

# Medical Policy



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## Title: Aqueous Shunts and Stents for Glaucoma

### **Professional**

Original Effective Date: January 1, 2012  
 Revision Date(s): June 7, 2013;  
 January 30, 2014; January 1, 2015;  
 December 28, 2015; April 27, 2016;  
 October 1, 2016; November 9, 2016;  
 April 12, 2017; July 1, 2017; April 24, 2019  
 Current Effective Date: November 9, 2016

### **Institutional**

Original Effective Date: January 1, 2012  
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Populations	Interventions	Comparators	Outcomes
Individuals: • With refractory open-angle glaucoma	Interventions of interest are: • 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 • Treatment-related morbidity

Populations	Interventions	Comparators	Outcomes
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 indications for glaucoma treatment other than cataract surgery or refractory open-angle glaucoma	Interventions of interest are: • Aqueous shunts or microstents	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 policy is to examine whether aqueous shunts or microstents improve health outcomes in individuals with open-angle glaucoma.

## **BACKGROUND**

### **Glaucoma**

Glaucoma is characterized by elevated intraocular pressure, 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's canal), drains into collector channels, and then into the aqueous veins. Increases in resistance in the trabecular meshwork and/or the inner wall of Schlemm's 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 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, 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 (eg, leaks or bleb-related endophthalmitis) and long-term failure. Other surgical procedures (not addressed in this policy) include trabecular laser ablation, deep sclerectomy, which removes the outer wall of Schlemm’s canal and excises deep sclera and peripheral cornea, and viscocanalostomy, which unroofs and dilates Schlemm’s 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 (eg, <15 mm Hg) and are not indicated for patients for whom very low IOP is desired (eg, 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 is 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 one 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 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) aqueous shunts were cleared for marketing by the U.S. Food and Drug Administration (FDA) through the 510(k) process between 1989 and 1993; modified Ahmed and Molteno devices were cleared in 2006. Their indication for use is "in patients with intractable glaucoma to reduce intraocular pressure where medical and conventional surgical treatments have failed." The AquaFlow™ Collagen Glaucoma Drainage Device was approved by FDA through the premarket approval (PMA) process for the maintenance of the subsclearal space following nonpenetrating deep sclerectomy. The EX-PRESS® Mini Glaucoma Shunt was cleared for marketing by FDA through the 510(k) process in 2003. 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 FDA through the 510(k) process as an aqueous shunt for management of refractory glaucoma. The approval was for patients with refractor glaucoma who failed previous surgical treatment or for patients with primary open-angle glaucoma unresponsive to maximum tolerated medical therapy. 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 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 labeling describes the following precautions<sup>1</sup>:

1. "The safety and effectiveness of the iStent® Trabecular Micro-Bypass Stent has not been established as an alternative to the primary treatment of glaucoma with medications. The effectiveness of this device has been demonstrated only in patients with mild-to-moderate open-angle glaucoma who are undergoing concurrent cataract surgery for visually significant cataract.
2. The safety and effectiveness of the iStent® Trabecular Micro-Bypass Stent has not been established in patients with the following circumstances or conditions, which were not studied in the pivotal trial:
  - In children
  - In eyes with significant prior trauma
  - In eyes with abnormal anterior segment
  - In eyes with chronic inflammation
  - In glaucoma associated with vascular disorders
  - In pseudophakic patients with glaucoma
  - In uveitic glaucoma
  - In eyes with prior incisional glaucoma surgery or cilioablative procedures
  - In eyes with prior laser trabeculoplasty with selective LT within 90 days prior to screening or prior to argon laser trabeculectomy at any time
  - In patients with medicated IOP greater than 24 mmHg
  - In patients with unmedicated IOP less than 21 mmHg nor greater than 36 mmHg after 'washout' of medications
  - For implantation of more or less than two stents
  - After complications during cataract surgery, including but not limited to, severe corneal burn, vitreous removal/vitreotomy required, corneal injuries, or complications requiring the placement of an anterior chamber IOL [intraocular lens]
  - When implantation has been without concomitant cataract surgery with IOL implantation for visually significant cataract
  - In patients with pseudoexfoliative glaucoma or pigmentary glaucoma, or in patients with other secondary open-angle glaucoma.

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 five-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.<sup>2</sup>

**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	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
CyPass®	Alcon	Suprachoroidal stent	PMA	2016
Hydrus™	Ivantis	Microstent	Not approved	
SOLX® Gold	SOLX	Micro-Shunt	Not approved	
iStent <i>supra</i> ®	Glaukos	Suprachoroidal stent	Not approved; in clinical trial	

FDA: Food and Drug Administration; PMA: premarket approval

FDA product codes: OGO, KYF.

## **POLICY**

- A. Insertion of aqueous shunts approved by the U.S. Food and Drug Administration (FDA) 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.
- B. Use of an aqueous shunt for all other conditions, including in patients with glaucoma when intraocular pressure is adequately controlled by medications, is considered **experimental / investigational**.
- C. 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.
- D. Use of a microstent for all other conditions 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**

The policy was updated with a literature review using MEDLINE; most recently through January 22, 2019.

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 a technology, two 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 PICOTS were 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 OAG 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 change in intraocular pressure (IOP) and change in medication use.

### Timing

Changes in IOP and medication use are measured for at least 12 months. Safety measures involve longer follow-up, for several years.

### Setting

Insertion of aqueous shunts and stents are performed in tertiary care centers.

### Study Selection Criteria

Methodologically credible studies were selected using the following principles:

- a. To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
- b. In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.
- c. To assess long-term outcomes and adverse effects, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.
- d. Studies with duplicative or overlapping populations were excluded.

## **AbExterno Aqueous Shunts**

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

### 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.<sup>3</sup> Trabeculectomy was found to lower mean IOP by 3.8 mm Hg more than the Ahmed shunt at one 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 one 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).<sup>4</sup> It indicated that IOP would generally settle at higher levels ( $\gg$ 18 mm Hg) with aqueous shunts than with standard trabeculectomy (14-16 mm Hg) or trabeculectomy with antifibrotic agents 5-fluorouacil 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.

