)	13.5 (3.4)	0.08	0.62	1.28
Year 4	11.4 (2.5)	11.6 (2.5)	0.69	0.69	1.33
Year 5	11.4 (2.2)	11.2 (2.2)	0.71	0.85	1.10
Netland et al (2014)[9,]					
Baseline	25.1 (6.0)	26.4 (6.9)	0.27	3.1 (1.1)	3.1 (1.2)
Month 6	13.8 (4.7)	11.9 (4.6)	0.03	NR	NR
Year 2	14.7 (4.6)	14.6 (7.1)	0.93	0.9 (1.3)	0.7 (1.2)
Wagschal et al (2015)[10,]; Gonzalez-Rodriguez e al (2016)[11,]					
Baseline	22.6 (10.2)	21.9 (6.8)	0.75	3.5 (0.9)	3.4 (1.3)
Year 1	11.2 (4.3)	10.7 (3.5)	0.85	0.4 (1.0)	0.6 (1.0)
Year 2	12.5 (5.1)	10.3 (3.7)	0.07	0.6 (1.3)	1.3 (1.5)
Year 3	13.3 (4.5)	11.1 (4.4)	0.10	1.4 (1.7)	1.2 (1.3)

IOP: intra-ocular pressure; NR: not reported; SD: standard deviation; RCT: randomized controlled trial.

Comparative Effectiveness Analyses

Five-year results of 2 RCTs comparing the Ahmed and Baerveldt shunts have been published. The Ahmed Baerveldt Comparison (ABC) study was a multicenter international RCT evaluating the comparative safety and efficacy of the Ahmed Glaucoma Valve and Baerveldt Glaucoma Implant in 276 adults with previous incisional eye surgery or refractory glaucoma.[12,13,] The ABC was funded by National Eye Institute, Research to Prevent Blindness, and New World Medical. The Ahmed Versus Baerveldt (AVB) study, reported by Christakis et al (2016), was an international, multicenter RCT enrolling 238 patients with uncontrolled glaucoma despite maximally tolerated medical therapy that was funded by the Glaucoma Research Society of Canada.[14,]

Christakis et al (2017) analyzed 5-year pooled data from the ABC and AVB trials comparing the relative efficacy of the 2 implants.[15,] At year 5, mean IOP was 15.8 mm Hg in the Ahmed group and 13.2 mm Hg in the Baerveldt group (p=.007). The cumulative failure rate in the Ahmed group was 49%; in the Baerveldt group, it was 37%. Mean glaucoma medication use was significantly lower in patients receiving the Baerveldt implant than in patients receiving the Ahmed implant (p=0.007). Visual acuity was similar between both groups. While efficacy measures were significantly better in the Baerveldt group, these patients experienced more hypotony (4.5%) than patients in the Ahmed group (0.4%; p=.002).

Section Summary: Ab Externo Aqueous Shunts

Evidence for the use of ab externo aqueous shunts for the treatment of OAG uncontrolled by medications consists of RCTs comparing shunts with trabeculectomy. Outcomes of interest are IOP and antiglaucoma medication use. Follow-up among the trials ranged from 1 to 5 years. Results from ab externo aqueous shunts are similar to trabeculectomy. Adverse event rates were higher among patients undergoing trabeculectomy.

The comparative effectiveness of 2 ab externo devices (the Ahmed and Baerveldt shunts) has been evaluated in 2 trials, the AVB, and the ABC trials. These trials reported similar results, with both devices lowering IOP significantly. Compared with patients receiving the Ahmed shunt, patients receiving the Baerveldt shunt experienced lower IOP and needed fewer medications. However, patients receiving the Baerveldt shunt experienced higher rates of hypotony-related complications.

Ab Interno Aqueous Stents

This section reviews the evidence for ab interno stents with the FDA approval or marketing clearance. At this time, the XEN gel stent and injector is the only stent system FDA approved as a stand-alone procedure for the treatment of refractory OAG.

REVIEW OF EVIDENCE

XEN GLAUCOMA TREATMENT SYSTEM

Observational Studies

Comparative Studies

Schlenker et al (2017) published a multicenter, retrospective comparative study that compared the risk, safety, and efficacy for stand-alone ab interno microstent implantation with mitomycin C (MMC) and trabeculectomy plus MMC (Table 4).[16,] Implantations of the ab interno XEN 45 gelatin microstent is a less invasive surgery than trabeculectomy. Outcomes included: IOP differences, medication reductions, interventions, complications, and the need for additional surgery. The

primary outcome was the hazard ratio of failure. Failure was defined as 2 consecutive IOP readings of less than 6 mm Hg, including vision loss. Success was measured by the withdrawal of glaucoma-related medications at 1 month postsurgery. The adjusted hazard ratio of failure of the microstent relative to trabeculectomy was 1.2 for complete success (95% CI, 0.7 to 2.0). Both surgeries had a 75% survival of approximately 10 months for complete success. During the last reported follow-up (varying times), antiglaucoma medications were being used by 25% of patients who received the microstent implantation and 33% of trabeculectomy patients. Patients in both groups reported similar numbers of postoperative interventions, such as laser suture lysis and needling. The need for reoperation was higher among those who had undergone microstent implantation-but this difference was not statistically significant. The authors concluded that the ab interno gelatin microstent with MMC was noninferior to trabeculectomy plus MMC. Changes in IOP and medication use appear in Table 5.

Noncomparative Studies

Mansouri et al (2018) reported on results from a study of 149 eyes (113 patients); 109 eyes received the XEN implant plus cataract surgery and 40 eyes received the implant alone (Table 4).[17,] There was a range of glaucoma severity represented in the study sample, with most patients in the mild-to-moderate stages. Of the 149 eyes, data for 87 (58%) eyes was available at 12 months. The high loss to follow-up was mainly due to high travel times for patients referred to the study treatment center from various provinces and countries, and to lack of interest among physicians to treat referred patients. At 12 months, mean IOP and mean medication use, both decreased (see Table 5). The proportion achieving 20% or more reduction in IOP was higher among patients receiving XEN alone than those undergoing cataract surgery and XEN implantation. Adverse events included bleb revision (n=5), choroidal detachment (n=2), and second glaucoma surgery (n=9).

Hengerer et al (2017) retrospectively analyzed 146 patients (242 eyes) receiving the XEN implant for treatment-refractory to antiglaucoma medication or glaucoma surgery (Table 4).[18,] In the subset of eyes with 12-month data (n=148), IOP reduction of 20% or more was achieved by 73.0% of patients. Mean antiglaucoma medications decreased (see Table 5). The decreases in IOP and medication use were statistically significant in patients receiving the XEN implant alone and in patients receiving the XEN implant while undergoing cataract surgery.

Table 4. Summary Characteristics for Observational Studies Using the XEN Implant as a Stand-Alone Procedure for Refractory Open-Angle Glaucoma

Study	Country	Participants	Treatment Delivery	FU
Schlenker et al (2017)[16,]	Austria, Belgium, Canada, Germany	Patients with OAG, pseudoexfoliation, pigment dispersion, normal-tension, angle-recession, combined mechanism, history of angle-closure, or juvenile glaucoma and no prior incisional surgery	• XEN alone (n=185) • Trabeculectomy (n=169)	Up to 30 mo (last visit in chart)
Mansouri et al (2018)[17,]	Switzerland	Patients with OAG and uncontrolled IOP, progressive glaucoma, and/or refractory to IOP medications	• XEN alone (n=40) • XEN plus cataract surgery (n=109)	12 mo

Study	Country	Participants	Treatment Delivery	FU
Hengerer et al (2017)[18,]	Germany	Patients with OAG and uncontrolled IOP, optic disc damage, and refractory to IOP medications or prior surgery	• XEN alone (n=203) • XEN plus cataract surgery (n=39)	12 mo

FU: follow-up; IOP: intraocular pressure; OAG: open-angle glaucoma.

Table 5. Summary of Results for the XEN Implant as Stand-Alone Procedure for Refractory Open-Angle Glaucoma

Study	Population	Median IOP (SD), mm Hg		Medication, Median (SD)	
		Baseline	*1 Year*[a]	*Baseline*	*1 Year*[a]
Schlenker et al (2017)[16,]	XEN alone	24.0 (IQR: 19 to 32)	13.0 (IQR: 10 to 15)	3.0 (IQR: 3 to 4)	0.0 (IQR: 0 to 1)
	Trabeculectomy	24.0 (IQR: 19 to 30))	13.0 (IQR: 10 to 16)	3.0 (IQR: 3 to 4)	0.0 (IQR: 0 to 0)
Mansouri et al (2018)[17,]	XEN alone	20 (IQR: 17 to 23)	40.0% reduction	2.5 (IQR: 1 to 4)	NR
Hengerer et al (2017)[18,]	XEN alone	31.5 (8.4)	14.3 (4.2)	3.1 (1.0)	0.3 (0.7)

[a] Follow-up for Schlenker (2017) was not 1 year, but last visit in retrospective chart review
IOP: intraocular pressure; IQR: interquartile range; NR: not reported; SD: standard deviation.

Section Summary: Ab Interno Aqueous Stents
Currently, the XEN gel stent is the only stent approved by the FDA for the treatment of refractory OAG as a stand-alone procedure. Clearance for the stent was based on a review in which the FDA concluded that while there were technical differences between the stent and predicate devices (shunts), the differences did not affect safety and effectiveness in lowering IOP and medication use. Evidence for the use of the XEN implant consists of a nonrandomized comparative study which retrospectively reviewed charts of patients either receiving the XEN implant or undergoing a trabeculectomy. Additional evidence consists of single-arm studies. The comparative study included patients with different types of glaucoma (57% with POAG) and reported that patients receiving the XEN implant experienced reductions in IOP and medication use similar to patients undergoing a trabeculectomy. However, there was no discussion on how patients were chosen to receive the different treatments and no subgroup analysis by glaucoma type was provided. The single-arm studies, with 12 months of follow-up, consistently showed that patients receiving the XEN implant experienced reductions in IOP and medication use, with reductions in IOP ranging from 4 mm Hg to over 15 mm Hg.

