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 (OAG) currently treated with ocular hypotensive medication.

OBJECTIVE

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

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 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 conditions is considered **investigational**.

**POLICY GUIDELINES**

None

**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 IOP where medical and conventional surgical treatments have failed.” The AquaFlow™ Collagen Glaucoma Drainage Device (STAAR Surgical) was approved by the FDA through the premarket approval process for the maintenance of the sub scleral 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 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:

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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 <91>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 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

<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>
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<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;</td>
<td>XEN injector</td>
<td>Aqueous glaucoma stent, ab interno</td>
<td>510(k)</td>
<td>2016</td>
</tr>
</tbody>
</table>
## RATIONALE

### Summary of Evidence

For individuals who have refractory open-angle glaucoma (OAG) 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 the 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 intraocular pressure (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 and meta-analyses of 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 the FDA approval for use in conjunction with cataract surgery for reduction of IOP in adults with mild-to-moderate OAG currently treated with ocular hypotensive medication. When compared to cataract surgery alone, the studies showed modest but statistically significant decreases in IOP and medication use through the first two years when stents were implanted in conjunction with cataract surgery. A decrease in topical medication application is considered to be an important outcome for patients and reduces the problem of non-compliance that can affect visual outcomes. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

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

SUPPLEMENTAL INFORMATION

Practice Guidelines and Position Statements

American Academy of Ophthalmology (AAO)

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). The AAO concluded that, based on level I evidence, aqueous shunts offer a valuable alternative to standard filtering surgery and cyclodestructive therapy for many patients with refractory glaucoma.

The AAO's (2015) preferred practice patterns on primary open-angle glaucoma indicated that the Academy considered laser trabeculoplasty as initial therapy in select patients or an alternative for patients who cannot or will not use medications reliably due to cost, memory problems, difficulty with installation, or intolerance to the medication. 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."

The National Institute for Health and Care Excellence(2018) published guidance entitled "Microinvasive subconjunctival insertion of a trans-scleral gelatin stent for primary open-angle glaucoma". 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.

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U.S. Preventive Services Task Force Recommendations

Not applicable.

Medicare National Coverage

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

REFERENCES


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POLICY HISTORY - THIS POLICY WAS APPROVED BY THE FEP® PHARMACY AND MEDICAL POLICY COMMITTEE ACCORDING TO THE HISTORY BELOW:

<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>Replace 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>
</tr>
<tr>
<td>December 2013</td>
<td>Replace policy</td>
<td>Policy updated with literature review, references 1-8, 10, 12, 15-16, and 18 added. Policy statements unchanged.</td>
</tr>
<tr>
<td>July 2015</td>
<td>Replace policy</td>
<td>Policy updated with literature review through August 5, 2014; references 5, 7, and 13 added; policy statements unchanged.</td>
</tr>
<tr>
<td>September 2016</td>
<td>Replace policy</td>
<td>Policy updated with literature review, references 8-10, 15-16, and 18 added. Policy statements unchanged.</td>
</tr>
<tr>
<td>September 2018</td>
<td>Replace policy</td>
<td>Policy updated with literature review through March 5, 2018; references 1, 6, 11-14, 17-27, 29, 31-33, 36, 40, and 46 added. Information about the FDA approval of CyPass® and Alcon withdrawl 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>
</tr>
<tr>
<td>March 2019</td>
<td>Replace 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 intero 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>
</tr>
<tr>
<td>December 2019</td>
<td>Replace policy</td>
<td>Policy updated with literature review through July 23, 2019; references added. Policy statements unchanged.</td>
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