A comparative effectiveness review on glaucoma treatments, prepared for the Agency for Healthcare Research and Quality by Boland et al (2012), found that available data on the role of aqueous drainage devices in OAG (primary studies, systematic review) were inadequate to permit conclusions on the comparative effectiveness of these treatments vs laser and other surgical treatments.<sup>5</sup>

### **Baerveldt Glaucoma Shunt**

#### Randomized Controlled Trials

Early results from the open-label, multicenter, randomized Tube Versus Trabeculectomy study were reviewed in the American Academy of Ophthalmology (2008) technology assessment and by Gedde et al (2012) who reported on the 5-year follow-up to Tube Versus Trabeculectomy.<sup>4,5,6</sup> 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 vision-related quality of life outcomes in the Tube Versus Trabeculectomy study.<sup>7</sup> 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 two 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.<sup>8</sup> 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). 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 (eg, 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 (see Table 2).<sup>9</sup> Five-year follow-up was reported by de Jong et al (2011).<sup>10</sup> 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 five 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) (see Table 2).<sup>11</sup> Comparator groups were similar at baseline. Throughout a two-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 one month after EX-PRESS implantation (median, 0.7 months) and at three 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),<sup>12</sup> presenting 1-year results, and by Gonzalez-Rodriguez et al (2016), presenting 3-year results (see Table 2).<sup>13</sup> 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 (see Table 3).

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

Study	Countries	Sites	Dates	Participants	Interventions	
					Active	Comparator
de Jong et al (2009) <sup>9</sup> ; de Jong et al (2011) <sup>10</sup> .	Netherlands	1	2003-2004	Patients with primary OAG not controlled by IOP medication	EX-PRESS (n=39)	Trabeculectomy (n=39)
Netland et al (2014) <sup>11</sup> .	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) <sup>12</sup> ; Gonzalez-Rodriguez et al(2016) <sup>13</sup> .	Canada	1	2011-2012	Patients with primary 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) <sup>9</sup> ; de Jong et al (2011) <sup>10</sup>					
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) <sup>11</sup>					
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) <sup>12</sup> ; Gonzalez-Rodriguez et al (2016) <sup>13</sup>					
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.

### Observational Studies

Dib Bustros et al (2017) published a retrospective chart review that offered 1-year results from 56 African American patients who underwent EX-PRESS (n=28) implantation or trabeculectomy (n=28).<sup>14</sup> Outcomes included IOP and glaucoma medication used presurgery, postsurgery, and at 12-months of follow-up. In both groups, IOP and glaucoma-related medication use dropped significantly. Postoperative and follow-up interventions included 5-fluorouracil injections and laser suture lysis. Patients who underwent trabeculectomy needed a significantly greater number of laser suture lysis and 5-fluorouracil interventions in the 3 months after surgery (trabeculectomy: 3.89; EX-PRESS: 2.36, p=0.007). The results showed that EX-PRESS was noninferior to trabeculectomy in reducing IOP and reducing the need for glaucoma-related medications.

Omatsu et al (2018) compared changes in corneal endothelial cells among patients undergoing trabeculectomy (n=60) and patients receiving EX-PRESS shunts (n=50).<sup>15</sup> Both groups experienced significant decreases in IOP compared with baseline. After two years of follow-up, patients undergoing trabeculectomy experienced significant decreases in corneal endothelial cells compared with baseline, while the EX-PRESS group did not.

### Comparative Effectiveness Analyses

Five-year results of two 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 FP7 and Baerveldt Glaucoma Implant BG 101-350 (1:1 ratio) in 276 adults with previous incisional eye surgery or refractory glaucoma.<sup>16,17</sup> The ABC was funded by National Eye Institute, Research to Prevent Blindness, and New World Medical. Mean IOP was 14.7 mm Hg in the Ahmed group and 12.7 mm Hg in the Baerveldt group at 5 years (p=0.01). The number of glaucoma medications in use at five years, the cumulative probability of failure at five years, and visual acuity at five years did not differ statistically between the two groups. The number of patients with inadequately controlled IOP or reoperation for glaucoma was 46 (80%) with the Ahmed shunt and 25 (53%) with the Baerveldt

shunt ( $p=0.003$ ). The 5-year cumulative reoperation rate for glaucoma was 21% in the Ahmed group and 9% in the Baerveldt group ( $p=0.01$ ).<sup>16</sup> Late complications were defined as those developing after three months. Such complications occurred in 56 (47%) patients in the Ahmed group and 67 (56%) patients in the Baerveldt group during 5 years of follow-up ( $p=0.08$ ). The cumulative incidences of serious complications at 5 years were 16% and 25% in the Ahmed and Baerveldt groups, respectively ( $p=0.03$ ).<sup>17</sup>

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.<sup>18</sup> AVB is funded by the Glaucoma Research Society of Canada. Patients were randomized in a 1:1 ratio to the Ahmed FP7 implant and the Baerveldt 350 implant. Failure of the shunt implant was the primary outcome, defined as any one of the following: IOP of less than 5 mm Hg or greater than 18 mm Hg or a reduction of less than 20% from baseline for 2 consecutive visits after 3 months; de novo glaucoma surgery required; removal of the implant; severe vision loss related to the surgery; or progression to no light perception for any reason. The cumulative failure rate was 53% in the Ahmed group and 40% in the Baerveldt group at 5 years ( $p=0.04$ ). In the Ahmed and Baerveldt shunts, the mean percent reduction in IOP was 47% and 57% ( $p=0.001$ ) and mean percent reduction in medication use was 44% and 61% ( $p=0.03$ ), all respectively. Hypotony was reported in 5 (4%) patients in the Baerveldt group but not in the Ahmed group ( $p=0.02$ ).