Aqueous Microstents in Conjunction with Cataract Surgery
The iStent and iStent *inject,* which is preloaded with 2 stents, have FDA approval for use in conjunction with cataract surgery. An additional stent, the CyPass, had FDA approval but was voluntarily recalled by the manufacturer in 2018, as follow-up data has shown significant endothelial cell loss among patients receiving the CyPass in conjunction with cataract surgery compared with patients receiving cataract surgery alone. Studies comparing implantation of stents during cataract surgery with cataract surgery alone are discussed below.

REVIEW OF EVIDENCE

ISTENT

Systematic Reviews

A 2019 Cochrane review on the iStent in patients with open-angle glaucoma was published by Le at al (2019, see Table 6). [19,] The authors identified 7 RCTs, all of which were considered to be at high or unclear risk of bias. Four of the trials compared iStent in combination with cataract surgery to cataract surgery alone, 2 RCTs compared treatment with iStent or iStent *inject* to medical therapy, and 1 RCT compared 1, 2, or 3 iStents. Results of the meta-analyses on use of the iStent in combination with cataract surgery are shown in Table 7. Implantation of 1 or 2 iStents resulted in a higher proportion of patients who were drop free (relative risk: 1.38) and reduced the mean number of drops when compared to phacoemulsification alone (-0.42 drops). The review concluded that based on the 4 trials, there was very low-quality evidence that iStent may result in a higher proportion of patients who are drop free or achieve better IOP control.

Table 6. Meta-analysis Characteristics

Study	Dates	Trials	Participants	N (Range)	Design	Duration
Le et al (2019)[19,]	- Aug 2018	7	Eyes with open-angle glaucoma	765 (33 to 239)	RCT	42 months

Table 7. Meta-analysis Results

Study	Drop Free Compared to Phacoemulsification Alone	Change in Drops Compared to Phacoemulsification Alone	Change in IOP Compared to Phacoemulsification Alone
Le et al (2019)[19,]			
N	239 (2 RCTs)	282 (2 RCTs)	284 (3 RCTs)
Pooled effect (95% CI)	RR: 1.38 (1.18 to 1.63)	-0.42 (-0.60 to -0.23)	-1.24 mmHg
I2 (p)	67% (p)	0%	

CI: confidence interval; IOP: intraocular pressure; RCT: randomized controlled trial; RR: relative risk

iStent and iStent inject Pivotal Trials

Included in the Cochrane review were results from the iStent U.S. investigational device exemption, open-label, 29-site, multicenter RCT. Results were reported to the FDA in 2010, with 1-year results published by Samuelson et al (2011) and 2-year results published by Craven et al (2012) (see Table 8).[20,21,] Trial objectives were to evaluate the incremental effect on IOP of iStent implantation compared to cataract surgery alone and to determine the potential benefit of combining 2 therapeutic treatments into a single surgical event. A total of 240 patients (mean age, 73 years) with cataracts and mild-to-moderate OAG (IOP ≤24 mm Hg controlled on 1-3 medications) underwent a medication washout period. Patients were randomized to cataract surgery plus iStent implantation or cataract surgery only. Follow-up visits were performed at 1, 3, 6, and 12 months. Results were assessed by intention-to-treat analysis with the last observation carried forward and per-protocol analysis. The proportion of eyes meeting both the primary (unmedicated IOP ≤21 mm Hg) and secondary outcomes (IOP reduction ≥20% without medication) was higher in the treatment group than in the control group through 1-year follow-

up (72% of treatment eyes vs 50% of control eyes achieved the primary efficacy endpoint, p<0.001). The proportion of patients achieving the secondary efficacy endpoint was 66% in the treatment group and 48% in the control group (p=0.003). Ocular hypotensive medications were initiated later in the postoperative period and used in a lower proportion of patients in the treatment group throughout 1-year follow-up (e.g., 15% vs 35% at 12 months). Mean reduction in IOP was similar in both groups, though the control group used slightly more medication (mean, 0.4 medications) than the treatment group (0.2 medications) at 1 year (see Table 9). At 2-year follow-up, 199 (83%) patients remained in the study. The primary endpoint (unmedicated IOP ≤21 mm Hg) was reached by 61% of patients in the treatment group and 50% of controls (p=0.036).[21,] Secondary outcomes ¾ IOP reduction of 20% or more without medication (53% vs 44%) and the mean number of medications used (0.3 vs 0.5)¾ no longer differed significantly between groups at 2 years. As noted by the FDA, this study was conducted in a restricted population with an unmedicated IOP of 22 mm Hg or higher and a medicated IOP of 36 mm Hg or lower.

The pivotal trial on the iStent *inject* was reported by Samuelson et al (2019).[22,] A total of 505 patients undergoing cataract surgery were randomized after lens implantation to insertion of 2 smaller iStents or control. Results were assessed by intention-to-treat analysis and per-protocol analysis, with patients requiring additional surgical procedures considered to be failures. The addition of medications was based on a standardized protocol. At the 2-year follow-up, a greater percentage of patients had achieved at least a 20% reduction in IOP (75.8% vs 61.9%, p=0.005), had a greater reduction in IOP (7.0 vs 5.4, p<0.001), and required fewer topical medications (0.4 vs 0.8, p<0.001).

Limitations of these studies are described in Tables 10 and 11. The 2 main limitations are that there was no masking to treatment and durability of these microstents after 2 years was not reported. Continued patency of the stents and need for additional treatments has been evaluated through 4 years in studies from the Microinvasive Glaucoma Surgery (MIGS) study group and are described below.

Table 8. Summary of Pivotal RCT Characteristics

Study	Countries	Sites	Dates	Participants	Interventions	
					Active	*Comparator*
Samuelson et al (2011)[20,]; Craven et al (2012)[21,]	U.S.	29	2005-2007	Patients with mild-to-moderate POAG, unmedicated IOP ≥22 and ≤36 mm Hg	iStent plus cataract surgery(n=116)	Cataract surgery alone (n=123)
Samuelson et al (2019)[22,]	U.S.		2011-	Patients with mild-to-moderate POAG, unmedicated IOP ≥21 and ≤36 mm Hg	iStent *inject* (2 stents) plus cataract surgery (n=387)	Cataract surgery alone (n=118)

IOP: intraocular pressure; POAG: primary open-angle glaucoma; RCT: randomized controlled trial.

Table 9. Summary of Pivotal RCT Results

Study	> 20% Reduction in Unmedicated IOP at 24 mo n (%)	Mean Reduction in IOP at 24 mo mm Hg (SD)	Mean IOP (SD), mm Hg		p	Mean Medication Use (SD)		p
			iStent	Cataract Alone		iStent	Cataract Alone	
Samuelson et al (2011)[20]; Craven et al (2012)[21]								
Baseline			18.6 (3.4)	17.9 (3.0)	NR	1.6 (0.8)	1.5 (0.6)	
Year 1			17.0 (2.8)	17.0 (3.1)	NR	0.2 (0.6)	0.4 (0.7)	0.016
Year 2			17.1 (2.9)	17.8 (3.3)	NR	0.3 (0.6)	0.5 (0.7)	
Samuelson et al (2019)[22] iStent inject	288/380 (75.8%)	7.0 (4.0)	17.1 (3.6)			0.4 (0.8)		
Cataract Alone	73/118 (61.9%)	5.4 (3.7)	17.8 (3.5)			0.8 (1.0)		
p-Value	0.005	<0.001				<0.001		

IOP: intraocular pressure; NR: not reported; SD: standard deviation.

Table 10. Study Relevance Limitations

Study	Population[a]	Intervention[b]	Comparator[c]	Outcomes[d]	Follow-Up[e]
Samuelson et al (2011)[20]					Patency after 2 years is unknown
Samuelson et al (2019)[22]					Patency after 2 years is unknown

The study limitations stated in this table are those notable in the current review; this is not a comprehensive gaps assessment.

a Population key: 1. Intended use population unclear; 2. Clinical context is unclear; 3. Study population is unclear; 4. Study population not representative of intended use.

b Intervention key: 1. Not clearly defined; 2. Version used unclear; 3. Delivery not similar intensity as comparator; 4.Not the intervention of interest.

c Comparator key: 1. Not clearly defined; 2. Not standard or optimal; 3. Delivery not similar intensity as intervention; 4. Not delivered effectively.

d Outcomes key: 1. Key health outcomes not addressed; 2. Physiologic measures, not validated surrogates; 3. No CONSORT reporting of harms; 4. Not establish and validated measurements; 5. Clinical significant difference not prespecified; 6. Clinical significant difference not supported.

e Follow-Up key: 1. Not sufficient duration for benefit; 2. Not sufficient duration for harms.

Table 11. Study Design and Conduct Limitations

Study	Allocation[a]	Blinding[b]	Selective Reporting[c]	Data Completeness[d]	Power[e]	Statistical[f]
Samuelson et al (2011)[20,]		2, 3. No blinding of assessors				
Samuelson et al (2019)[22,]		2, 3. No blinding of assessors				

The study limitations stated in this table are those notable in the current review; this is not a comprehensive gaps assessment.
a Allocation key: 1. Participants not randomly allocated; 2. Allocation not concealed; 3. Allocation concealment unclear; 4. Inadequate control for selection bias.
b Blinding key: 1. Not blinded to treatment assignment; 2. Not blinded outcome assessment; 3. Outcome assessed by treating physician.
c Selective Reporting key: 1. Not registered; 2. Evidence of selective reporting; 3. Evidence of selective publication.
d Data Completeness key: 1. High loss to follow-up or missing data; 2. Inadequate handling of missing data; 3. High number of crossovers; 4. Inadequate handling of crossovers; 5. Inappropriate exclusions; 6. Not intent to treat analysis (per protocol for noninferiority trials).
e Power key: 1. Power calculations not reported; 2. Power not calculated for primary outcome; 3. Power not based on clinically important difference.
f Statistical key: 1. Analysis is not appropriate for outcome type: (a) continuous; (b) binary; (c) time to event; 2. Analysis is not appropriate for multiple observations per patient; 3. Confidence intervals and/or p values not reported; 4. Comparative treatment effects not calculated.

