Aqueous Shunts and Stents for Glaucoma

Summary

Glaucoma surgery is intended to reduce intraocular pressure (IOP) when the target IOP cannot be reached with 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.

The evidence for aqueous shunts in individuals who have open-angle glaucoma includes randomized controlled trials (RCTs). Relevant outcomes are 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 leads to slightly less reduction in IOP than standard filtering surgery (trabeculectomy). Reported shunt success rates are as good as trabeculectomy in the long term. FDA-approved shunts have a different adverse effect profile and avoid some of the most problematic complications of trabeculectomy. The evidence is sufficient to determine quantitatively that the technology results in a meaningful improvement in the net health outcome.

The evidence for aqueous microstents in individuals who have open-angle glaucoma includes RCTs. Relevant outcomes are change in disease status, functional outcomes, medication use, and treatment-related morbidity. A microstent has received FDA approval 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. RCTs have been conducted in patients with cataracts and less advanced glaucoma, where IOP is at least partially controlled with medication. Trial results indicate that IOP may be lowered below baseline with decreased need for medication, although the benefit appears to diminish after the first year. One RCT compared a single microstent to multiple microstents. This study reported no difference on the primary outcome (percentage of patients with ≥20% reduction in IOP); secondary outcomes favored the microstent group. The evidence is insufficient to determine the effects of the technology on health outcomes.

FDA 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. They are indicated for use “in patients with intractable glaucoma to reduce intraocular pressure where medical and conventional surgical treatments have failed.” The
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AquaFlow™ Collagen Glaucoma Drainage Device was approved by FDA through the premarket approval process for the maintenance of the sub scleral space following nonpenetrating deep sclerectomy. In 2003, the EX-PRESS® Mini Glaucoma Shunt was cleared for marketing by 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. The Cypass™ received premarket approval July 29, 2016, for primary open angle glaucoma to reduce intraocular pressure when implanted in eyes which have not failed conventional medical and surgical treatment.

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>
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<tr>
<td>Trabectome™</td>
<td>NeoMedix</td>
<td>Electrocautery device</td>
<td>510(k)</td>
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<td>Ahmed™</td>
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<td>Baerveldt®</td>
<td>Advanced Medical Optics</td>
<td>Aqueous glaucoma shunt</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</td>
<td>510(k)</td>
<td>&lt;1993</td>
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<tr>
<td>Molteno®</td>
<td>Molteno Ophthalmics</td>
<td>Aqueous glaucoma shunt</td>
<td>510(k)</td>
<td>&lt;1993</td>
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<td>EX-PRESS®</td>
<td>Alcon</td>
<td>Mini-glaucoma shunt</td>
<td>510(k)</td>
<td>2003</td>
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<tr>
<td>iStent®</td>
<td>Glaukos</td>
<td>Microstent</td>
<td>PMA</td>
<td>2012</td>
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<td>Hydrus™</td>
<td>Ivantis</td>
<td>Microstent</td>
<td>Not approved</td>
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<tr>
<td>SOLX® Gold</td>
<td>SOLX</td>
<td>Micro-Shunt</td>
<td>Not approved</td>
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<td>iStent inject®</td>
<td>Glaukos</td>
<td>Suprachoroidal stent</td>
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<td>iStent supra®</td>
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<td>Transcend Medical</td>
<td>Suprachoroidal stent</td>
<td>PMA</td>
<td>2016</td>
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<tr>
<td>XEN Gel Stent</td>
<td>AqueSys</td>
<td>Subconjunctival</td>
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</table>

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

In 2012, the FDA approved the Glaukos Corporation’s iStent® Trabecular Micro-Bypass Stent, PMA P080030, as indicated for use in conjunction with cataract surgery for the reduction of IOP in adult patients 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 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 intraocular pressure greater than 24 mm Hg
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- 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

Note: Use of the iStent has subsequently been reported for many of the circumstance or conditions listed above; most of the publications are case series.

The SOLX® DeepLight® Gold Micro-Shunt, Hydrus™ Microstent, and XEN Gel Stent are currently in FDA-regulated trials. They have received regulatory approval in Europe, but have not been cleared by FDA for use in the United States.

