

Protocol

Aqueous Shunts and Stents for Glaucoma

(90321)

Medical Benefit		Effective Date: 04/01/19	Next Review Date: 01/20
Preauthorization	No	Review Dates: 03/10, 03/11, 07/11, 01/12, 09/12, 01/13, 01/14, 11/14, 11/15, 11/16, 11/17, 07/18, 01/19	

Preauthorization is not required.

The following protocol contains medical necessity criteria that apply for this service. The criteria are also applicable to services provided in the local Medicare Advantage operating area for those members, unless separate Medicare Advantage criteria are indicated. If the criteria are not met, reimbursement will be denied and the patient cannot be billed. Please note that payment for covered services is subject to eligibility and the limitations noted in the patient's contract at the time the services are rendered.

Populations	Interventions	Comparators	Outcomes
Individuals: • With refractory open-angle glaucoma	Interventions of interest are: • Ab externo aqueous shunts	Comparators of interest are: • Ocular medication • Trabeculectomy	Relevant outcomes include: • Change in disease status • Functional outcomes • Medication use • Treatment-related morbidity
Individuals: • With refractory open-angle glaucoma	Interventions of interest are: • Ab interno aqueous stents	Comparators of interest are: • Ocular medication • Trabeculectomy	Relevant outcomes include: • Change in disease status • Functional outcomes • Medication use • Treatment-related morbidity
Individuals: • With mild-to-moderate open-angle glaucoma who are undergoing cataract surgery	Interventions of interest are: • Aqueous microstents	Comparators of interest are: • Cataract surgery alone	Relevant outcomes include: • Change in disease status • Functional outcomes • Medication use • Treatment-related morbidity
Individuals: • With 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 of 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 (e.g., 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 currently treated with ocular hypotensive medication.

SUMMARY OF EVIDENCE

For individuals who have refractory open-angle glaucoma who receive ab externo aqueous shunts, the evidence includes randomized controlled trials (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 U.S. Food and Drug Administration (FDA)–approved shunts have shown that the use of large externally placed shunts reduces IOP to slightly less than standard filtering surgery (trabeculectomy). Reported shunt success rates show that these devices are noninferior to trabeculectomy in the long term. Food and Drug Administration–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 open-angle glaucoma 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 four 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 open-angle glaucoma 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 open-angle glaucoma 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 open-angle glaucoma 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 20% or more 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.

POLICY

Insertion of ab externo 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 medi-

cal therapy has failed to adequately control intraocular pressure.

Use of an ab externo aqueous shunt for all other conditions, including in patients with glaucoma when intraocular pressure is adequately controlled by medications, is considered **investigational**.

Insertion of ab interno aqueous stents approved by the FDA as a method to reduce intraocular pressure in patients with glaucoma where medical therapy has failed to adequately control intraocular pressure, is considered **medically necessary**.

Implantation of one or two FDA-approved ab interno stents in conjunction with cataract surgery may be considered **medically necessary** in patients with mild to moderate open-angle glaucoma treated with ocular hypotensive medication.

Use of ab interno stents for all other indications is considered **investigational**.

POLICY GUIDELINES

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

MEDICARE ADVANTAGE

For Medicare Advantage, the above statements apply, except for the following:

One XEN45 device per eye may be considered **medically necessary** for the management of refractory glaucoma, defined as prior failure of filtering/cilioablative procedure and/or uncontrolled IOP (progressive damage and mean diurnal medicated IOP ≥ 20 mm Hg) on maximally tolerated medical therapy (i.e., \geq four classes of topical IOP-lowering medications, or fewer in the case of tolerability or efficacy issues).

One iStent, Hydrus or CyPass device per eye may be considered **medically necessary** for the treatment of adults with mild or moderate open-angle glaucoma and a cataract when the individual is currently being treated with an ocular hypotensive medication and the procedure is being performed in conjunction with cataract surgery.

For Medicare Advantage, the following procedures are considered **investigational**:

- insertion of an anterior segment aqueous drainage device, without extraocular reservoir, internal approach, suprachoroidal space;
- insertion of an anterior segment aqueous drainage device, without extraocular reservoir, internal approach, into the trabecular meshwork; each additional device insertion;
- insertion of an aqueous drainage device, without extraocular reservoir, internal approach into the subconjunctival space; each additional device.