One non-randomized comparative study was reported by Hooshmand et al (2019) on outcomes with the use of the iStent inject, which simultaneously injects 2 stents through a single ab interno opening, compared to the first generation single iStent (see Table 12).[23,] The iStent inject was developed to provide easier ab interno insertion and comes preloaded with 2 stents that are smaller than the first-generation iStent. There was no significant difference between the earlier model and the second generation device on outcomes at 12 months (see Table 13) but Kaplan-Meier analysis found an earlier time to add topical medications in the iStent inject patients. Limitations of the study include the length of follow-up, which was limited by the time that the iStent inject had been available, and the non-randomized design (see Tables 14 and 15). In addition, the study compared 2 cohorts from different time periods, those who had been treated with the first generation device and those who had been treated with the second-generation device. Efficacy of the iStent inject at longer follow-up is unknown.

Table 12. Summary of Comparative Study Characteristics

Study; Trial	Countries	Sites	Dates	Participants	Interventions	
					Active	Comparator
Hooshmand et al (2019)[23,]	AU	2		Patients with POAG undergoing cataract surgery	iStent at the time of cataract surgery (n=145)	iStent inject at the time of cataract surgery (n=100)

POAG: primary open-angle glaucoma

Table 13. Summary of Comparative Study Results

Study	IOP < 18 mm Hg without medication at 12 months n (%)	IOP < 18 mm Hg with medication at 12 months n (%)	> 20% reduction in IOP at 12 months n (%)
Hooshmand et al (2019)[23,]	N=219	N=219	N=219
iStent	79 (56.0)	89 (63.1)	49 (34.8)
iStent inject	40 (51.3)	45 (57.7)	23 (29.5)
p-Value	0.50	0.43	0.43

CI: confidence interval; IOP: intraocular pressure.
1 Include number analyzed, effect in each group, and measure of effect (absolute or relative) with CI,
2 Describe the range of sample sizes, effects, and other notable features in text.

Table 14. Study Relevance Limitations

Study	Population[a]	Intervention[b]	Comparator[c]	Outcomes[d]	Follow-Up[e]
Hooshmand et al (2019)[23,]					1. Follow-up was limited by the time that the iStent inject was available.

The study limitations stated in this table are those notable in the current review; this is not a comprehensive gaps assessment.
a Population key: 1. Intended use population unclear; 2. Clinical context is unclear; 3. Study population is unclear; 4. Study population not representative of intended use.
b Intervention key: 1. Not clearly defined; 2. Version used unclear; 3. Delivery not similar intensity as comparator; 4.Not the intervention of interest.
c Comparator key: 1. Not clearly defined; 2. Not standard or optimal; 3. Delivery not similar intensity as intervention; 4. Not delivered effectively.
d Outcomes key: 1. Key health outcomes not addressed; 2. Physiologic measures, not validated surrogates; 3. No CONSORT reporting of harms; 4. Not establish and validated measurements; 5. Clinical significant difference not prespecified; 6. Clinical significant difference not supported.
e Follow-Up key: 1. Not sufficient duration for benefit; 2. Not sufficient duration for harms.

Table 15. Study Design and Conduct Limitations

Study	Allocation[a]	Blinding[b]	Selective Reporting[c]	Data Completeness[d]	Power[e]	Statistical[f]
Hooshmand et al (2019)[23,]	1. Study was not randomized	1, 2, 3. No blinding of assessors			1. Post-hoc power calculations	

The study limitations stated in this table are those notable in the current review; this is not a comprehensive gaps assessment.
a Allocation key: 1. Participants not randomly allocated; 2. Allocation not concealed; 3. Allocation concealment unclear; 4. Inadequate control for selection bias.
b Blinding key: 1. Not blinded to treatment assignment; 2. Not blinded outcome assessment; 3. Outcome assessed by treating physician.
c Selective Reporting key: 1. Not registered; 2. Evidence of selective reporting; 3. Evidence of selective publication.
d Data Completeness key: 1. High loss to follow-up or missing data; 2. Inadequate handling of missing data; 3. High number of crossovers; 4. Inadequate handling of crossovers; 5. Inappropriate exclusions; 6. Not intent to treat analysis (per protocol for noninferiority trials).
e Power key: 1. Power calculations not reported; 2. Power not calculated for primary outcome; 3. Power not based on clinically important difference.

f Statistical key: 1. Analysis is not appropriate for outcome type: (a) continuous; (b) binary; (c) time to event; 2. Analysis is not appropriate for multiple observations per patient; 3. Confidence intervals and/or p values not reported; 4. Comparative treatment effects not calculated.

HYDRUS MICROSTENT

Systematic Reviews

A Cochrane review by Otarola et al (2020) included 3 studies with 808 participants.[24,] Two studies (described below) were conducted in patients with cataracts and OAG (n=653), and compared the Hydrus microsent combined with cataract surgery to cataract surgery alone.[25,26,] They found moderate-certainty evidence that adding the Hydrus microstent to cataract surgery in patients with mild or moderate OAG increased the proportion of participants who were medication-free at 12 month (risk ratio 1.59, 95% confidence interval 1.39 to 1.83) and 24 month follow-up (risk ratio 1.63, 95% confidence interval 1.40 to 1.888), and reduced unmedicated IOP by 2 mm Hg, the number of medications by -0.41, and the need for secondary glaucoma surgery.

The third study compared the Hydrus microstent with the iStent in patients without cataract surgery.[27,] This study is described in the next section on microstents as a stand-alone procedure.

Randomized Controlled Trials

Pfeiffer et al (2015) reported on a single-masked, randomized trial with 100 patients (100 eyes) that compared the effectiveness of the Hydrus Microstent plus cataract surgery with cataract surgery alone (Table 16).[25,] At the 24-month follow-up, the proportion of patients with a 20% reduction in IOP was significantly higher with the Hydrus Microstent (80% vs 46%, p<0.001) and the mean IOP after medication washout was lower (16.9 mm Hg vs 19.2 mm Hg, p=0.009) compared with cataract surgery alone, respectively. The microstent group used significantly fewer medications (0.5 vs 1.0, p=0.019) and had a higher proportion of patients taking no hypotensive medications at the time of cataract surgery (73% vs 38%, p=0.001). Comparisons of mean washed out IOP and the mean number of medications used are presented in Table 17.

Samuelson et al (2019) reported on a multicenter RCT (HORIZON) comparing implantation of a single Hydrus Microstent following cataract surgery vs cataract surgery alone (Table 16).[26,] Patients were masked to treatment assignment for the course of the study. The primary endpoint was percent demonstrating a 20% reduction in unmedicated IOP. Significantly more patients receiving the microstent following cataract surgery experienced a 20% reduction in unmedicated IOP compared with patients undergoing cataract surgery alone (77% vs 58%; p<0.001). Additional results (mean washed out IOP and the mean number of medications used) are presented in Table 17.

Table 16. Summary of Key RCT Characteristics for the Hydrus Microstent

Study	Countries	Sites	Dates	Participants	Interventions	
					Active	Comparator
Pfeiffer (2015)[25,]	Germany, Italy, Spain, the Netherlands	7	2011 to 2012	Patients with concurrent open-angle glaucoma and cataract	Cataract surgery plus Hydrus Microstent implantation (n=50)	Cataract surgery alone (n=50)

Study	Countries	Sites	Dates	Participants	Interventions	
Samuelson (2019)[26,]	Germany, Italy, Mexico, Philippines, Poland, Spain, United Kingdom, United States	26	2012 to 2015	Patients with age-related cataract and mild to moderate primary open-angle glaucoma	Cataract surgery plus Hydrus Microstent implantation (n=369)	Cataract surgery alone (n=187)

RCT: randomized controlled trial.

Table 17. Summary of Key RCT Results for the Hydrus Microstent

Study	Mean washed out IOP			Mean medication use		
	Hydrus Microstent	Cataract alone	p	Hydrus Microstent	Cataract alone	p
Pfeiffer (2015)[25,]						
Baseline	26.3 +/- 4.4	26.6 +/- 4.2	0.7	2.0 +/- 1.0	2.0 +/ - 1.1	0.8
Year 2	16.9 +/- 3.3	19.2 +/- 4.7	0.009	0.5 +/- 1.0	1.0 +/- 1.0	0.02
Samuelson (2019)[26,]						
Baseline mean	25.5 +/- 3.0	25.4 +/- 2.9	NS	1.7 +/- 0.9	1.7 +/- 0.9	NS
Year 2	17.4 +/- 3.7	19.2 +/- 3.8	NR	0.3 +/- 0.8	0.7 +/- 0.9	<0.001

IOP: intraocular pressure; NR: not reported; NS: not significant; RCT: randomized controlled trial.

Observational Study

Fea et al (2017) conducted a retrospective review of 92 patients undergoing cataract surgery plus Hydrus Microstent implantation.[28,] Two year follow-up showed improvements in IOP and medication use. Mean IOP at baseline was 19.4 mm Hg, decreasing significantly by 6 months to 15.6 mm Hg, which was maintained at 2 years of follow-up (15.7 mm Hg). The mean number of medications was 2.1 at baseline, decreasing significantly by 6 months to 0.5, which was maintained through 2 years of follow-up (0.7).

XEN GLAUCOMA TREATMENT SYSTEM

Observational Studies

Mansouri et al (2018)[17,] and Hengerer et al (2017)[18,], are described above in the section on aqueous stents used as a stand-alone treatment for refractory OAG. These studies also included patients who received the XEN implant in conjunction with cataract surgery and study characteristics and results for this subgroup appear in Tables 18 and 19.