FDA product codes: OGO KYF

POLICY STATEMENT

*This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

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.

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

Implantations of a single FDA approved microstent (iStent Trabecular Micro-Bypass Stent) in conjunction with cataract surgery is considered medically necessary in patients with mild to moderate open-angle glaucoma currently treated with ocular hypotensive medication.

The use of other non–approved micro-stents is considered 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.

Procedures using the Trabectome device are considered similar to trabecular laser ablation and are not within the scope of this policy.

RATIONALE

FDA-Approved/Cleared Aqueous Shunts
This section reviews the evidence on aqueous shunts with FDA approval. Evidence on nonapproved devices is included in a later section.

A 2006 Cochrane review evaluated 15 randomized or pseudo-randomized controlled trials (RCTs), on 1,153 participants, on the Ahmed, Baerveldt, Molteno, and Schocket shunts (1). Trabeculectomy was found to result in a lower mean intraocular pressure (IOP) (by 3.8 mm Hg) than the Ahmed shunt at 1 year. A limitation of this report is that complications were not compared, as the authors considered them to be too variably reported to allow comparative tabulation. There was no evidence of superiority of one shunt over another.
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A literature review on commercially available aqueous shunts, including the Ahmed, Baerveldt, Krupin, and Molteno devices, for an American Academy of Ophthalmology (AAO) technology assessment was published in 2008 (2). This review indicated that the IOP would generally settle at higher levels (approximately 18 mm Hg) with aqueous shunts than after standard trabeculectomy (14-16 mm Hg) or after trabeculectomy with anti-fibrotic agents 5-fluorouracil or mitomycin C (8-10 mm Hg). In one study, mean IOPs with the Baerveldt shunt and adjunct medications were found to be equivalent to trabeculectomy with mitomycin C (13 mm Hg). Five-year success rates for the two procedures were found to be similar (50%). The assessment concluded that aqueous shunts were comparable with trabeculectomy for IOP control and duration of benefit. The risk of postoperative infection was less with aqueous shunts than after trabeculectomy. Complications of aqueous shunts were noted to include 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 described as accelerated damage to the corneal endothelium over time.

A comparative effectiveness review (CER) on glaucoma treatments was prepared by the Johns Hopkins Evidence-based Practice Center for the Agency for Healthcare Research and Quality (AHRQ) in 2012. (3) The CER found that the data available on the role of aqueous drainage devices in open-angle glaucoma (primary studies, systematic review) were inadequate to draw conclusions on the comparative effectiveness of these treatments in comparison with laser and other surgical treatments.

Baerveldt Glaucoma Shunt
Early results from the open-label multicenter randomized Tube Versus Trabeculectomy (TVT) study were reviewed in the 2008 AAO technology assessment, and in 2012, Gedde et al. reported 5-year follow-up from this study. (2, 4) The study included 212 eyes of 212 patients (18-85 years) who had previous 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 maximum tolerated medical therapy. Excluding patients who had died, the study had 82% follow-up 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 tube group and 13.6 mm Hg in the trabeculectomy group) nor number of glaucoma medications (1.4 in the tube group and 1.2 in the trabeculectomy group) were significantly different with intent-to-treat analysis. The cumulative probability of failure over the 5 years was lower in the tube group than the trabeculectomy group (29.8% vs. 46.9%), and the rate of reoperation was lower (9% vs. 29%). The rate of loss of 2 or more lines of visual acuity was similar in the 2 groups (46% in the tube group and 43% in the trabeculectomy group).

Ex-PRESS Mini Shunt
A 2014 publication described a U.S. multicenter randomized trial of trabeculectomy compared with EX-PRESS® implantation in 120 patients (120 eyes). (5) The groups were comparable at baseline, with a preoperative IOP of 25.1 mm Hg on a mean of 3.1 medications for the EX-PRESS® group, compared with 26.4 mm Hg on a mean of 3.1 medications in the trabeculectomy group. Throughout 2 years of follow-up after surgery, the average IOP and number of medications were similar in the 2 groups. At 2 years, mean IOP was 14.7 mm Hg on 0.9 medications in the EX-PRESS® group and 14.6 mm Hg on 0.7 medications in the trabeculectomy group. 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 1 month after EX-PRESS® implantation and 3 months after trabeculectomy (p=0.041), with a median time to return to baseline vision of 0.7 months and 2.2 months, respectively. Postoperative complications were higher after trabeculectomy (41%) than after EX-PRESS® implantation (18.6%).