Christakis et al (2017) analyzed 5-year pooled data from the ABC and AVB trials comparing the relative efficacy of the 2 implants.<sup>19</sup> Patients were randomized to an Ahmed implant ( $n=267$ ) or a Baerveldt implant ( $n=247$ ). IOP, glaucoma medication use and visual acuity were compared. 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%;  $p=.002$ ).

A small RCT by Bo et al (2018) randomizing 68 patients compared the EX-PRESS shunt ( $n=33$ ) and the Ahmed shunt ( $n=35$ ).<sup>20</sup> Follow-up at nine months showed no difference in best-corrected visual acuity or in postoperative complications. Control of IOP was superior in EX-PRESS compared with the Ahmed shunt.

#### *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 one to five years. Results showed that ab externo aqueous shunts are noninferior to trabeculectomy. Adverse event rates were higher among patients undergoing trabeculectomy.

The comparative effectiveness of two ab externo devices (the Ahmed and Baerveldt shunts) has been evaluated in two 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. Evidence for stents not approved as stand-alone procedures is discussed in the Appendix.

### **Xen Glaucoma Treatment System**

#### Observational Studies

##### Comparative Studies

Schlenker et al (2017) published a multicenter, retrospective interventional cohort 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).<sup>21</sup> 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 two consecutive IOP readings of less than 6 mm Hg, including vision loss. Success was measured by the withdrawal of glaucoma-related medications at one 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 (see Table 4).<sup>22</sup> 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).

Grover et al (2017) published results from the single-arm, open-label clinical study evaluating the effectiveness and safety of the XEN Glaucoma Treatment System in 65 patients with refractory glaucoma (see Table 4).<sup>22</sup> Effectiveness data were collected for 12 months and safety data for 18 months. Forty-six (75%) patients of 61 with available data had a 12-month mean diurnal IOP reduction of 20% or more without increasing IOP-lowering medications. The mean IOP reduction

at 12 months was -9.1 mm Hg (95% CI, -10.7 to -7.5 mm Hg) on a mean of 1.7 medications (see Table 5). Efficacy was consistent across age groups, baseline IOP, baseline medication use, sex, and ethnicity. The most common adverse events were glaucoma surgery, hypotony, IOP increase of 10 mm Hg or more, and needling procedures. The FDA cited results from this study to conclude that the XEN System was as safe and effective as predicate devices.

Hengerer et al (2017) retrospectively analyzed 146 patients (242 eyes) receiving the XEN implant for treatment-refractory to antiglaucoma medication or glaucoma surgery (see Table 4).<sup>23</sup> 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.

Additional smaller case series assessing the use of the XEN implant are described in Tables 4 and 5. These case series, by Galal et al (2017),<sup>24</sup> Ozal et al (2017),<sup>25</sup> and Tan et al (2018),<sup>26</sup> reported significant reductions in IOP and medication use. Low rates of the following complications were reported: hypotony (which resolved), need for bleb intervention, iris tissue obstruction, implant extrusion, and choroidal detachment.

**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) <sup>21</sup>	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	<ul style="list-style-type: none"> <li>· XEN alone (n=185)</li> <li>· Trabeculectomy (n=169)</li> </ul>	Up to 30 mo (last visit in chart)
Mansouri et al (2018) <sup>27</sup>	Switzerland	Patients with OAG and uncontrolled IOP, progressive glaucoma, and/or refractory to IOP medications	<ul style="list-style-type: none"> <li>· XEN alone (n=40)</li> <li>· XEN plus cataract surgery (n=109)</li> </ul>	12 mo
Grover et al (2017) <sup>22</sup>	U.S.	Patients with OAG and uncontrolled IOP, refractory to IOP medications	<ul style="list-style-type: none"> <li>· XEN alone, (N=65)</li> </ul>	12 mo
Hengerer et al (2017) <sup>23</sup>	Germany	Patients with OAG and uncontrolled IOP, optic disc damage, and refractory to IOP medications or prior surgery	<ul style="list-style-type: none"> <li>· XEN alone (n=203)</li> <li>· XEN plus cataract surgery (n=39)</li> </ul>	12 mo
Galal et al (2017) <sup>24</sup>	Germany	Patients with OAG	<ul style="list-style-type: none"> <li>· XEN alone (n=3)</li> <li>· XEN plus cataract surgery (n=10)</li> <li>· Both groups also received subconjunctival mitomycin-C</li> </ul>	12 mo
Ozal et al (2017) <sup>25</sup>	Turkey	Patients with OAG and uncontrolled IOP, progressive glaucoma, and/or refractory to IOP medications or prior surgery	<ul style="list-style-type: none"> <li>· XEN alone (n=9)</li> <li>· XEN plus cataract surgery (n=6)</li> </ul>	12 mo
Tan et al (2018) <sup>26</sup>	U.K.	Patients with OAG and taking at least 1 IOP-lowering medication	<ul style="list-style-type: none"> <li>· XEN alone (N=39)</li> </ul>	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 <sup>a</sup>	Baseline	1 Year <sup>a</sup>
Schlenker et al (2017) <sup>21</sup> ,	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) <sup>27</sup> ,	XEN alone	20 (IQR: 17 to 23)	40.0% reduction	2.5 (IQR: 1 to 4)	NR
Grover et al (2017) <sup>22</sup> ,	XEN alone	25.1 (3.7)	15.9 (5.2)	3.5	1.7
Hengerer et al (2017) <sup>23</sup> ,	XEN alone	31.5 (8.4)	14.3 (4.2)	3.1 (1.0)	0.3 (0.7)
Galal et al (2017) <sup>24</sup> ,	All patients	16 (4)	12 (3)	1.9 (1)	0.3 (0.5)
Ozal et al (2017) <sup>25</sup> ,	All patients	36.1	16.7	3.6 (0.5)	0.3 (0.9)
Tan et al (2018) <sup>26</sup> ,	XEN alone	24.9 (7.8)	14.5 (3.4)	3	0.7

<sup>a</sup> 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 several single-arm studies. The comparative study included patients with different types of glaucoma (57% with OAG) 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 with Cataract Surgery

Several stents have the FDA approval for use in conjunction with cataract surgery and are discussed below. The iStent inject device is preloaded with two stents. An additional stent, the CyPass, had the FDA approval but has been 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.