Table 18. Summary of Key Study Characteristics for the XEN Implant with Cataract Surgery

Study	Country	Participants	Treatment Delivery	FU
Mansouri et al (2018)[17,]	Switzerland	Patients with POAG and uncontrolled IOP, progressive	· XEN alone (n=40)· XEN plus cataract surgery (n=109)	12 mo

Study	Country	Participants	Treatment Delivery	FU
		glaucoma, and/or refractory to IOP medications		
Hengerer et al (2017)[18,]	Germany	Patients with POAG and uncontrolled IOP, optic disc damage, and refractory to IOP medications or prior surgery	· XEN alone (n=203)· XEN plus cataract surgery (n=39)	12 mo

FU: follow-up; IOP: intraocular pressure; POAG: primary open-angle glaucoma.

Table 19. Summary of Key Study Results for the XEN Implant with Cataract Surgery

Study	Population	IOP (SD), mm Hg		Medication, Median (SD)	
		Baseline	1 Year	Baseline	1 Year
Mansouri et al (2018)[17,]	XEN + cataract	18 (IQR: 14 to 23)	22.9% reduction	2 (IQR: 1 to 3)	NR
Hengerer et al (2017)[18,]	XEN + cataract	35.7 (12)	13.9 (2.5)	3.3 (1.0)	0.4 (0.7)

IOP: intraocular pressure; IQR: interquartile range; NR: not reported; SD: standard deviation.

CyPass

The FDA evaluated the clinical performance of the CyPass Micro-Stent system based on the pivotal Clinical Study to Assess the Safety and Effectiveness of the Transcend CyPass Glaucoma Implant in Patients With Open-Angle Glaucoma Undergoing Cataract Surgery (COMPASS) trial (NCT01085357). COMPASS was a multicenter RCT comparing the safety and efficacy of CyPass Micro-Stent plus cataract surgery with cataract surgery alone for treating mild-to-moderate primary OAG in patients undergoing cataract surgery. Evidence from the RCT supported the use of the CyPass stent in conjunction with cataract surgery; however, in August 2018, the manufacturer voluntarily withdrew the device from the market because a long-term study showed that patients receiving CyPass in conjunction with cataract surgery experienced statistically significant endothelial cell loss compared with patients who underwent cataract surgery alone.

Section Summary: Ab Interno Aqueous Microstents

Implantation of 1 or 2 microstents has received the FDA approval for use in conjunction with cataract surgery for reduction of IOP in adults with mild-to-moderate OAG currently treated with ocular hypotensive medication. RCTs and meta-analyses of RCTs have compared cataract surgery alone to microstent implantation in conjunction with cataract surgery when IOP is at least partially controlled with medication. When compared to cataract surgery alone, the studies showed modest but statistically significant decreases in IOP and medication use through the first 2 years when stents were implanted in conjunction with cataract surgery. A decrease in topical medication application is considered to be an important outcome for patients and reduces the problem of non-compliance that can affect visual outcomes.

MICROSTENT IMPLANTATION AS A STAND-ALONE PROCEDURE

iStent

The iStent was approved by the FDA to be used in conjunction with cataract surgery to reduce IOP in patients with mild-to-moderate open-angle glaucoma. The studies described below evaluated the use of the iStent or iStent inject as a stand-alone procedure.

The Cochrane review by Le et al (2019) on the iStent in patients with open-angle glaucoma identified 2 RCTs that compared treatment with iStent or iStent inject to medical therapy and 1 RCT that compared 1, 2, or 3 iStents.[19,] Results of the meta-analyses are shown in Table 20. Meta-analysis was not performed due to heterogeneity. However, in both trials, iStent implantation resulted in a higher proportion of patients who were drop free and reduced the mean number of drops when compared to medical therapy. One RCT indicated that compared to implantation of 1 stent, implantation of 2 or 3 stents resulted in a similar proportion of patients who were drop free at 36 months or less, but a higher proportion of patients who were drop free after 36 months. The 2 studies included in the 2019 Cochrane review are described in greater detail below (Tables 21 and 22). Limitations of these studies are described in Tables 23 and 24.

Table 20. Meta-analysis Results

Study	Drop Free Compared to Medical Therapy	Drop Free with 2 Stents Compared to 1 Stent at 42 months	Drop Free with 3 Stents Compared to 1 Stent at 42 months
Le et al (2019)[19,]			
N	2 RCTs	1 RCT	1 RCT
Pooled effect (95% CI)	90% of patients in the iStent groups were drop free	RR:0.51 (0.34 to 0.75)	RR:0.49 (0.34 to 0.73)

CI: confidence interval; RCT: randomized controlled trial; RR: relative risk.

A 2014 industry-sponsored, multicenter, unblinded, randomized trial compared implantation of 2 iStent inject devices to 2 ocular hypotensive agents.[29,] The 192 patients enrolled in this unmasked trial had an IOP not controlled by 1 hypotensive medication. At 12-month follow-up, the 2 groups were comparable for IOP reduction of at least 20%, IOP of 18 mm Hg or less, and mean decrease in IOP. A greater proportion of patients in the iStent inject group achieved an IOP reduction of at least 50% (53.2% vs 35.7%, respectively). One patient in the iStent inject group experienced elevated IOP (48 mm Hg) and 4 required ocular hypotensive medication. Longer-term studies are in progress.

Vold et al (2016) reported results of an RCT comparing 2 stand-alone iStent inject implants to topical travoprost (1:1 ratio) in 101 phakic eyes with an IOP between 21 and 40 mm Hg and newly diagnosed POAG, pseudoexfoliative glaucoma, or ocular hypertension that had not been treated previously.[30,] The patients were not undergoing cataract surgery. The trial was unmasked, and methods for allocation concealment and calculation of power were not described. One hundred patients (54 iStent; 47 travoprost) completed 24 months of follow-up and 73 completed 36 months of follow-up. The trial was performed at a single-center in Armenia with visiting surgeons from the U.S. Statistical analyses were not provided. Baseline mean IOP was 25 mm Hg in both groups. Mean IOP at 3 years was 15 mm Hg in both groups. Medication (or second medication) was added to 6 eyes in the iStent group and 11 eyes in the travoprost group.

Progression of cataract was reported in 11 eyes in the iStent group and 8 eyes in the travoprost group, with cataract surgery being performed in 5 eyes in the iStent group and 1 eye in the travoprost group. The results would suggest that 2 iStents might reduce the number of medications required to maintain target IOP compared with travoprost but also hasten time to cataract surgery. However, the study methods were poorly reported, and statistical analyses were not reported.

Four year follow-up of iStent inject is reported in 2 phase 4 publications from the MIGS study group.[31,32,] Berdahl et al (2020) reported on 53 patients who were on 2 preoperative medications who received 2 iStent inject implants and started on travoprost on postoperative Day 1. At 48 month follow-up, 85% of eyes had reduced IOP (> 20%) with a single medication as compared to the baseline IOP on 2 medications. Mean IOP on 1 medication was 11.9 to 13.0 mm Hg, compared to 19.7 on 2 medications preoperatively. Lindstrom et al (2020) reported on 57 patients who were on 1 preoperative medication before implantation of 2 iStent inject devices. Month 48 IOP without medication was reduced (> 20%) in 95% of eyes with iStent inject. There were no adverse events that were considered to be related to the devices.

Hydrus versus iStent

Hydrus microstent was compared with the iStent in a double-blind multicenter RCT by Ahmed et al (COMPARE, 2020).[27,] Eyes (n=152) with mild-to-moderate glaucoma and an IOP of 23 to 39 after washout of medication were randomized to either 1 Hydrus stent or 2 iStents as a stand-alone treatment. Both stents have FDA approval in the U.S. when used in conjunction with cataract surgery but not as a stand-alone procedure. Follow-up was performed through 12 months post-operatively with medications added at the investigator's discretion. The Hydrus outperformed 2 iStents in nearly every measure (see Table 22). Eyes implanted with the Hydrus microstent were able to maintain IOP < 18 mm Hg on fewer medications and a greater percentage of patients were medication-free compared to the iStent group (46.6% vs 24.0%, p<0.001). The decision to increase medications was up to the investigator and not pre-specified, but post hoc analysis indicated that the IOP at which medications were increased was similar in the 2 groups.

Table 21. Summary of RCT Characteristics

Study; Trial	Countries	Sites	Dates	Participants	Interventions	
					Active	Comparator
Fea et al (2014)[29,]	EU, Armenia	8		Patients with OAG not controlled on one medication, Post-washout IOP >22 and <38 mmHg	iStent inject (n=94)	Two medications (n=98)
Vold et al (2016)[30,]	Armenia with U.S. surgeons	1		Patients with Patients with OAG (n=101) or PEX (n=1) who were naive to therapy with	Two iStents (n=54)	One medication (n=47)

Study; Trial	Countries	Sites	Dates	Participants	Interventions	
				IOP > 21 and < 40 mmHg		
Ahmed et al (2019)[27,]	U.S., E.U., Canada, Asia	12	2013-2015	152 patients with mild-to-moderate glaucoma (OAG, PEX, or PG and IOP 23 to 39 mmHg after washout	Hydrus (n=75)	Two iStents (n=77)

IOP: intraocular pressure; PEX: pseudoexfoliative glaucoma; PG: pigmentary glaucoma; OAG: open-angle glaucoma; RCT: randomized controlled trial.

Table 22. Summary of RCT Results

Study	>20% reduction in IOP n (%)	IOP < 18 mmHg	Mean IOP mmHg (SD)	Mean reduction in IOP from baseline mmHg (SD)	Mean number of medications at 12 months	Percent Medication Free at 12 months n (%)
Fea et al (2014) [29,]	*at 12 months*	*at 12 months* n (%)	*at 12 months*			
iStent inject	89/94 (94.7)	87/94 (92.6)	13.0 (2.3)	8.1 (2.6)		
Medical therapy	88/98 (91.8)	88/98 (89.8)	13.2 (2.0)	7.3 (2.2)		
p-Value	0.02	NR	NR	0.43		
Vold et al (2016)[30,]	IOP < 18 mmHg n (%) at 24 months	*at 36 months*	*at 36 months*			
iStent	90%	91%	14.6 mmHg			
Medical therapy	87%	79%	15.3 mmHg			
p-Value						
Ahmed et al (2020)[27,]		*without medication*				
Hydrus	39.7%	30.1%	17.3 (3.7).	-8.2 (3.7)	1.0	34 (46.6)
2 iStents	13.3%	9.3%	19.2 (2.4)	-5.1 (2.9)	1.7	18 (24.0)
p-Value	<0.001	<0.001	0.037	0.003	<0.001	0.006

IOP: intraocular pressure; NR: not reported; RCT: randomized controlled trial; SD: standard deviation.