In 2009, de Jong reported a randomized study of the EX-PRESS® mini shunt compared with standard trabeculectomy in 78 patients (80 eyes) with a diagnosis of open-angle glaucoma that could not be controlled with maximal-tolerated medical therapy. (6) Five-year follow-up was reported in 2011. (7) The 2 groups were similar after randomization, with the exception of difference in the mean age (62 years for...
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the EX-PRESS® group, 69 years for the trabeculectomy group). At an average 12 months’ follow-up, mean IOP had improved from 23 to 12 mm Hg in the EX-PRESS® group and from 22 to 14 mm Hg in the trabeculectomy group. Both groups of patients used fewer antiglaucoma medications postoperatively than before the procedure (from 2.8 at baseline to 0.3 in the EX-PRESS® group and from 3.0 at baseline to 0.6 in the trabeculectomy group). Twelve-month Kaplan-Meier success rates (defined as an IOP of >4 mm Hg and ≤18 mm Hg without use of antiglaucoma medications) were 82% for the EX-PRESS® shunt and 48% for trabeculectomy. At 5 years, the success rates were not significantly different between the 2 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). There were more complications after trabeculectomy than after EX-PRESS® implantation.

Two additional small RCTs were published in 2015 by Gonzalez-Rodriguez et al (8) (N=63) and Wagschal et al (N=64). (9) Both studies corroborated the results of the earlier RCTs, reporting no differences between trabeculectomy and Ex-PRESS shunt groups on the outcomes of mean IOP, success rates, number of medications used, or complication rates.

A 2015 Cochrane review evaluated the efficacy of adjunctive procedures for trabeculectomy. (10) The EX-PRESS Mini Shunt was included and 3 RCTs included that compared trabeculectomy alone with trabeculectomy plus EX-PRESS Mini Shunt. The 3 trials were rated as having high or unclear risk of bias using the Cochrane risk of bias tool. None of the RCTs reported a significant improvement for the EX-PRESS group. Pooled analysis, IOP was slightly 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).

Section Summary: Aqueous Shunts
Evidence from RCTs exists for each of the FDA-approved aqueous shunts. Trial results are fairly consistent that the magnitude of reduction in IOP following aqueous shunt placement is similar, or slightly inferior, to that following trabeculectomy. Shunts have fewer complications than trabeculectomy, and reduced the need for future operations. Overall, the risk-benefit ratio for shunts does not appear to differ substantially from that for trabeculectomy.

Aqueous Microstents
iStent
Results from the iStent U.S. investigational device exemption (IDE) open-label 29 site multicenter randomized clinical trial were reported to the FDA in 2010, with 1-year results published in 2011 and 2-year results published in 2012. (11-13) The objective of the trial was to measure the incremental effect on IOP from iStent implantation over that of cataract surgery alone and to determine the potential benefit of combining 2 therapeutic treatments into 1 surgical event. A total of 240 patients (mean age of 73 years) with cataracts and mild to moderate open-angle glaucoma (IOP < 24 mm Hg controlled on 1 to 3 medications) underwent a medication washout period. Patients were randomized to undergo cataract surgery with iStent implantation or cataract surgery only if the unmedicated IOP was 22 mm Hg or higher and 36 mm Hg or lower. The mean number of medications at baseline was 1.5. The medicated IOP at baseline was 18.7 mm Hg in the stent group and 18.04 in the control group. After washout, the mean IOP was 25 mm Hg and mean visual acuity (logMAR) was 0.36. Follow-up visits were performed at 1, 3, 6, and 12 months. Results were assessed by intent-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 study because of complications of cataract surgery. Of the remaining 114 subjects, 112 (91%) completed the 12-month visit. The proportion of eyes meeting both the primary (unmedicated IOP ≤ 21 mm Hg) and secondary outcomes (IOP reduction ≥ 20% without hypotensive
medications) was higher in the treatment group than in the control group through 1-year follow-up. At 1-year follow-up, 72% of treatment eyes and 50% of control eyes achieved the primary efficacy endpoint. The proportion of patients achieving the secondary efficacy endpoint at 1 year was 66% in the treatment group versus 48% in the control group. 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 (e.g., 15% vs. 35% at 12 months). The mean reduction in IOP was similar in the 2 groups, with a slightly higher level of medication used in the control group (mean of 0.4 medications) in comparison with the treatment group (0.2 medications) at 1 year.