BACKGROUND

GLAUCOMA

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

Treatment

Ocular Medication

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

Surgery

Surgical intervention may be indicated in patients with glaucoma when the target IOP cannot be reached pharmacologically. Surgical procedures for glaucoma aim to reduce IOP from impaired aqueous humor drainage in the trabecular meshwork and/or Schlemm canal. Trabeculectomy (guarded filtration surgery) is the most established surgical procedure for glaucoma, which involves dissecting the conjunctiva, creating a scleral flap and scleral ostomy then suturing down the flap and closing the conjunctiva, allowing aqueous humor to directly enter the subconjunctival space. This procedure creates a subconjunctival reservoir, which can effectively reduce IOP, but commonly results in filtering “blebs” on the eye, and is associated with numerous complications (e.g., hemorrhage, scarring, hypotony, infection, leaks, bleb-related endophthalmitis) and long-term failure. Other surgical procedures (not addressed herein) include trabecular laser ablation, deep sclerectomy (which removes the outer wall of the Schlemm canal and excises deep sclera and peripheral cornea), and visco-canalostomy (which unroofs and dilates the Schlemm canal without penetrating the trabecular meshwork or anterior chamber) (see the Visco-canalostomy and Canaloplasty Protocol). 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 (see the Visco-canalostomy and Canaloplasty Protocol).

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 ($\approx 10\%$ 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 pempfigoid.

Minimally Invasive Glaucoma Surgeries

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 protocol 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 one-mm long stent inserted into the end of the Schlemm canal through the cornea and anterior chamber; the CyPass suprachoroidal stent; and XEN gelatin stent.

Because aqueous humor outflow is pressure-dependent, the pressure in the reservoir and venous system is critical for reaching the target IOP. Therefore, some devices may be unable to reduce IOP below the pressure of the distal outflow system used (e.g., less than 15 mm Hg) and are not indicated for patients for whom very low IOP is desired (e.g., those with advanced glaucoma). It has been proposed that stents such as the iStent, CyPass, and Hydrus Microstent may be useful in patients with early-stage glaucoma to reduce the burden of medications and problems with compliance. One area of investigation 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 ab externo and ab interno aqueous shunts and microstents is summarized in Table 1. The first-generation Ahmed™ (New World Medical), Baerveldt® (Advanced Medical Optics), Krupin (Eagle Vision), and Molteno® (Molteno Ophthalmic) ab externo aqueous shunts were cleared for marketing by the FDA through the 510(k) process between 1989 and 1993; modified Ahmed and Molteno devices were cleared in 2006. They are indicated for use “in patients with intractable glaucoma to reduce intraocular pressure where medical and conventional surgical treatments have failed.” The AquaFlow™ Collagen Glaucoma Drainage Device (STAAR Surgical) was approved by the FDA through the premarket approval process for the maintenance of the subsclearal space following nonpenetrating deep sclerectomy. In 2003, the ab externo EX-PRESS® Mini Glaucoma Shunt was cleared for marketing by the FDA through the 510(k) process. In 2016, the XEN® Glaucoma Treatment System (Allergan), which consists of the XEN45 Gel Stent preloaded into the XEN Injector, was cleared for marketing by the FDA through the 510(k) process as an ab interno aqueous stent for management of refractory glaucoma. The approval was for patients with refractory glaucoma who failed previous surgical treatment or for patients with primary open-angle glaucoma unresponsive to maximum tolerated medical therapy. The FDA determined that this device was substantially equivalent to existing devices, specifically the Ahmed™ Glaucoma Valve and the EX-PRESS® Glaucoma Filtration Device.

In 2018, the 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 precautions¹:

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 mm Hg
- In patients with unmedicated IOP less than 21 mm Hg nor greater than 36 mm Hg 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.²

Table 1. Regulatory Status of Aqueous Shunts and Stents

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

FDA: Food and Drug Administration; PMA: premarket approval.

FDA product codes: OGO, KYF.

RELATED PROTOCOL

Viscocanalostomy and Canaloplasty

Services that are the subject of a clinical trial do not meet our Technology Assessment Protocol criteria and are considered investigational. *For explanation of experimental and investigational, please refer to the Technology Assessment Protocol.*

It is expected that only appropriate and medically necessary services will be rendered. We reserve the right to conduct prepayment and postpayment reviews to assess the medical appropriateness of the above-referenced procedures. **Some of this protocol may not pertain to the patients you provide care to, as it may relate to products that are not available in your geographic area.**

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We are not responsible for the continuing viability of web site addresses that may be listed in any references below.

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58. National Government Services, Inc. (Primary Geographic Jurisdiction 06 & K - Illinois, Minnesota, Wisconsin, Connecticut, New York - Entire State, Maine, Massachusetts, New Hampshire, Rhode Island, Vermont) Local Coverage Determination (LCD): Micro-Invasive Glaucoma Surgery (MIGS) (L37244), Revision Effective Date for services performed on or after 11/08/2018.