Table 23. Study Relevance Limitations

Study	Population[a]	Intervention[b]	Comparator[c]	Outcomes[d]	Follow-Up[e]
Fea et al (2014)[29,]					1. Follow-up was limited to 12 months. Monitoring for occlusion of the stents at longer follow-up is needed
Vold et al (2016)[30,]		4. Not the currently marketed device			
Ahmed et al (2019)[27,]			4. Not the currently marketed device		1. Follow-up was through 12 months, longer follow-up is continuing.

The study limitations stated in this table are those notable in the current review; this is not a comprehensive gaps assessment
a Population key: 1. Intended use population unclear; 2. Clinical context is unclear; 3. Study population is unclear; 4. Study population not representative of intended use.
b Intervention key: 1. Not clearly defined; 2. Version used unclear; 3. Delivery not similar intensity as comparator; 4.Not the intervention of interest.
c Comparator key: 1. Not clearly defined; 2. Not standard or optimal; 3. Delivery not similar intensity as intervention; 4. Not delivered effectively.
d Outcomes key: 1. Key health outcomes not addressed; 2. Physiologic measures, not validated surrogates; 3. No CONSORT reporting of harms; 4. Not establish and validated measurements; 5. Clinical significant difference not prespecified; 6. Clinical significant difference not supported.
e Follow-Up key: 1. Not sufficient duration for benefit; 2. Not sufficient duration for harms.

Table 24. Study Design and Conduct Limitations

Study	Allocation[a]	Blinding[b]	Selective Reporting[c]	Data Completeness[d]	Power[e]	Statistical[f]
Fea et al (2014) [29,]	3. Randomization procedure was not described	1, 2, 3. Study could not be blinded		1. Unequal loss to follow-up in the 2 groups, and the subjects lost to follow-up were treated as failures	1. Power calculations not reported	
Vold et al (2016)[30,]	3. Randomization procedure was not described	1, 2, 3. Study could not be blinded		1. There was 27% loss to follow-up at 36 months	1. Power calculations not reported	4. Statistical analysis not reported
Ahmed et al (2020)[27,]		2, 3. Investigators were not blinded and there was no independent				2. Did not use repeated measures for multiple assessments

Study	Allocation[a]	Blinding[b]	Selective Reporting[c]	Data Completeness[d]	Power[e]	Statistical[f]
		adjudication or preset criteria for increase in medication				

The study limitations stated in this table are those notable in the current review; this is not a comprehensive gaps assessment.
a Allocation key: 1. Participants not randomly allocated; 2. Allocation not concealed; 3. Allocation concealment unclear; 4. Inadequate control for selection bias.
b Blinding key: 1. Not blinded to treatment assignment; 2. Not blinded outcome assessment; 3. Outcome assessed by treating physician.
c Selective Reporting key: 1. Not registered; 2. Evidence of selective reporting; 3. Evidence of selective publication.
d Data Completeness key: 1. High loss to follow-up or missing data; 2. Inadequate handling of missing data; 3. High number of crossovers; 4. Inadequate handling of crossovers; 5. Inappropriate exclusions; 6. Not intent to treat analysis (per protocol for noninferiority trials).
e Power key: 1. Power calculations not reported; 2. Power not calculated for primary outcome; 3. Power not based on clinically important difference.
f Statistical key: 1. Analysis is not appropriate for outcome type: (a) continuous; (b) binary; (c) time to event; 2. Analysis is not appropriate for multiple observations per patient; 3. Confidence intervals and/or p values not reported; 4. Comparative treatment effects not calculated.

Greater Than Two Stents

An RCT comparing the efficacy of 1 iStent with multiple iStent devices was published by Katz et al (2015).[33,] This trial, from a single-institution in Armenia, randomized 119 patients with mild-to-moderate OAG and an IOP between 22 and 38 mm Hg (off medications) to 1 stent (n=38), 2 stents (n=41), or 3 stents (n=40). Randomization was performed using a pseudorandom number generator. The primary endpoint was the percentage of patients with a reduction of 20% or more in IOP off medications at 12 months. This endpoint was reached by 89.2% of the 1-stent group, by 90.2% of the 2-stent group, and by 92.1% of the 3-stent group. The secondary endpoint (percentage of patients achieving an IOP £15 mm Hg off medication) was reached by 64.9% of the 1-stent group, by 85.4% of the 2-stent group, and by 92.1% of the 3-stent group. Forty-two-month follow-up results for 109 patients were published by Katz et al (2018).[34,] Post-washout IOP was 17.4±0.9, 15.8±1.1 and 14.2±1.5 mmHg, for 1, 2, or 3 stents, respectively. The need for additional medication increased in single-stent eyes from 4 eyes at 12 months to 18 eyes at 42 months, suggesting a reduction in patency of the microstents over time. The need for additional medication did not increase from months 12 and 42 in multi-stent eyes. No between-group statistical comparisons were reported.

Section Summary: Microstent Implantation as a Stand-Alone Procedure

The evidence on microstents as a stand-alone procedure in patients with mild-to-moderate glaucoma that is controlled on medical therapy includes RCTs and a systematic review of 3 heterogeneous RCTs. Two RCTs indicate that implantation of a microstent can reduce IOP at a level similar to ocular medications at 12-month follow-up. Reduction in medications is an important outcome for patients with glaucoma, both for the patients themselves and because lack of compliance can lead to adverse health outcomes. Whether microstents remain patent after 12 months is uncertain, and whether additional stents can subsequently be safely implanted is unknown. Some evidence on longer-term outcomes is provided by an RCT that compared implantation of a single iStent with multiple iStents. At longer-term (42-month) follow-up, the need for additional medication increased in eyes implanted with a single iStent but not with multiple iStents. The durability of multiple iStents is unknown. A fourth RCT compared

implantation of the Hydrus microstent to 2 iStents. Outcomes from the Hydrus microstent were significantly better than 2 iStents, both statistically and clinically, for all outcome measures. The primary limitation of this study is that the duration of follow-up in the present publication is limited to 12 months. Longer-term follow-up from this study is continuing and will answer important questions on the durability of the procedure. Corroboration in an independent study and comparison with a medical therapy control group would also increase confidence in the results.

Summary of Evidence

For individuals who have refractory OAG who receive ab externo aqueous shunts, the evidence includes randomized controlled trials (RCTs), retrospective studies, and systematic reviews. Relevant outcomes are a change in disease status, functional outcomes, medication use, and treatment-related morbidity. RCTs assessing U.S. Food and Drug Administration (FDA) approved shunts have shown that the use of large externally placed shunts reduces IOP to slightly less than standard filtering surgery (trabeculectomy). Reported shunt success rates show that these devices are noninferior to trabeculectomy in the long-term. The FDA approved shunts have different adverse event profiles and avoid some of the most problematic complications of trabeculectomy. Two trials have compared the Ahmed and Baerveldt shunts. Both found that eyes treated with the Baerveldt shunt had slightly lower average IOP at 5 years than eyes treated with the Ahmed but the Baerveldt also had a higher rate of serious hypotony-related complications. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals who have refractory OAG who receive ab interno aqueous stents, the evidence includes a nonrandomized retrospective comparative study and several single-arm studies. Relevant outcomes are a change in disease status, functional outcomes, medication use, and treatment-related morbidity. The comparative study reported that patients receiving the stent experienced similar reductions in IOP and medication use as patients undergoing trabeculectomy. The single-arm studies, with 12-month follow-up results, consistently showed that patients receiving the stents experienced reductions in IOP and medication use. Reductions in IOP ranged from 4 mm Hg to over 15 mm Hg. In addition, the FDA has given clearance to a gel stent based on equivalent IOP and medication use reductions as seen with ab externo shunts. Clearance for the stent was based on a review in which the FDA concluded that while there were technical differences between the stent and predicate devices (shunts), the differences did not affect safety and effectiveness in lowering IOP and medication use. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals who have mild-to-moderate OAG who are undergoing cataract surgery who receive aqueous microstents, the evidence includes RCTs and meta-analyses of RCTs. Relevant outcomes are a change in disease status, functional outcomes, medication use, and treatment-related morbidity. Implantation of 1 or 2 microstents has received the FDA approval for use in conjunction with cataract surgery for reduction of IOP in adults with mild-to-moderate OAG currently treated with ocular hypotensive medication. When compared to cataract surgery alone, the studies showed modest but statistically significant decreases in IOP and medication use through the first 2 years when stents were implanted in conjunction with cataract surgery. A decrease in topical medication application is considered to be an important outcome for patients and reduces the problem of non-compliance that can affect visual outcomes. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals with mild-to-moderate OAG who are not undergoing cataract surgery who receive aqueous microstents as a stand-alone procedure, the evidence includes RCTs and a systematic review of 3 heterogeneous RCTs. Relevant outcomes are a change in disease status, functional outcomes, medication use, and treatment-related morbidity. Several RCTs have evaluated the use of multiple microstents but comparators differed. Two RCTs indicate that implantation of a microstent can reduce IOP at a level similar to ocular medications at 12-month follow-up. Reduction in medications is an important outcome for patients with glaucoma. Whether microstents remain patent after 12 months is uncertain, and whether additional stents can subsequently be safely implanted is unknown. Some evidence on longer-term outcomes is provided by an RCT that compared implantation of a single iStent to implantation of multiple iStents. At longer-term (42-month) follow-up, the need for additional medication increased in eyes implanted with a single microstent but not with multiple microstents. The durability of multiple iStents is unknown. A fourth RCT compared implantation of the Hydrus microstent to 2 iStents. Outcomes from the Hydrus microstent were significantly better than 2 iStents, both statistically and clinically, for all outcome measures. The primary limitation of this study is that the duration of follow-up in the present publication is limited to 12 months. Longer-term follow-up from this study is continuing and will answer important questions on the durability of the procedure. Corroboration in an independent study and comparison with a medical therapy control group would also increase confidence in the results. The evidence is insufficient to determine the effects of the technology on health outcomes.