At 2-year follow-up, there were 199 of the original 239 patients (83%) remaining in the study. The primary endpoint, IOP of 21 mm Hg or less without use of medication, was reached by 61% of patients in the treatment group compared to 50% of controls ($p=0.036$). The secondary outcomes of IOP reduction of 20% or more without medication (53% vs. 44%) and mean number of medications used (0.3 vs. 0.5) were no longer significantly different between the groups at 2 years. As noted by the FDA, this study was conducted in a restricted population of patients who had an unmedicated IOP of 22 mm Hg or higher and 36 mm Hg or lower. The results of this study indicate that treatment of this specific population with a microstent is likely to improve outcomes at 1 year compared to cataract surgery alone. However, given the 2-year results of this study, it is not possible to conclude with certainty that health outcomes are improved at longer periods of follow-up.

In 2010, Fea et al reported a randomized, double-blind, trial of 36 cataract surgery patients who did or did not receive an iStent implantation (2:1 ratio). Inclusion criteria were a previous diagnosis of primary open-angle glaucoma 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). At baseline, IOP averaged 17.9 mm Hg with 2.0 medications in the stent group and 17.3 mm Hg with 1.9 medications in the control group. Mean IOP at 15 months was 14.8 mm Hg with 0.4 medications in the stent group and 15.7 mm Hg with 1.3 medications in the control group. 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. After washout of medications, mean IOP was 16.6 in the stent group and 19.2 in the control group. No adverse events related to stent implantation were reported. Four-year follow-up from this study was published in 2015. Twenty-four of 36 patients were available at 4 years. Differences between treatment groups remained nonsignificant (mean IOP, 15.9 mm Hg in the stent group vs 17 mm Hg in the control group).

**Multiple Stents**

One RCT comparing the efficacy of 1 iStent to multiple iStents was published in 2015. This study, from a single institution in Armenia, randomized 119 patients with open-angle glaucoma and an IOP between 22 mm Hg and 38 mm Hg (off medications) to 1 shunt (n=38), 2 shunts (n=41), or 3 shunts (n=40). Randomization was performed using a pseudorandom number generator. The main outcome measure was IOP at 12 months. The primary end point was percentage of patients with a 20% or more reduction in IOP off medications. This end point 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 end point (percentage of patients achieving an IOP ≤15 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. No between-group statistical comparisons were reported.

Use of multiple iStent devices with cataract surgery was reported in an open-label, prospective series of 53 eyes (47 patients) in 2012. Eight-eight of 53 eyes had implantation of 2 stents and 25 had implantation of 3 stents, based on the need for greater IOP control, as determined by the operating
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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 1 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 in 72% in the 3-stent group. Stent blockage occurred in the early postoperative period in 15% of eyes and was successfully treated with laser. At least 1 other prospective case series has been published. (18) It enrolled 39 patients with open-angle glaucoma and IOP between 18 mm Hg and 30 mm Hg. Each patient received 2 microstents and medications as needed, and was followed for 3 years. At study completion, mean reduction in IOP was 9.1 mm Hg (95% CI, 8.0 to 10.1). There was 1 postoperative complication (hyphema), which resolved without further intervention.