Agrawal et al (2018) conducted a systematic review of Micro-Invasive Glaucoma Surgery in conjunction with cataract surgery compared to cataract surgery alone for patients with primary OAG.<sup>28</sup> The literature search identified nine RCTs (seven using the iStent, one using Hydrus, and one using Cypass). The RCTs were assessed for risk of bias, with all studies considered low-risk for selection, performance, and detection biases. Eight of the nine trials were

also considered low-risk for attrition and reporting biases. No meta-analyses were conducted. Key RCTs are discussed in detail below.

## **iStent**

### Randomized Controlled Trials with One iStent

Results from the iStent U.S. investigational device exemption, open-label, 29-site, multicenter RCT 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 6).<sup>30,31</sup> Trial objectives were to compare the incremental effect on IOP of iStent implantation with that of cataract surgery alone and to determine the potential benefit of combining two therapeutic treatments into a single surgical event. A total of 240 patients (mean age, 73 years) with cataracts and mild-to-moderate OAG (IOP  $\leq$ 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 if unmedicated IOP was between 22 mm and 36 mm Hg. 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. Of the 117 subjects randomized to iStent implantation, 111 underwent cataract surgery with stent implantation, and 106 (91%) completed the 12-month postoperative visit. Of the 123 subjects randomized to cataract surgery only, 117 underwent cataract surgery, and 3 exited the trial because of surgical complications. Of the remaining 114 subjects, 112 (91%) completed the 12-month visit. The proportion of eyes meeting both the primary (unmedicated IOP  $\leq$ 21 mm Hg) and secondary outcomes (IOP reduction  $\geq$ 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 (eg, 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 one year (see Table 7).

At 2-year follow-up, 199 (83%) patients remained in the study. The primary endpoint (unmedicated IOP  $\leq$ 21 mm Hg) was reached by 61% of patients in the treatment group and 50% of controls ( $p = 0.036$ ).<sup>29</sup> Secondary outcomes<sup>3/4</sup>IOP reduction of 20% or more without medication (53% vs 44%) and mean number of medications used (0.3 vs 0.5)<sup>3/4</sup>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. Study results suggested that microstent treatment in this specific group likely improved outcomes at one year compared with cataract surgery alone; however, two-year results make it difficult to conclude with certainty that health outcomes improved (see Table 7).

Fea et al (2010) reported on a randomized, double-blind, trial of 36 cataract surgery patients who did or did not receive an iStent implantation (2:1 ratio) (see Table 6).<sup>32</sup> Inclusion criteria were a previous diagnosis of primary OAG with an IOP above 18 mm Hg at 3 separate visits and taking 1 or more hypotensive medications. Investigators were masked to the treatment condition and conducted follow-up at 24 hours, 1 week, and 1, 2, 3, 6, 9, 12, and 15 months. Prescription of hypotensive medications was performed according to preset guidelines. Primary outcomes were IOP and reduction in medication use over 15 months and IOP after a 1-month washout of ocular hypotensive agents (16 months postoperatively). Mean IOP at 15 months decreased in both

treatment groups (see Table 7). Eight (67%) of 12 patients in the stent group and 5 (24%) of 21 in the control group did not require ocular hypotensive medication. Because treatment compliance is an ongoing concern for most ophthalmologists, trialists sought to keep patients as medication free as possible postoperatively. Patients in the stent group had significantly lower medication use than patients in the cataract alone group. After washout of medications, mean IOP was 16.6 mm Hg in the stent group and 19.2 mm Hg in the control group. No adverse events related to stent implantation were reported. Four-year follow-up from this study was published by Fea et al (2015).<sup>30</sup> Twenty-four of 36 patients were available at 4 years. Differences between treatment groups remained statistically nonsignificant (mean IOP, 15.9 mm Hg in the stent group vs 17 mm Hg in the control group).

**Table 6.** Summary of Key RCT Characteristics for the iStent

Study	Countries	Sites	Dates	Participants	Interventions	
					Active	Comparator
Samuelson et al (2011) <sup>31</sup> ; Craven et al (2012) <sup>29</sup>	U.S.	29	2005-2007	Patients with mild-to-moderate OAG, IOP $\geq$ 22 and $\leq$ 36 mm Hg	iStent plus cataract (n=116)	Cataract alone (n=123)
Fea et al (2010) <sup>32</sup> ; Fea et al (2015) <sup>30</sup>	Italy	1	NR	Patients with primary OAG	iStent plus cataract (n=24)	Cataract alone (n=12)

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

**Table 7.** Summary of Key RCT Results for the iStent

Study	Mean IOP (SD), mm Hg		p	Mean Medication Use (SD)		p
	iStent	Cataract Alone		iStent	Cataract Alone	
Samuelson et al (2011) <sup>31</sup> ; Craven et al (2012) <sup>29</sup>						
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)	
Fea et al (2010) <sup>32</sup> ; Fea et al (2015) <sup>30</sup>						
Baseline	17.9 (2.6)	17.3 (3.0)	0.51	1.9 (0.9)	1.8 (0.7)	NS
Month 15	14.8 (1.2)	15.7 (1.1)	0.03	0.4 (0.7)	1.3 (1.0)	0.007
Year 4	17.5 (2.3)	20.4 (3.2)	0.02	0.5 (0.8)	0.9 (1.0)	