SUPPLEMENTAL INFORMATION

Clinical Input From Physician Specialty Societies and Academic Medical Centers

While the various physician specialty societies and academic medical centers may collaborate with and make recommendations during this process, through the provision of appropriate reviewers, input received does not represent an endorsement or position statement by the physician specialty societies or academic medical centers, unless otherwise noted.

In response to requests, input was received from 1 physician specialty society and 2 academic medical centers while this policy was under review in 2013. Input supported the use of aqueous shunts in patients with glaucoma uncontrolled by medication. Input supported the use of a single microstent in patients with mild-to-moderate glaucoma undergoing cataract surgery to reduce the adverse events of medications and to avoid noncompliance.

Practice Guidelines and Position Statements

American Academy of Ophthalmology

The AAO (2008) published a technology assessment on commercially available aqueous shunts, including the Ahmed, Baerveldt, Krupin, and Molteno devices.[2,] The assessment indicated that, in general, IOP would settle at higher levels (»18 mm Hg) with shunts than after standard trabeculectomy (14-16 mm Hg). Five-year success rates of 50% were found for the 2 procedures, indicating that aqueous shunts are comparable with trabeculectomy for IOP control and duration of benefit (based on level I evidence; well-designed randomized controlled trials). The assessment also indicated that although aqueous shunts have generally been reserved for intractable glaucoma when prior medical or surgical therapy has failed, indications for shunts have broadened (based on level III evidence; case series, case reports, and poor-quality case-control or cohort studies). The AAO concluded that, based on level I evidence, aqueous shunts

offer a valuable alternative to standard filtering surgery and cyclodestructive therapy for many patients with refractory glaucoma.

The AAO's (2015) preferred practice patterns on primary open-angle glaucoma indicated that the Academy 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.[35,] 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.

National Institute for Health and Care Excellence
The National Institute for Health and Care Excellence (2017) updated guidance on trabecular stent bypass microsurgery for open-angle glaucoma.[36,] The guidance stated that "Current evidence on trabecular stent bypass microsurgery for open-angle glaucoma raises no major safety concerns. Evidence of efficacy is adequate in quality and quantity.

The National Institute for Health and Care Excellence(2018) published guidance entitled "Microinvasive subconjunctival insertion of a trans-scleral gelatin stent for primary open-angle glaucoma"[37,]. The guidance states that evidence is limited in quantity and quality and therefore, the procedure should only be used with special arrangements and that patients should be informed of the uncertainty of the procedure.

U.S. Preventive Services Task Force Recommendations
Not applicable.

Ongoing and Unpublished Clinical Trials
Some currently ongoing and unpublished trials that might influence this review are listed in Table 25.

Table 25. Summary of Key Trials

NCT No.	Trial Name	Planned Enrollment	Completion Date
Ongoing			
NCT01461278[a]	A Prospective, Randomized, Single-Masked, Controlled, Parallel Groups, Multicenter Clinical Investigation of the Glaukos® Suprachoroidal Stent Model G3 In Conjunction With Cataract Surgery	1200	Dec 2020
NCT01841450[a]	A Prospective, Randomized, Controlled, Parallel Groups, Multicenter Post-Approval Study Of The Glaukos® iStent® Trabecular Micro-Bypass Stent System In Conjunction With Cataract Surgery	360	Jul 2021

NCT No.	Trial Name	Planned Enrollment	Completion Date
NCT04440527	Intraocular Pressure After Preserflo/Innfocus Microshunt vs Trabeculectomy: a Prospective, Randomised Control-trial (PAINT-Study)	70	Jul 2024
Unpublished			
NCT01444040[a]	A Prospective, Randomized Evaluation of Subjects With Open-angle Glaucoma, Pseudoexfoliative Glaucoma, or Ocular Hypertension Naïve to Medical and Surgical Therapy, Treated With Two Trabecular Micro-bypass Stents (iStent Inject) or Travoprost Ophthalmic Solution 0.004%	200	Jun 2018(unknown)
NCT01461291[a]	A Prospective, Randomized, Single-Masked, Controlled, Parallel Groups, Multicenter Clinical Investigation of the Glaukos® Trabecular Micro-Bypass Stent Model GTS400 Using the G2-M-IS Injector System in Conjunction With Cataract Surgery	1200	Dec 2019

NCT: national clinical trial.
[a] Denotes industry-sponsored or cosponsored trial.

CODING

The following codes for treatment and procedures applicable to this policy are included below for informational purposes. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

CPT/HCPCS

66179	Aqueous shunt to extraocular equatorial plate reservoir, external approach; without graft
66180	Aqueous shunt to extraocular equatorial plate reservoir, external approach; with graft
66183	Insertion of anterior segment aqueous drainage device, without extraocular reservoir, external approach
66184	Revision of aqueous shunt to extraocular equatorial plate reservoir; without graft
66185	Revision of aqueous shunt to extraocular equatorial plate reservoir; with graft
0191T	Insertion of anterior segment aqueous drainage device, without extraocular reservoir; internal approach, into the trabecular meshwork; initial insertion
0253T	Insertion of anterior segment aqueous drainage device, without extraocular reservoir; internal approach, into the suprachoroidal space
0376T	Insertion of anterior segment aqueous drainage device, without extraocular reservoir; internal approach, into the trabecular meshwork; each additional device insertion (List separately in addition to code for primary procedure)
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)

0474T	Insertion of anterior segment aqueous drainage device, with creation of intraocular reservoir, internal approach, into the supraciliary space
C1783	Ocular implant, aqueous drainage assist device

ICD-10 Diagnoses

H25.011	Cortical age-related cataract, right eye
H25.012	Cortical age-related cataract, left eye
H25.013	Cortical age-related cataract, bilateral
H25.031	Anterior subcapsular polar age-related cataract, right eye
H25.032	Anterior subcapsular polar age-related cataract, left eye
H25.033	Anterior subcapsular polar age-related cataract, bilateral
H25.041	Posterior subcapsular polar age-related cataract, right eye
H25.042	Posterior subcapsular polar age-related cataract, left eye
H25.043	Posterior subcapsular polar age-related cataract, bilateral
H25.091	Other age-related incipient cataract, right eye
H25.092	Other age-related incipient cataract, left eye
H25.093	Other age-related incipient cataract, bilateral
H25.11	Age-related nuclear cataract, right eye
H25.12	Age-related nuclear cataract, left eye
H25.13	Age-related nuclear cataract, bilateral
H25.21	Age-related cataract, morgagnian type, right eye
H25.22	Age-related cataract, morgagnian type, left eye
H25.23	Age-related cataract, morgagnian type, bilateral
H25.811	Combined forms of age-related cataract, right eye
H25.812	Combined forms of age-related cataract, left eye
H25.813	Combined forms of age-related cataract, bilateral
H25.89	Other age-related cataract
H25.9	Unspecified age-related cataract
H26.001	Unspecified infantile and juvenile cataract, right eye
H26.002	Unspecified infantile and juvenile cataract, left eye
H26.003	Unspecified infantile and juvenile cataract, bilateral
H26.011	Infantile and juvenile cortical, lamellar, or zonular cataract, right eye
H26.012	Infantile and juvenile cortical, lamellar, or zonular cataract, left eye
H26.013	Infantile and juvenile cortical, lamellar, or zonular cataract, bilateral
H26.031	Infantile and juvenile nuclear cataract, right eye
H26.032	Infantile and juvenile nuclear cataract, left eye
H26.033	Infantile and juvenile nuclear cataract, bilateral
H26.041	Anterior subcapsular polar infantile and juvenile cataract, right eye
H26.042	Anterior subcapsular polar infantile and juvenile cataract, left eye
H26.043	Anterior subcapsular polar infantile and juvenile cataract, bilateral
H26.051	Posterior subcapsular polar infantile and juvenile cataract, right eye
H26.052	Posterior subcapsular polar infantile and juvenile cataract, left eye
H26.053	Posterior subcapsular polar infantile and juvenile cataract, bilateral
H26.061	Combined forms of infantile and juvenile cataract, right eye
H26.062	Combined forms of infantile and juvenile cataract, left eye
H26.063	Combined forms of infantile and juvenile cataract, bilateral
H26.101	Unspecified traumatic cataract, right eye
H26.102	Unspecified traumatic cataract, left eye
H26.103	Unspecified traumatic cataract, bilateral

H26.111 Localized traumatic opacities, right eye
H26.112 Localized traumatic opacities, left eye
H26.113 Localized traumatic opacities, bilateral
H26.121 Partially resolved traumatic cataract, right eye
H26.122 Partially resolved traumatic cataract, left eye
H26.123 Partially resolved traumatic cataract, bilateral
H26.131 Total traumatic cataract, right eye
H26.132 Total traumatic cataract, left eye
H26.133 Total traumatic cataract, bilateral
H26.211 Cataract with neovascularization, right eye
H26.212 Cataract with neovascularization, left eye
H26.213 Cataract with neovascularization, bilateral
H26.221 Cataract secondary to ocular disorders (degenerative) (inflammatory), right eye
H26.222 Cataract secondary to ocular disorders (degenerative) (inflammatory), left eye
H26.223 Cataract secondary to ocular disorders (degenerative) (inflammatory), bilateral
H26.231 Glaucomatous flecks (subcapsular), right eye
H26.232 Glaucomatous flecks (subcapsular), left eye
H26.233 Glaucomatous flecks (subcapsular), bilateral
H26.31 Drug-induced cataract, right eye
H26.32 Drug-induced cataract, left eye
H26.33 Drug-induced cataract, bilateral
H26.40 Unspecified secondary cataract
H26.411 Soemmering's ring, right eye
H26.412 Soemmering's ring, left eye
H26.413 Soemmering's ring, bilateral
H26.491 Other secondary cataract, right eye
H26.492 Other secondary cataract, left eye
H26.493 Other secondary cataract, bilateral
H26.8 Other specified cataract
H26.9 Unspecified cataract
H40.001 Preglaucoma, unspecified, right eye
H40.002 Preglaucoma, unspecified, left eye
H40.003 Preglaucoma, unspecified, bilateral
H40.011 Open angle with borderline findings, low risk, right eye
H40.012 Open angle with borderline findings, low risk, left eye
H40.013 Open angle with borderline findings, low risk, bilateral
H40.021 Open angle with borderline findings, high risk, right eye
H40.022 Open angle with borderline findings, high risk, left eye
H40.023 Open angle with borderline findings, high risk, bilateral
H40.031 Anatomical narrow angle, right eye
H40.032 Anatomical narrow angle, left eye
H40.033 Anatomical narrow angle, bilateral
H40.041 Steroid responder, right eye
H40.042 Steroid responder, left eye
H40.043 Steroid responder, bilateral
H40.051 Ocular hypertension, right eye
H40.052 Ocular hypertension, left eye
H40.053 Ocular hypertension, bilateral
H40.061 Primary angle closure without glaucoma damage, right eye