Section Summary: Aqueous Microstents
Two identified RCTs compared cataract surgery plus a single iStent to cataract surgery alone. Results of these trials were mixed, with 1 showing a significant benefit in the stent group and the other reporting no significant benefit. One RCT compared a single iStent to 2 or 3 stents; it reported similar rates of the primary outcome among groups (percentage of patients with ≥20% reduction in IOP). There were some numerical group differences in secondary outcomes, but statistical testing was not reported. A low rate of complications (eg, stent malposition, hyphema) was reported in all trials, but this evidence is insufficient to determine rates of complications with confidence. Larger studies with longer follow-up are required to determine the true rate of complications.

Aqueous Shunts and Stents Not Approved by FDA

iStent inject®
An industry-sponsored multicenter unblinded randomized trial compared implantation of 2 iStent inject® devices versus 2 ocular hypotensive agents.(19) The 192 patients enrolled in this unmasked trial had an IOP that was not controlled by 1 hypotensive medication. At 12-month follow-up, the 2 groups were comparable for IOP reduction of at least 20%, IOP of 18 mm Hg or less, and mean decrease in IOP. A greater proportion of patients in the iStent inject® group achieved an IOP reduction of at least 50% (53.2% vs 35.7%). One patient in the iStent inject® group experienced elevated IOP (48 mm Hg) and 4 required ocular hypotensive medication. Longer-term studies are in progress.

Hydrus Microstent
In 2015, Pfeiffer et al reported a single-masked, randomized trial with 100 patients (100 eyes) that evaluated the effectiveness of the Hydrus Microstent when combined with cataract surgery to cataract surgery alone. (20) 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).

Other Shunts and Stents Case series have been identified on the EyePass and CyPass micro-stent. (21,22) The CyPass recently received FDA approval. The EyePass is no longer being developed.

Summary of Evidence
The evidence for aqueous shunts in individuals who have open-angle glaucoma includes randomized controlled trials (RCTs). Relevant outcomes are 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 leads to slightly less reduction in intraocular pressure (IOP) than standard filtering surgery (trabeculectomy). Reported shunt
success rates are as good as trabeculectomy in the long term. FDA-approved shunts have a different adverse effect profile and avoid some of the most problematic complications of trabeculectomy. The evidence is sufficient to determine quantitatively that the technology results in a meaningful improvement in the net health outcome.

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**SUPPLEMENTAL INFORMATION**

**Ongoing and Unpublished Clinical Trials**

Some currently unpublished trials that might influence this review are listed in Table 2.

**Table 2. Summary of Key Trials**

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<thead>
<tr>
<th>NCT No.</th>
<th>Trial Name</th>
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<td>NCT01282346a</td>
<td>Clinical Evaluation of the SOLX Gold Shunt for the Reduction of Intraocular Pressure (IOP) in Refractory Glaucoma</td>
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<td>Dec 2015 (ongoing)</td>
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<td>NCT02024464a</td>
<td>A Prospective, Multicenter, Randomized Comparison of the Hydrus Microstent to the iStent for Lowering Intraocular Pressure in Glaucoma Patients Undergoing Cataract Surgery</td>
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<td>NCT01444040a</td>
<td>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%</td>
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<td>April 2017</td>
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<td>NCT01456390</td>
<td>A Prospective Evaluation of Open-Angle Glaucoma Subjects With One Prior Trabeculectomy Treated Concurrently With One Suprachoroidal Stent and Two Trabecular Micro-bypass Stents and a Postoperative Prostaglandin</td>
<td>80</td>
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<tr>
<td>NCT02023242a</td>
<td>A Prospective, Multicenter, Randomized Comparison of the Hydrus to the iStent® for Lowering Intraocular Pressure in Primary Open Angle Glaucoma</td>
<td>100</td>
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<td>NCT01461291a</td>
<td>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</td>
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<tr>
<td>NCT01461278a</td>
<td>A Prospective, Randomized, Single Masked, Controlled, Parallel Groups, Multicenter Clinical Investigation of the Glaukos® Suprachoroidal Stent Model G3 In Conjunction With Cataract Surgery</td>
<td>1200</td>
<td>Apr 2019</td>
</tr>
</tbody>
</table>
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NCT: national clinical trial.

a Denotes industry-sponsored or cosponsored trial.

