Aqueous Shunts and Stents for Glaucoma

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.

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

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

POLICY STATEMENT
Insertion of ab externo aqueous shunts approved by the U.S. Food and Drug Administration may be considered medically necessary as a method to reduce intraocular pressure in patients with glaucoma where medical therapy has failed to adequately control intraocular pressure.

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 Food and Drug Administration 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 1 or 2 Food and Drug Administration approved 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 conditions is considered investigational.

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

BENEFIT APPLICATION
Experimental or investigational procedures, treatments, drugs, or devices are not covered (See General Exclusion Section of brochure).

FDA 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 subscleral space following nonpenetrating deep sclerectomy. In 2003, the ab externo EX-PRESS® Mini Glaucoma Shunt was cleared for marketing by the FDA through the 510(k) process. In 2016, the XEN® Glaucoma Treatment System (Allergan), which consists of the XEN45 Gel Stent preloaded into the XEN Injector, was cleared for marketing by the FDA through the 510(k) process as an ab interno aqueous stent for management of refractory glaucoma. The approval was for patients with refractory glaucoma who failed previous surgical treatment or for patients with primary open-angle glaucoma unresponsive to maximum tolerated medical therapy. The FDA determined that this device was substantially equivalent to existing devices, specifically the Ahmed™ Glaucoma Valve and the EX-PRESS® Glaucoma Filtration Device.

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In 2018, the iStent® Trabecular Micro-Bypass Stent preloaded into the iStent inject device (Glaukos) was approved by the FDA through the Premarket approval 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:

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 cilioablatiputive 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/vitrectomy 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 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 density.
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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

<table>
<thead>
<tr>
<th>Device</th>
<th>Manufacturer</th>
<th>Type</th>
<th>FDA Status</th>
<th>Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>AquaFlow™</td>
<td>STAAR Surgical</td>
<td>Drainage device</td>
<td>PMA</td>
<td>2001</td>
</tr>
<tr>
<td>Ahmed™</td>
<td>New World Medical</td>
<td>Aqueous glaucoma shunt, ab externo</td>
<td>510(k)</td>
<td>&lt;1993</td>
</tr>
<tr>
<td>Baerveldt®</td>
<td>Advanced Medical Optics</td>
<td>Aqueous glaucoma shunt, ab externo</td>
<td>510(k)</td>
<td>&lt;1993</td>
</tr>
<tr>
<td>Krupin</td>
<td>Eagle Vision</td>
<td>Aqueous glaucoma shunt, ab externo</td>
<td>510(k)</td>
<td>&lt;1993</td>
</tr>
<tr>
<td>Molteno®</td>
<td>Molteno Ophthalmic</td>
<td>Aqueous glaucoma shunt, ab externo</td>
<td>510(k)</td>
<td>&lt;1993</td>
</tr>
<tr>
<td>EX-PRESS®</td>
<td>Alcon</td>
<td>Mini-glaucoma shunt, ab externo</td>
<td>510(k)</td>
<td>2003</td>
</tr>
<tr>
<td>XEN® Gel Stent; XEN injector</td>
<td>AqueSys/Allergan</td>
<td>Aqueous glaucoma stent, ab interno</td>
<td>510(k)</td>
<td>2016</td>
</tr>
<tr>
<td>iStent®; iStent inject®</td>
<td>Glaukos</td>
<td>Microstent, ab interno</td>
<td>PMA- in conjunction with cataract surgery</td>
<td>2018</td>
</tr>
<tr>
<td>iStent supra®</td>
<td>Glaukos</td>
<td>Suprachoroidal stent</td>
<td>Not approved; in clinical trial</td>
<td></td>
</tr>
<tr>
<td>CyPass®</td>
<td>Alcon</td>
<td>Suprachoroidal stent, ab interno</td>
<td>Company voluntarily recalled</td>
<td>2018</td>
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<tr>
<td>Hydrus™</td>
<td>Ivantis</td>
<td>Microstent, ab interno</td>
<td>PMA approval</td>
<td>2018</td>
</tr>
<tr>
<td>SOLX® Gold</td>
<td>SOLX</td>
<td>Micro-Shunt, ab externo</td>
<td>Not approved; in clinical trial</td>
<td></td>
</tr>
</tbody>
</table>

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

RATIONALITY

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. 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 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 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 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% 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.

SUPPLEMENTAL INFORMATION

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. 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. The assessment indicated that, in general, IOP would settle at higher levels (18 mm Hg) with shunts than after standard trabeculectomy (14-16 mm Hg). Five-year success rates of 50% were found for the 2 procedures, indicating that aqueous shunts are comparable with trabeculectomy for IOP control and duration of benefit (based on level I evidence; well-designed randomized controlled trials). The assessment also indicated that although aqueous shunts have generally been reserved for intractable glaucoma when prior medical or surgical therapy has failed, indications for shunts have broadened (based on level III evidence; case series, case reports, and poor-quality case-control or cohort studies). 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. Included in their 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 Mini Glaucoma 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 stage (<=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. 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. 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.”

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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. The guidelines were updated in 2017. 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.

Medicare National Coverage

There is no national coverage determination (NCD). In the absence of an NCD, coverage decisions are left to the discretion of local Medicare carriers.

REFERENCES


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39. Vlasov A, Kim WI. The efficacy of two trabecular bypass stents compared to one in the management of open-angle glaucoma. Mil Med. Mar 2017;182(S1):222-225. PMID 28291477


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**POLICY HISTORY**

<table>
<thead>
<tr>
<th>Date</th>
<th>Action</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>March 2012</td>
<td>New Policy</td>
<td>Policy updated with literature search through December 2012; some references removed and re-numbered; references 6, 8, 12, 16, and 17 added. FDA approval of iStent updated; “stent” added to title and new not medically necessary statement added.</td>
</tr>
<tr>
<td>March 2013</td>
<td>Update Policy</td>
<td>Policy updated with literature search with references added. Policy statement and summary revised to: iStent may be considered medically necessary in patients with mild to moderate glaucoma when implanted in conjunction with cataract surgery.</td>
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<tr>
<td>December 2013</td>
<td>Update Policy</td>
<td>Policy updated with literature review through August 5, 2014; references 5, 7, and 13 added; policy statements unchanged.</td>
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<tr>
<td>September 2016</td>
<td>Update Policy</td>
<td>Policy updated with literature review, references 8-10, 15-16, and 18 added. Policy statements unchanged.</td>
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<tr>
<td>September 2018</td>
<td>Update Policy</td>
<td>Policy updated with literature review through March 5, 2018; references 1, 6, 11-14, 17-27, 29, 31-33, 36, 40, 46 added. Information about the FDA approval of CyPass® and Alcon withdrawal of CyPass from market Aug. 2018 added. Policy statements were changed. The term “aqueous shunts” modified with “ab externo” and “ab interno”; Previously, ab externo and ab interno devices were combined in one policy statement. There are now 2 separate policy statements, one for ab externo devices and one for ab interno devices.</td>
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<tr>
<td>March 2019</td>
<td>Update Policy</td>
<td>Policy updated with literature review through October 1, 2018; references 15 and 20 were added. Policy statements were edited to clarify the differences between ab externo shunts and ab interno stents. In addition, the use of an FDA-approved stent in a stand-alone procedure to reduce IOP pressure is now considered medically necessary.</td>
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