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

### Observational Studies with One iStent

Kurji et al (2017) reported on 2 surgical methods, phaco-trabectome and phaco-iStent, to control IOP in patients with OAG undergoing cataract surgery.<sup>33</sup> Fifty-five patients (70 eyes) were analyzed in this retrospective comparative case series, 36 receiving phaco-trabectome and 34 receiving phaco-iStent. Outcomes included IOP reduction, glaucoma medication reduction, patients' safety profile, and best-corrected visual acuity. At baseline, the mean IOP of patients in the phaco-trabectome group (30 patients [36 eyes], 20.92 mm Hg) was higher than those in the phaco-iStent group (25 patients [34 eyes], 17.47 mm Hg;  $p=0.026$ ). At 12-month follow-up, both groups experienced significant reductions in IOP; however, there was no statistically

significant difference between groups (phaco-trabectome, -5.09 mm Hg 24% relative reduction vs Phaco-iStent, -3.84 mm Hg, 22% relative reduction;  $p=0.331$ ). Glaucoma medication usage did not decrease significantly from baseline to 12 months in either group; moreover, there was no significant difference in reduction between the groups. Phaco-iStent patients had fewer individual complications.

Ferguson et al (2018) reported on a series of 59 patients with severe primary OAG who were implanted with 1 trabecular micro-bypass stent (iStent) during cataract surgery.<sup>34</sup> Patients were followed for two years. IOP at baseline was 19.3 mm Hg at baseline, decreasing significantly to 14.4 mm Hg at 12 months and 14.9 mm Hg at 24 months ( $p<0.01$ ). Mean number of glaucoma medications also decreased, from 2.3 at baseline to 1.6 at 24 months.

#### Randomized Controlled Trials with Two iStents

Fernández-Barrientos et al (2010) randomized 33 patients with OAG or ocular hypertension to 2 iStent devices plus cataract surgery or cataract surgery alone.<sup>35</sup> The study was performed at a single-center in Spain. Eligible eyes had a medicated IOP between 17 mm and 31 mm Hg (exclusive) and between 21 mm and 35 mm Hg after medication washout. Mean IOP reduction was greater in the iStent plus surgery group (6.6 mm Hg) than in the surgery alone group (3.9 mm Hg;  $p=0.002$ ). The mean number of IOP-lowering medications was also significantly lower in the iStent group (0.0 vs 0.7, respectively;  $p=0.007$ ).

#### Observational Studies with Two iStents

Use of multiple iStent devices with cataract surgery was reported in an open-label, prospective series of 53 eyes (47 patients) by Belovay et al (2012).<sup>36</sup> Twenty-eight of 53 eyes were implanted with 2 stents and 25 with 3 stents, based on the need for greater IOP control, as determined by the operating surgeon. Best-corrected visual acuity improved or remained stable in 89% of eyes. IOP decreased from a mean of 18.0 to 14.3 mm Hg, and the number of hypotensive medications decreased from a mean of 2.7 to 0.7 at 1 year postoperatively. Target IOP was reached in 77% of eyes, while 59% of patients discontinued all medications for the study eye. At one year, the mean number of hypotensive medications decreased to 1.0 in the 2-stent group and 0.4 in the 3-stent group. Medication use ceased in 46% of eyes in the 2-stent group and 72% in the 3-stent group. Stent blockage occurred in the early postoperative period in 15% of eyes and was successfully treated with laser.

Donnenfeld et al (2015) published a prospective case series enrolling 39 patients with OAG and IOP between 18 and 30 mm Hg.<sup>37</sup> Each patient received two microstents and medications as needed, and was followed for three years. At trial completion, the mean reduction in IOP was 9.1 mm Hg (95% CI, 8.0 to 10.1 mm Hg). There was one postoperative complication (hyphema), which resolved without further intervention.

Vlasov et al (2017) conducted a retrospective chart review of patients with OAG receiving either 1 iStent ( $n=39$ ) or 2 iStents ( $n=30$ ) during cataract surgery.<sup>38</sup> Both groups experienced statistically significant reductions in IOP, and there was no significant difference between them in IOP reduction. Only the group receiving two iStents experienced a statistically significant reduction in medication use.

## Hydrus Microstent

### 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 8).<sup>39</sup> 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 mean number of medications used are presented in Table 9.

Samuelson et al (2019) reported on a multicenter RCT comparing implantation of a single Hydrus Microstent following cataract surgery vs cataract surgery alone (Table 8).<sup>40</sup> Patients were blinded 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 mean number of medications used) are presented in Table 9.

**Table 8.** Summary of Key RCT Characteristics for the Hydrus Microstent

Study	Countries	Sites	Dates	Participants	Interventions	Comparator
Pfeiffer (2015) <sup>39</sup>	Germany, Italy, Spain, the Netherlands	7	2011 to 2012	Patients with concurrent open-angle glaucoma and cataract	Active Cataract surgery plus Hydrus Microstent implantation (n=50)	Cataract surgery alone (n=50)
Samuelson (2019) <sup>40</sup>	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 9.** 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) <sup>39</sup>						
Baseline	26.3 +/- 4.4	26.6 +/- 4.2	0.7	2.0 +/- 1.0	2.0 +/- 1.1	0.8
Year 2 change	16.9 +/- 3.3	19.2 +/- 4.7	0.009	0.5 +/- 1.0	1.0 +/- 1.0	0.02
Samuelson (2019) <sup>40</sup>						
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.<sup>41</sup> 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). Mean number of

medications was 2.1 at baseline, decreasing significantly by six months to 0.5, which was maintained through two years of follow-up (0.7).

## Xen Glaucoma Treatment System

### Observational Studies

Mansouri et al (2018)<sup>27</sup>, Hengerer et al (2017)<sup>23</sup>, Galal et al (2017)<sup>24</sup>, and Ozal et al (2017)<sup>25</sup>, are described above in the section on aqueous shunts 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 10 and 11.

Additional single-arm studies (Perez-Torregrosa et al [2016]<sup>42</sup>, and De Gregorio et al [2017]<sup>43</sup>,) evaluating the use of the XEN implant in conjunction with cataract surgery are also described in Tables 10 and 11 below.

