**Aqueous Shunts and Stents for Glaucoma**

**Medical Benefit**
- **Effective Date:** 10/01/18
- **Next Review Date:** 07/19
- **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

**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.

<table>
<thead>
<tr>
<th>Populations</th>
<th>Interventions</th>
<th>Comparators</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Individuals:</td>
<td>Interventions of interest are:</td>
<td>Comparators of interest are:</td>
<td>Relevant outcomes include:</td>
</tr>
<tr>
<td>• With refractory open-angle glaucoma</td>
<td>• Ab externo aqueous shunts</td>
<td>• Ocular medication</td>
<td>• Change in disease status</td>
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<td>• Trabeculectomy</td>
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<tr>
<td>Individuals:</td>
<td>Interventions of interest are:</td>
<td>Comparators of interest are:</td>
<td>• Medication use</td>
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<tr>
<td>• With refractory open-angle glaucoma</td>
<td>• Ab interno aqueous shunts</td>
<td>• Ocular medication</td>
<td>• Treatment-related morbidity</td>
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<td>Individuals:</td>
<td>Interventions of interest are:</td>
<td>Comparators of interest are:</td>
<td>Relevant outcomes include:</td>
</tr>
<tr>
<td>• With mild-to-moderate open-angle glaucoma</td>
<td>• Aqueous microstents</td>
<td>• Cataract surgery alone</td>
<td>• Change in disease status</td>
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<td>who are undergoing cataract surgery</td>
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<td>• Functional outcomes</td>
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</tr>
<tr>
<td>• With indications for glaucoma treatment</td>
<td>• Aqueous shunts or microstents</td>
<td>• Standard of care</td>
<td>• Change in disease status</td>
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<tr>
<td>other than cataract surgery or refractory</td>
<td></td>
<td></td>
<td>• Functional outcomes</td>
</tr>
<tr>
<td>open-angle glaucoma</td>
<td></td>
<td></td>
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<td>• Treatment-related morbidity</td>
</tr>
</tbody>
</table>

**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. Relevant outcomes are change in disease status, functional outcomes, medication use, and treatment-related morbidity. RCTs assessing U.S. Food and Drug Administration–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 comparative study and several single-arm studies. Relevant outcomes are 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. However, there was no discussion on how the patients were chosen to receive the different treatments. The single-arm studies have reported 12-month follow-up results and found that patients receiving the stents experienced reductions in IOP and medication use. Comparative studies with longer follow-up periods are needed. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have mild-to-moderate open-angle glaucoma who are undergoing cataract surgery who receive aqueous microstents, the evidence includes RCTs. Relevant outcomes are change in disease status, functional outcomes, medication use, and treatment-related morbidity. Two microstents have received the Food and Drug Administration 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 RCTs. Relevant outcomes are 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. One RCT compared two iStents with travoprost. This trial did not report statistical comparisons. 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 medical therapy has failed to adequately control intraocular pressure.

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 **investigational**.

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

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 treated with ocular hypotensive medication.

Use of a microstent 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., ≥ four classes of topical IOP-lowering medications, or fewer in the case of tolerability or efficacy issues).

**BACKGROUND**

**GLAUCOMA**

Surgical procedures for glaucoma aim to reduce IOP resulting from impaired aqueous humor drainage in the trabecular meshwork and/or Schlemm canal. 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**

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

Currently, minimally invasive glaucoma surgeries (MIGS) are alternative, less invasive techniques that are being developed and evaluated. Similar to trabeculectomy, the objective of MIGS is to lower IOP by improving outflow of eye fluid; however, MIGS involves less surgical manipulation of the sclera and the conjunctiva compared than a trabeculectomy. MIGS can either be performed outside the eye (ab externo) or inside the eye (ab interno).

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.

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., < 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 (PMA) 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. The EX-PRESS® shunt is placed under a partial thickness scleral flap and transports aqueous fluid from the anterior chamber of the eye into a conjunctival filtering bleb. 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 shunt 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. FDA determined that this device was substantially equivalent to existing devices, specifically the Ahmed™ Glaucoma Valve and the EX-PRESS® Glaucoma Filtration Device.

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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<td>Baerveldt®</td>
<td>Advanced Medical Optics</td>
<td>Aqueous glaucoma shunt, ab externo</td>
<td>510(k)</td>
<td>&lt; 1993</td>
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<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>
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<tr>
<td>EX-PRESS®</td>
<td>Alcon</td>
<td>Mini-glaucoma shunt, ab externo</td>
<td>510(k)</td>
<td>2003</td>
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<tr>
<td>XEN® Gel Stent</td>
<td>AqueSys/Allergan</td>
<td>Aqueous glaucoma shunt, ab interno</td>
<td>510(k)</td>
<td>2016</td>
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<tr>
<td>iStent®</td>
<td>Glaukos</td>
<td>Microstent, ab interno</td>
<td>PMA</td>
<td>2012</td>
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<tr>
<td>CyPass®</td>
<td>Transcend Medical</td>
<td>Suprachoroidal stent, ab interno</td>
<td>PMA</td>
<td>2016</td>
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<td>Hydrus™</td>
<td>Ivantis</td>
<td>Microstent, ab interno</td>
<td>Not approved; PMA submission</td>
<td>2017</td>
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<td>SOLX® Gold</td>
<td>SOLX</td>
<td>Micro-Shunt, ab externo</td>
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<tr>
<td>iStent inject®</td>
<td>Glaukos</td>
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<td>iStent supra®</td>
<td>Glaukos</td>
<td>Suprachoroidal stent</td>
<td>Not approved; in clinical trial</td>
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</table>

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

In 2012, the iStent® Trabecular Micro-Bypass Stent (Glaukos) was approved by the FDA through the PMA 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 currently treated with ocular hypotensive medication and 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 patients with prior glaucoma surgery of any type, including argon laser trabeculoplasty
   - In patients with medicated IOP greater than 24 mm Hg
• In patients with unmedicated IOP less than 22 mm Hg nor greater than 36 mm Hg after ‘washout’ of medications
• For implantation of more than a single stent
• 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”

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.

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


40. 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(51):222-225. PMID 28291477