Practice Guidelines and Position Statements

American Glaucoma Society
A 2012 position statement by the American Glaucoma Society (AGS) states that new technology whose intraocular pressure-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 advantages to glaucoma patients. (23) If effective and safe, the AGS believe that these benefits and the fact that these technologies will not have bleb-related complications would represent an “improvement in net health outcomes.” In addition, the AGS states that some categories of new surgical devices and techniques are utilized at the time of concomitant cataract surgery. Since cataract surgery alone has been shown to lower intraocular pressure, a control group of patients with similar entry criteria undergoing cataract surgery alone may be appropriate for these technologies.

American Academy of Ophthalmology
The American Academy of Ophthalmology (AAO) published a 2008 technology assessment on commercially available aqueous shunts, including the Ahmed, Baerveldt, Krupin, and Molteno devices. (2) The assessment indicated that in general, the IOP would settle at higher levels (approximately 18 mm Hg) with shunts than after standard trabeculectomy (14–16 mm Hg). Five-year success rates of 50% have been found for the two 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 indicated that although aqueous shunts have been generally 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 or to cyclodestructive therapy for many patients with refractory glaucoma.

AAO’s 2010 Preferred Practice Patterns on primary open-angle glaucoma from the AAO states that glaucoma surgical procedures currently under evaluation are canaloplasty with a tensioning suture (Prolene [Ethicon Inc., Somerville, NJ]), ab interno trabeculotomy using the Trabectome (NeoMedix, Tustin, CA), trabecular meshwork bypass stent, and the Ex-PRESS mini glaucoma shunt (Alcon Laboratories, Inc., Ft. Worth, TX). (24) The AAO considers laser trabeculoplasty as initial therapy in selected 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 considers nonpenetrating glaucoma surgery to be an alternative to trabeculectomy, although the precise role of nonpenetrating surgery in the surgical management of glaucoma remains to be determined. Nonpenetrating glaucoma surgery avoids a continuous passageway from the anterior chamber to the subconjunctival space, reducing the incidence of complications such as bleb-related problems and hypotony. The nonpenetrating procedures have a higher degree of surgical difficulty compared with trabeculectomy and require special instrumentation. The two main types of nonpenetrating glaucoma surgery are viscocanalostomy and nonpenetrating deep sclerectomy.

A 2011 technology assessment from the AAO (literature search up to October 2009) reviewed the evidence on novel, or emerging, glaucoma procedures. (25) Included in the technology assessment were devices and procedures that either had FDA clearance or were in phase III clinical trials in the U.S. at the time. These included the Ex-PRESS™ mini glaucoma shunt, the SOLX Gold Shunt, and the iStent, along with various surgical procedures. The technology assessment concluded that these techniques and devices are still in the initial state (<5 years) of clinical experience and lacking widespread use. The clinical studies generally provided only level III evidence in support of the procedures. Based on the literature available at the time, it was not possible to conclude whether the novel procedures were superior, equal to, or inferior to surgery such as trabeculectomy or to one another.
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**National Institute for Health and Clinical Excellence**
The U.K.’s National Institute for Health and Clinical Excellence provided guidance on trabecular stent bypass microsurgery for open angle glaucoma in 2011. (26) The guidance states that current evidence on trabecular stent bypass microsurgery for open angle glaucoma raises no major safety concerns. There is evidence of efficacy in the short term, but this is based on small numbers of patients. Therefore, this procedure should only be used with special arrangements for clinical governance, consent, and audit or research.

**U.S. Preventive Services Task Force Recommendations**
Use of aqueous shunts and stents in the treatment of glaucoma is not a preventive service.

**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**

9.03.21 Aqueous Shunts and Stents for Glaucoma


POLICY HISTORY

<table>
<thead>
<tr>
<th>Date</th>
<th>Action</th>
<th>Description</th>
</tr>
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<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>
</tr>
<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>
</tr>
<tr>
<td>July 2015</td>
<td>Update 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>
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September 2016 Update Policy

Policy updated with literature review, references 8-10, 15-16, and 18 added. Policy statements unchanged.