**Table 10.** Summary of Key Case Series Characteristics for the XEN Implant with Cataract Surgery

Study	Country	Participants	Treatment Delivery	FU
Mansouri et al (2018) <sup>27</sup> ,	Switzerland	Patients with OAG and uncontrolled IOP, progressive glaucoma, and/or refractory to IOP medications	<ul style="list-style-type: none"> <li>• XEN alone (n=40)</li> <li>• XEN plus cataract surgery (n=109)</li> </ul>	12 mo
Hengerer et al (2017) <sup>23</sup> ,	Germany	Patients with OAG and uncontrolled IOP, optic disc damage, and refractory to IOP medications or prior surgery	<ul style="list-style-type: none"> <li>• XEN alone (n=203)</li> <li>• XEN plus cataract surgery (n=39)</li> </ul>	12 mo
Perez-Torregrosa et al (2016) <sup>42</sup> ,	Spain	Patients with OAG and cataract and taking at least 2 IOP-lowering medications	<ul style="list-style-type: none"> <li>• XEN plus cataract (n=30)</li> </ul>	12 mo
De Gregorio et al (2017) <sup>26</sup> ,	Italy	Patients with OAG under maximally tolerated medical therapy and with cataract	<ul style="list-style-type: none"> <li>• XEN plus cataract (n=41)</li> </ul>	12 mo
Galal et al (2017) <sup>24</sup> ,	Germany	Patients with OAG	<ul style="list-style-type: none"> <li>• XEN alone (n=3)</li> <li>• XEN plus cataract surgery (n=10)</li> <li>• Both groups also received subconjunctival mitomycin-C</li> </ul>	12 mo
Ozal et al (2017) <sup>25</sup> ,	Turkey	Patients with OAG and uncontrolled IOP, progressive glaucoma, and/or refractory to IOP medications or prior surgery	<ul style="list-style-type: none"> <li>• XEN alone (n=9)</li> <li>• XEN plus cataract surgery (n=6)</li> </ul>	12 mo

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

**Table 11.** Summary of Key Case Series 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) <sup>27</sup> ,	XEN + cataract	18 (IQR: 14 to 23)	22.9% reduction	2 (IQR: 1 to 3)	NR
Hengerer et al (2017) <sup>23</sup> ,	XEN + cataract	35.7 (12)	13.9 (2.5)	3.3 (1.0)	0.4 (0.7)
Perez-Torregrosa et al (2016) <sup>42</sup> ,	XEN + cataract	21.2 (3.4)	8.1 (3.0)	3.1	0.2 (0.7)
De Gregorio et al (2017) <sup>43</sup> ,	XEN + cataract	22.5 (3.7)	13.1 (2.4)	2.6 (0.9)	0.4 (0.8)
Galal et al (2017) <sup>24</sup> ,	All patients	16 (4)	12 (3)	1.9 (1)	0.3 (0.5)
Ozal et al (2017) <sup>25</sup> ,	All patients	36.1	16.7	3.6 (0.5)	0.3 (0.9)

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

## **CyPass**

### Randomized Controlled Trials

The FDA evaluated the clinical performance of the CyPass Micro-Stent system based on the pivotal 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. Vold et al (2016) published the 2-year results.<sup>44</sup> A total of 505 patients (1 eye per patient) were assigned in a 1:3 ratio to phacoemulsification only (control) or supraciliary micro stenting with phacoemulsification (microstent). Baseline mean IOPs and number of IOP-lowering medications were similar in both treatment groups (»24.4 mm Hg and 1.4 medications, respectively). In the intention-to-treat analysis, 58% of controls vs 73% of microstent patients achieved 20% or greater unmedicated IOP-lowering at 24 months compared with baseline ( $p=0.002$ ). The difference in mean IOP reduction at 24 months was 1.8 mm Hg (95% CI, 1.0 to 2.6 mm Hg;  $p<0.001$ ), favoring the microstent group. In the control group, 59% were medication free at 24 months vs 85% in the microstent group. Mean medication use decreased to 0.6 drugs at 24 months in the control group and to 0.2 drugs in the microstent group ( $p<0.001$ ). There were no vision-threatening microstent-related adverse events. Thirty-nine percent of microstent patients vs 36% of control patients experienced ocular adverse events in the 24-month period. The following ocular adverse events were reported: hypotony (3% microstent vs 0% control), maculopathy (1.3% microstent vs 0.8% control), corneal edema (4% microstent vs 2% control), cyclodialysis cleft greater than 2 mm in circumference (2% microstent vs 0% control), iritis (9% microstent vs 4% control), and subconjunctival hemorrhage (2% microstent vs 1% control). Best-corrected visual acuity was 20/40 or better in more than 98% of all patients. Eleven patients in the microstent group and 1 patient in the control group died during the 24-month period; however, the deaths were classified as unrelated to the intervention.

### *Section Summary: Aqueous Microstents with Cataract Surgery*

Currently, the FDA has approved several stents for the treatment of patients with mild-to-moderate OAG considering cataract surgery. Several RCTs and single-arm studies have compared cataract surgery alone with stent implantation in conjunction with cataract surgery. When compared to cataract surgery alone, a majority of the studies showed significant decreases in IOP and medication use when stents were implanted in conjunction with the cataract surgery.

Evidence from an RCT supported the use of the CyPass stent in conjunction with cataract surgery; however, in August 2018, the manufacturer of CyPass voluntarily withdrew CyPass 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.

## **Other Indications for Glaucoma Treatment**

Glaucoma shunts and microstent have also been studied in patients for indications other than cataract surgery or refractory OAG. The following section describes implantation of more than two stents. The use of shunts and stents for procedures that are not FDA approved are discussed in the Appendix.