H40.062 Primary angle closure without glaucoma damage, left eye
H40.063 Primary angle closure without glaucoma damage, bilateral
H40.10X0 Unspecified open-angle glaucoma, stage unspecified
H40.10X1 Unspecified open-angle glaucoma, mild stage
H40.10X2 Unspecified open-angle glaucoma, moderate stage
H40.10X3 Unspecified open-angle glaucoma, severe stage
H40.10X4 Unspecified open-angle glaucoma, indeterminate stage
H40.1110 Primary open-angle glaucoma, right eye, stage unspecified
H40.1111 Primary open-angle glaucoma, right eye, mild stage
H40.1112 Primary open-angle glaucoma, right eye, moderate stage
H40.1113 Primary open-angle glaucoma, right eye, severe stage
H40.1114 Primary open-angle glaucoma, right eye, indeterminate stage
H40.1120 Primary open-angle glaucoma, left eye, stage unspecified
H40.1121 Primary open-angle glaucoma, left eye, mild stage
H40.1122 Primary open-angle glaucoma, left eye, moderate stage
H40.1123 Primary open-angle glaucoma, left eye, severe stage
H40.1124 Primary open-angle glaucoma, left eye, indeterminate stage
H40.1130 Primary open-angle glaucoma, bilateral, stage unspecified
H40.1131 Primary open-angle glaucoma, bilateral, mild stage
H40.1132 Primary open-angle glaucoma, bilateral, moderate stage
H40.1133 Primary open-angle glaucoma, bilateral, severe stage
H40.1134 Primary open-angle glaucoma, bilateral, indeterminate stage
H40.1210 Low-tension glaucoma, right eye, stage unspecified
H40.1211 Low-tension glaucoma, right eye, mild stage
H40.1212 Low-tension glaucoma, right eye, moderate stage
H40.1213 Low-tension glaucoma, right eye, severe stage
H40.1214 Low-tension glaucoma, right eye, indeterminate stage
H40.1220 Low-tension glaucoma, left eye, stage unspecified
H40.1221 Low-tension glaucoma, left eye, mild stage
H40.1222 Low-tension glaucoma, left eye, moderate stage
H40.1223 Low-tension glaucoma, left eye, severe stage
H40.1224 Low-tension glaucoma, left eye, indeterminate stage
H40.1230 Low-tension glaucoma, bilateral, stage unspecified
H40.1231 Low-tension glaucoma, bilateral, mild stage
H40.1232 Low-tension glaucoma, bilateral, moderate stage
H40.1233 Low-tension glaucoma, bilateral, severe stage
H40.1234 Low-tension glaucoma, bilateral, indeterminate stage
H40.1310 Pigmentary glaucoma, right eye, stage unspecified
H40.1311 Pigmentary glaucoma, right eye, mild stage
H40.1312 Pigmentary glaucoma, right eye, moderate stage
H40.1313 Pigmentary glaucoma, right eye, severe stage
H40.1314 Pigmentary glaucoma, right eye, indeterminate stage
H40.1320 Pigmentary glaucoma, left eye, stage unspecified
H40.1321 Pigmentary glaucoma, left eye, mild stage
H40.1322 Pigmentary glaucoma, left eye, moderate stage
H40.1323 Pigmentary glaucoma, left eye, severe stage
H40.1324 Pigmentary glaucoma, left eye, indeterminate stage
H40.1330 Pigmentary glaucoma, bilateral, stage unspecified
H40.1331 Pigmentary glaucoma, bilateral, mild stage

H40.1332 Pigmentary glaucoma, bilateral, moderate stage
H40.1333 Pigmentary glaucoma, bilateral, severe stage
H40.1334 Pigmentary glaucoma, bilateral, indeterminate stage
H40.1410 Capsular glaucoma with pseudoexfoliation of lens, right eye, stage unspecified
H40.1411 Capsular glaucoma with pseudoexfoliation of lens, right eye, mild stage
H40.1412 Capsular glaucoma with pseudoexfoliation of lens, right eye, moderate stage
H40.1413 Capsular glaucoma with pseudoexfoliation of lens, right eye, severe stage
H40.1414 Capsular glaucoma with pseudoexfoliation of lens, right eye, indeterminate stage
H40.1420 Capsular glaucoma with pseudoexfoliation of lens, left eye, stage unspecified
H40.1421 Capsular glaucoma with pseudoexfoliation of lens, left eye, mild stage
H40.1422 Capsular glaucoma with pseudoexfoliation of lens, left eye, moderate stage
H40.1423 Capsular glaucoma with pseudoexfoliation of lens, left eye, severe stage
H40.1424 Capsular glaucoma with pseudoexfoliation of lens, left eye, indeterminate stage
H40.1430 Capsular glaucoma with pseudoexfoliation of lens, bilateral, stage unspecified
H40.1431 Capsular glaucoma with pseudoexfoliation of lens, bilateral, mild stage
H40.1432 Capsular glaucoma with pseudoexfoliation of lens, bilateral, moderate stage
H40.1433 Capsular glaucoma with pseudoexfoliation of lens, bilateral, severe stage
H40.1434 Capsular glaucoma with pseudoexfoliation of lens, bilateral, indeterminate stage
H40.151 Residual stage of open-angle glaucoma, right eye
H40.152 Residual stage of open-angle glaucoma, left eye
H40.153 Residual stage of open-angle glaucoma, bilateral
H40.20X0 Unspecified primary angle-closure glaucoma, stage unspecified
H40.20X1 Unspecified primary angle-closure glaucoma, mild stage
H40.20X2 Unspecified primary angle-closure glaucoma, moderate stage
H40.20X3 Unspecified primary angle-closure glaucoma, severe stage
H40.20X4 Unspecified primary angle-closure glaucoma, indeterminate stage
H40.211 Acute angle-closure glaucoma, right eye
H40.212 Acute angle-closure glaucoma, left eye
H40.213 Acute angle-closure glaucoma, bilateral
H40.2210 Chronic angle-closure glaucoma, right eye, stage unspecified
H40.2211 Chronic angle-closure glaucoma, right eye, mild stage
H40.2212 Chronic angle-closure glaucoma, right eye, moderate stage
H40.2213 Chronic angle-closure glaucoma, right eye, severe stage
H40.2214 Chronic angle-closure glaucoma, right eye, indeterminate stage
H40.2220 Chronic angle-closure glaucoma, left eye, stage unspecified
H40.2221 Chronic angle-closure glaucoma, left eye, mild stage
H40.2222 Chronic angle-closure glaucoma, left eye, moderate stage
H40.2223 Chronic angle-closure glaucoma, left eye, severe stage
H40.2224 Chronic angle-closure glaucoma, left eye, indeterminate stage
H40.2230 Chronic angle-closure glaucoma, bilateral, stage unspecified
H40.2231 Chronic angle-closure glaucoma, bilateral, mild stage
H40.2232 Chronic angle-closure glaucoma, bilateral, moderate stage
H40.2233 Chronic angle-closure glaucoma, bilateral, severe stage
H40.2234 Chronic angle-closure glaucoma, bilateral, indeterminate stage
H40.231 Intermittent angle-closure glaucoma, right eye
H40.232 Intermittent angle-closure glaucoma, left eye
H40.233 Intermittent angle-closure glaucoma, bilateral
H40.241 Residual stage of angle-closure glaucoma, right eye
H40.242 Residual stage of angle-closure glaucoma, left eye