## **Greater than two Stents**

### Randomized Controlled Trial

An RCT comparing the efficacy of 1 iStent with multiple iStent devices was published by Katz et al (2015).<sup>45</sup> 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 main outcome was IOP at 12 months. The primary endpoint was the percentage of patients with a reduction of 20% or more in IOP off medications. This endpoint was reached by 89.2% (95% CI, 74.6% to 97.0%) of the 1-stent group, by 90.2% (95% CI, 76.9% to 97.3%) of the 2-stent group, and by 92.1% (95% CI, 78.6% to 98.3%) of the 3-stent group. The secondary endpoint (percentage of patients achieving an IOP  $\leq$  15 mm Hg off medication) was reached by 64.9% (95% CI, 47.5% to 79.8%) of the 1-stent group, by 85.4% (95% CI, 70.8% to 94.4%) of the 2-stent group, and by 92.1% (95% CI, 78.6% to 98.3%) of the 3-stent group. Forty-two-month follow-up results for 109 patients were published by Katz et al(2018).<sup>46</sup> Mean medicated IOPs for the 1-stent, 2-stent, and 3-stent groups were  $15.0 \pm 2.8$  mm Hg,  $15.7 \pm 1.0$  mm Hg, and  $14.8 \pm 1.3$  mm Hg, respectively. No between-group statistical comparisons were reported.

### Observational Studies

Use of multiple iStent devices with cataract surgery was reported in an open-label, prospective series of 53 eyes (47 patients) by Belovay et al (2012).<sup>37</sup> Twenty-eight of 53 eyes were implanted with 2 stents and 25 with 3 stents, based on the need for greater IOP control, as determined by the operating surgeon. Best-corrected visual acuity improved or remained stable in 89% of eyes. IOP decreased from a mean of 18.0 to 14.3 mm Hg, and the number of hypotensive medications decreased from a mean of 2.7 to 0.7 at 1 year postoperatively. Target IOP was reached in 77% of eyes, while 59% of patients discontinued all medications for the study eye. At one year, the mean number of hypotensive medications decreased to 1.0 in the 2-stent group and 0.4 in the 3-stent group. Medication use ceased in 46% of eyes in the 2-stent group and 72% in the 3-stent group. Stent blockage occurred in the early postoperative period in 15% of eyes and was successfully treated with laser.

### *Section Summary: Other Indications for Glaucoma Treatment*

Studies have evaluated the use of more than two stents, but comparators differed. One RCT compared implantation of a single iStent with 2 or 3 stents; it reported similar rates of patients with a 20% or more reduction in IOP. There were some group differences in secondary outcomes, but statistical testing was not reported. An observational study described implantation of two or three stents, at the discretion of the operating surgeon.

## **SUMMARY OF EVIDENCE**

For individuals who have refractory OAG who receive an external aqueous shunt, the evidence includes RCTs, retrospective studies, and systematic reviews. The relevant outcomes are a change in disease status, functional outcomes, medication use, and treatment-related morbidity. RCTs assessing FDA-approved shunts have shown 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

five 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. The 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. The relevant outcomes are a change in disease status, functional outcomes, medication use, and treatment-related morbidity. Implantation of one or two microstents has received 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 have been conducted in patients with cataracts and less advanced glaucoma, where IOP is at least partially controlled with medication. Trial results have shown that IOP may be lowered below baseline with a decreased need for medication through the first two years. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals with indications for glaucoma treatment other than cataract surgery or refractory OAG who receive aqueous shunts or microstents, the evidence includes an RCT and an observational study. The 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. One RCT compared a single microstent with multiple microstents. This trial reported no difference in the primary outcome (percentage of patients with  $\geq 20\%$  reduction in IOP); secondary outcomes favored the multiple microstent groups. An observational study described implantation of two or three stents, at the discretion of the operating surgeon. The evidence is insufficient to determine the effects of the technology on health outcomes.

### **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 societies and 2 academic medical centers while this policy was under review in 2013. The input supported use of aqueous shunts in patients with moderate-to-severe glaucoma uncontrolled by medication. Input supported use of a single microstent in patients with mild- to-moderate glaucoma undergoing cataract surgery to reduce side effects of medications and avoid noncompliance.

## **PRACTICE GUIDELINES AND POSITION STATEMENTS**

### American Glaucoma Society

A position statement by the AGS (2012) indicated that new technology whose intraocular pressure (IOP)-lowering effect allows for a reduction in medications, or a reduction in the need for more advanced surgical care, or improves patient adherence to care, would provide benefits to glaucoma patients.<sup>47</sup> If effective and safe, AGS suggested these benefits and the fact that these technologies would not have bleb-related complications would represent an "improvement in net health outcomes." Also, AGS stated that some categories of new surgical devices and techniques are used at the time of concomitant cataract surgery. Because cataract surgery alone has been shown to lower IOP, a control group of patients with similar entry criteria undergoing cataract surgery alone may be appropriate for these technologies.

### American Academy of Ophthalmology

The AAO (2008) published a technology assessment on commercially available aqueous shunts, including the Ahmed, Baerveldt, Krupin, and Molteno devices.<sup>4</sup> The assessment indicated that, in general, IOP would settle at higher levels ( $\approx 18$  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). 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.

A 2011 technology assessment from AAO (literature search to October 2009) reviewed the evidence on novel or emerging, glaucoma procedures.<sup>48</sup> Included in the assessment were devices and procedures with U.S. Food and Drug Administration clearance or in phase 3 clinical trials in the United States. Devices included the EX-PRESS MiniGlaucoma shunt, the SOLX Gold Shunt, and the iStent, as well as various surgical procedures. The assessment concluded that these devices and techniques were still in the initial state ( $\leq 5$  years) of clinical experience and lacked widespread use. The clinical studies generally provided only level III evidence in support of the procedures. Based on the literature available at the time, AAO could not determine whether the novel procedures were superior, equal to, or inferior to surgery (eg, trabeculectomy) or one another.

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 instillation, or intolerance to the medication.<sup>49</sup> 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.<sup>50</sup> 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 a guidance entitled "Microinvasive subconjunctival insertion of a trans-scleral gelatin stent for primary open-angle glaucoma"<sup>51</sup>. 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.

#### European Glaucoma Society

The European Glaucoma Society's *Terminology and Guidelines for Glaucoma* (2014) provided evidence-based guidelines on the treatment of primary open-angle glaucoma.<sup>52</sup> The guidelines were updated in 2017.<sup>53</sup> The guidelines stated that there are no well-controlled comparative trials to support the superiority in safety or efficacy of minimally invasive glaucoma surgery, including both ab interno and ab externo procedures, over trabeculectomy.

### **U.S. PREVENTIVE SERVICES TASK FORCE RECOMMENDATIONS**

Not applicable.

### **ONGOING AND UNPUBLISHED CLINICAL TRIALS**

Some currently unpublished trials that might influence this policy are listed in Table 12.

**Table 12.** Summary of Key Trials

<b>NCT No.</b>	<b>Trial Name</b>	<b>Planned Enrollment</b>	<b>Completion Date</b>
<b>Ongoing</b>			
NCT01444040 <sup>a</sup>	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 (ongoing)
NCT01461291 <sup>a</sup>	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 2018
NCT02024464 <sup>a</sup>	A Prospective, Multicenter, Randomized Comparison of the Hydrus Microstent to the iStent for Lowering Intraocular Pressure in Glaucoma Patients Undergoing Cataract Surgery	300	Jul 2018 (ongoing)
NCT01539239 <sup>a</sup>	The Safety and Effectiveness of the Hydrus Aqueous Implant for Lowering Intraocular Pressure in Glaucoma Patients Undergoing Cataract Surgery, A Prospective, Multicenter, Randomized, Controlled Clinical Trial	1143	Jun 2020

NCT No.	Trial Name	Planned Enrollment	Completion Date
NCT01461278 <sup>a</sup>	A Prospective, Randomized, Single-Masked, Controlled, Parallel Groups, Multicenter Clinical Investigation of the Glaukos® Suprachoroidal Stent Model G3 In Conjunction With Cataract Surgery	1200	Apr 2019
NCT01841450 <sup>a</sup>	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
<b>Unpublished</b>			
NCT02023242 <sup>a</sup>	A Prospective, Multicenter, Randomized Comparison of the Hydrus to the iStent® for Lowering Intraocular Pressure in Primary Open Angle Glaucoma	152	Jan 2018 (completed)
NCT01282346 <sup>a</sup>	Clinical Evaluation of the SOLX Gold Shunt for the Reduction of Intraocular Pressure (IOP) in Refractory Glaucoma	60	Dec 2015 (completed)

NCT: national clinical trial.

<sup>a</sup> 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

E08.36	Diabetes mellitus due to underlying conditions with diabetic cataract
E09.36	Drug or chemical induced diabetes mellitus with diabetic cataract
E10.36	Type 1 diabetes mellitus with diabetic cataract
E11.36	Type 2 diabetes mellitus with diabetic cataract
E13.36	Other specified diabetes mellitus with diabetic cataract
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
Q15.0	Congenital glaucoma

**REVISIONS**

06-07-2013	Policy added to the bcbsks.com website.
01-30-2014	Updated Description section. In Policy section: <ul style="list-style-type: none"> <li>▪ 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."</li> <li>▪ 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."</li> </ul>

	Updated Rationale section.
	In Coding section: <ul style="list-style-type: none"> <li>▪ Noted CPT code 0192T will be a deleted code, effective December 31, 2013</li> <li>▪ Added CPT code 66183 (<i>New code, effective January 1, 2014</i>)</li> <li>▪ Added Diagnosis codes: 366.00-366.9</li> <li>▪ Added ICD-10 Diagnosis (<i>Effective October 1, 2014</i>)</li> </ul>
	Updated Reference section.
01-01-2015	Policy posted to the website February 10, 2014.
	In Coding section: <ul style="list-style-type: none"> <li>▪ Added CPT Codes: 66179, 66184, 0376T (Effective January 1, 2015)</li> <li>▪ Added CPT Code: 66185 (coding correction)</li> <li>▪ Revised CPT Codes: 66180, 0191T, 0253T (Effective January 1, 2015)</li> <li>▪ Deleted CPT Codes: 66170, 66172 (not applicable to the policy)</li> </ul>
12-28-2015	Updated Description section.
	In Policy section: <ul style="list-style-type: none"> <li>▪ In Item A, removed "The iStent shunt is FDA approved, only when used in conjunction with cataract surgery."</li> <li>▪ 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."</li> <li>▪ 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."</li> </ul>
	Updated Rationale section.
	Updated References section.
04-27-2016	Updated Description section.
	Updated Rationale section.
	In Coding section: <ul style="list-style-type: none"> <li>▪ Coding bullets removed.</li> </ul>
	Updated References section.
10-01-2016	In Coding section: <ul style="list-style-type: none"> <li>▪ 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</li> <li>▪ Removed ICD-10 codes: H40.11x0, H40.11x1, H40.11x2, H40.11x3, H40.11x4</li> </ul>
11-09-2016	In Policy section: <ul style="list-style-type: none"> <li>▪ Moved previous Item C to become current Item B.</li> <li>▪ 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."</li> </ul>
	In Coding section: <ul style="list-style-type: none"> <li>▪ Added CPT codes: 0449T, 0450T (<i>Effective January 1, 2017</i>).</li> </ul>
	Updated References section.
04-12-2017	Updated Description section.
	Updated Rationale section.
	Updated References section.
07-01-2017	In Coding section: <ul style="list-style-type: none"> <li>▪ Added CPT code: 0474T (Effective July 1, 2017).</li> </ul>
04-24-2019	Updated Description section.

	Updated Rationale section.
	In Coding section: ▪ ICD-9 codes removed.
	Updated References section.

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