H40.243 Residual stage of angle-closure glaucoma, bilateral
H40.31X0 Glaucoma secondary to eye trauma, right eye, stage unspecified
H40.31X1 Glaucoma secondary to eye trauma, right eye, mild stage
H40.31X2 Glaucoma secondary to eye trauma, right eye, moderate stage
H40.31X3 Glaucoma secondary to eye trauma, right eye, severe stage
H40.31X4 Glaucoma secondary to eye trauma, right eye, indeterminate stage
H40.32X0 Glaucoma secondary to eye trauma, left eye, stage unspecified
H40.32X1 Glaucoma secondary to eye trauma, left eye, mild stage
H40.32X2 Glaucoma secondary to eye trauma, left eye, moderate stage
H40.32X3 Glaucoma secondary to eye trauma, left eye, severe stage
H40.32X4 Glaucoma secondary to eye trauma, left eye, indeterminate stage
H40.33X0 Glaucoma secondary to eye trauma, bilateral, stage unspecified
H40.33X1 Glaucoma secondary to eye trauma, bilateral, mild stage
H40.33X2 Glaucoma secondary to eye trauma, bilateral, moderate stage
H40.33X3 Glaucoma secondary to eye trauma, bilateral, severe stage
H40.33X4 Glaucoma secondary to eye trauma, bilateral, indeterminate stage
H40.41X0 Glaucoma secondary to eye inflammation, right eye, stage unspecified
H40.41X1 Glaucoma secondary to eye inflammation, right eye, mild stage
H40.41X2 Glaucoma secondary to eye inflammation, right eye, moderate stage
H40.41X3 Glaucoma secondary to eye inflammation, right eye, severe stage
H40.41X4 Glaucoma secondary to eye inflammation, right eye, indeterminate stage
H40.42X0 Glaucoma secondary to eye inflammation, left eye, stage unspecified
H40.42X1 Glaucoma secondary to eye inflammation, left eye, mild stage
H40.42X2 Glaucoma secondary to eye inflammation, left eye, moderate stage
H40.42X3 Glaucoma secondary to eye inflammation, left eye, severe stage
H40.42X4 Glaucoma secondary to eye inflammation, left eye, indeterminate stage
H40.43X0 Glaucoma secondary to eye inflammation, bilateral, stage unspecified
H40.43X1 Glaucoma secondary to eye inflammation, bilateral, mild stage
H40.43X2 Glaucoma secondary to eye inflammation, bilateral, moderate stage
H40.43X3 Glaucoma secondary to eye inflammation, bilateral, severe stage
H40.43X4 Glaucoma secondary to eye inflammation, bilateral, indeterminate stage
H40.51X0 Glaucoma secondary to other eye disorders, right eye, stage unspecified
H40.51X1 Glaucoma secondary to other eye disorders, right eye, mild stage
H40.51X2 Glaucoma secondary to other eye disorders, right eye, moderate stage
H40.51X3 Glaucoma secondary to other eye disorders, right eye, severe stage
H40.51X4 Glaucoma secondary to other eye disorders, right eye, indeterminate stage
H40.52X0 Glaucoma secondary to other eye disorders, left eye, stage unspecified
H40.52X1 Glaucoma secondary to other eye disorders, left eye, mild stage
H40.52X2 Glaucoma secondary to other eye disorders, left eye, moderate stage
H40.52X3 Glaucoma secondary to other eye disorders, left eye, severe stage
H40.52X4 Glaucoma secondary to other eye disorders, left eye, indeterminate stage
H40.53X0 Glaucoma secondary to other eye disorders, bilateral, stage unspecified
H40.53X1 Glaucoma secondary to other eye disorders, bilateral, mild stage
H40.53X2 Glaucoma secondary to other eye disorders, bilateral, moderate stage
H40.53X3 Glaucoma secondary to other eye disorders, bilateral, severe stage
H40.53X4 Glaucoma secondary to other eye disorders, bilateral, indeterminate stage
H40.60X0 Glaucoma secondary to drugs, unspecified eye, stage unspecified
H40.60X1 Glaucoma secondary to drugs, unspecified eye, mild stage
H40.60X2 Glaucoma secondary to drugs, unspecified eye, moderate stage

H40.60X3	Glaucoma secondary to drugs, unspecified eye, severe stage
H40.60X4	Glaucoma secondary to drugs, unspecified eye, indeterminate stage
H40.61X0	Glaucoma secondary to drugs, right eye, stage unspecified
H40.61X1	Glaucoma secondary to drugs, right eye, mild stage
H40.61X2	Glaucoma secondary to drugs, right eye, moderate stage
H40.61X3	Glaucoma secondary to drugs, right eye, severe stage
H40.61X4	Glaucoma secondary to drugs, right eye, indeterminate stage
H40.62X0	Glaucoma secondary to drugs, left eye, stage unspecified
H40.62X1	Glaucoma secondary to drugs, left eye, mild stage
H40.62X2	Glaucoma secondary to drugs, left eye, moderate stage
H40.62X3	Glaucoma secondary to drugs, left eye, severe stage
H40.62X4	Glaucoma secondary to drugs, left eye, indeterminate stage
H40.63X0	Glaucoma secondary to drugs, bilateral, stage unspecified
H40.63X1	Glaucoma secondary to drugs, bilateral, mild stage
H40.63X2	Glaucoma secondary to drugs, bilateral, moderate stage
H40.63X3	Glaucoma secondary to drugs, bilateral, severe stage
H40.63X4	Glaucoma secondary to drugs, bilateral, indeterminate stage
H40.811	Glaucoma with increased episcleral venous pressure, right eye
H40.812	Glaucoma with increased episcleral venous pressure, left eye
H40.813	Glaucoma with increased episcleral venous pressure, bilateral
H40.821	Hypersecretion glaucoma, right eye
H40.822	Hypersecretion glaucoma, left eye
H40.823	Hypersecretion glaucoma, bilateral
H40.831	Aqueous misdirection, right eye
H40.832	Aqueous misdirection, left eye
H40.833	Aqueous misdirection, bilateral
H40.89	Other specified glaucoma
H42	Glaucoma in diseases classified elsewhere

REVISIONS

06-07-2013	Policy added to the bcbsks.com website.
01-30-2014	Updated Description section.
	In Policy section: ▪ Added new Item B, "Implantation of a single FDA-approved microstent in conjunction with cataract surgery may be considered medically necessary in patients who are intolerant of medications." ▪ Inserted in new Item D, " for all other conditions, including patients with glaucoma when intraocular pressure is adequately controlled by medication" to read "Use of microstent for all other conditions, including patients with glaucoma when intraocular pressure is adequately controlled by medication, is considered experimental / investigational."
	Updated Rationale section.
	In Coding section: ▪ Noted CPT code 0192T will be a deleted code, effective December 31, 2013 ▪ Added CPT code 66183 *(New code, effective January 1, 2014)* ▪ Added Diagnosis codes: 366.00-366.9 ▪ Added ICD-10 Diagnosis *(Effective October 1, 2014)*
	Updated Reference section.
01-01-2015	Policy posted to the website February 10, 2014.
	In Coding section:

	▪ Added CPT Codes: 66179, 66184, 0376T (Effective January 1, 2015) ▪ Added CPT Code: 66185 (coding correction) ▪ Revised CPT Codes: 66180, 0191T, 0253T (Effective January 1, 2015) ▪ Deleted CPT Codes: 66170, 66172 (not applicable to the policy)
12-28-2015	Updated Description section.
	In Policy section: ▪ In Item A, removed "The iStent shunt is FDA approved, only when used in conjunction with cataract surgery." ▪ In Item B, added "with mild to moderate open-angle glaucoma currently treated with ocular hypotensive medication" and removed "who are intolerant of medications" to read, "Implantation of a single FDA-approved microstent in conjunction with cataract surgery may be considered medically necessary in patients with mild to moderate open-angle glaucoma currently treated with ocular hypotensive medication." ▪ In Item D, removed ", including patients with glaucoma when intraocular pressure is adequately controlled by medication," to read, "Use of a microstent for all other conditions is considered experimental/investigational."
	Updated Rationale section.
	Updated References section.
04-27-2016	Updated Description section.
	Updated Rationale section.
	In Coding section: ▪ Coding bullets removed.
	Updated References section.
10-01-2016	In Coding section: ▪ Added ICD-10 codes: H40.1110, H40,1111, H40.1112, H40.1113, H40.1114, H40.1120, H40.1121, H40.1122, H40.1123, H40.1124, H40.1130, H40.1131, H40.1132, H40.1133, H40.1134 ▪ Removed ICD-10 codes: H40.11x0, H40.11x1, H40.11x2, H40.11x3, H40.11x4
11-09-2016	In Policy section: ▪ Moved previous Item C to become current Item B. ▪ In current Item C, removed "treated with ocular hypotensive medication" and added "requiring treatment" to read, "Implantation of a single FDA-approved microstent in conjunction with cataract surgery may be considered medically necessary in patients with mild to moderate open-angle glaucoma currently requiring treatment."
	In Coding section: ▪ Added CPT codes: 0449T, 0450T *(Effective January 1, 2017)*.
	Updated References section.
04-12-2017	Updated Description section.
	Updated Rationale section.
	Updated References section.
07-01-2017	In Coding section: ▪ Added CPT code: 0474T (Effective July 1, 2017).
04-24-2019	Updated Description section.
	Updated Rationale section.
	In Coding section: ▪ ICD-9 codes removed.
	Updated References section.
06-19-2019	Updated Description section.
05-28-2020	Updated Description Section
	Update Rationale Section
	In Policy section: Removed

	• Insertion of ab externo/ ab interno aqueous shunts approved by the U.S. Food and Drug Administration may be considered **medically necessary** as a method to reduce intraocular pressure in patients with glaucoma where medical therapy has failed to adequately control intraocular pressure. • Insertion of ab interno aqueous stents approved by the U.S. Food and Drug Administration as a method to reduce intraocular pressure in patients with glaucoma may be considered **medically necessary** as an adjunct or alternative to medical therapy to adequately control intraocular pressure. • Use of an ab interno/ ab interno aqueous shunt or stent for any condition not listed above all other conditions, including in patients with glaucoma when intraocular pressure is adequately controlled by medications, is considered **experimental / investigational**. • Implantation of 1 or 2 a single FDA-approved interno microstents in conjunction with cataract surgery may be considered **medically necessary** in patients with mild to moderate open-angle glaucoma currently requiring treatment. • Use of an interno/ ab interno microstents for any all other conditions not listed above is considered **experimental / investigational.** Replaced • In conjunction with cataract surgery, the implantation of 1 or 2 FDA approved ab interno stents may be considered **medically necessary** in patients with mild to moderate open-angle glaucoma currently receiving treatment • As a stand alone surgery, the insertion of FDA approved ab externo / ab interno aqueous shunts, including the Xen gel Stents, may be considered **medically necessary** as a method to reduce the intraocular pressure in patients with glaucoma where medical therapy has failed to adequately control intraocular pressure • Use of the ab external / ab interno aqueous shunts or stents for any other condition not listed above, is considered **experimental/ investigational**
	Updated coding sections: • Removed CPT/HCPS: 66179, 66180, 66183, 66184, 66185 • Removed ICD 10: E08.36, E09.36, E10.36, E11.36, E13.36, Q15.0
	Updated References section.
06-21-2021	Updated Description section.
	Updated Rationale section.
	In coding section: Added codes: 66179, 66180, 66183, 66184, 66185.
	Updated References section.
07-08-2021	In the policy section • Removed "currently receiving treatment" from Item A

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