BlueCross BlueShield of Louisiana

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Aqueous Shunts and Stents for Glaucoma

Policy # 00421
Original Effective Date: 05/21/2014
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Applies to all products administered or underwritten by Blue Cross and Blue Shield of Louisiana and its subsidiary, HMO Louisiana, Inc.(collectively referred to as the "Company"), unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

Note: Ophthalmologic Techniques for Evaluating Glaucoma and Viscocanalostomy and Canaloplasty are addressed separately in medical policies 00089 and 00280, respectively.

When Services Are Eligible for Coverage
Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:

- *Benefits are available in the member's contract/certificate, and*
- *Medical necessity criteria and guidelines are met.*

Based on review of available data, the Company may consider insertion of aqueous shunts approved by the U.S. Food and Drug Administration (FDA) as a method to reduce intraocular pressure (IOP) in patients with glaucoma where medical therapy has failed to adequately control intraocular pressure (IOP) to be **eligible for coverage.**

Based on review of available data, the Company may consider implantation of a single U.S. Food and Drug Administration (FDA)-approved microstent in conjunction with cataract surgery in patients with mild to moderate open-angle glaucoma currently treated with ocular hypotensive medication to be **eligible for coverage.**

When Services Are Considered Investigational
Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Company considers the use of an aqueous shunt for all other conditions, including in patients with glaucoma when intraocular pressure (IOP) is adequately controlled by medications, to be **investigational.***

Based on review of available data, the Company considers the use of a microstent for all other conditions to be **investigational.***

Background/Overview

Glaucoma surgery is intended to reduce IOP when the target IOP cannot be reached with medications. Due to complications with established surgical approaches such as trabeculectomy, a variety of devices, including aqueous 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.

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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's canal), drains into collector channels, and then into the aqueous veins. Increases in resistance in the trabecular meshwork and/or the inner wall of Schlemm canal can disrupt the balance of aqueous humor inflow and outflow, resulting in an increase in IOP and glaucoma risk.

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, 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 (eg, leaks or bleb-related endophthalmitis) and long-term failure. Other surgical procedures (not addressed in this policy) include trabecular laser ablation, deep sclerectomy, (which removes the outer wall of Schlemm's canal and excises deep sclera and peripheral cornea), and viscocanalostomy (which unroofs and dilates Schlemm's canal without penetrating the trabecular meshwork or anterior chamber).

More recently the Trabectome™‡, an electrocautery device with irrigation and aspiration, has been used to selectively ablate the trabecular meshwork and inner wall of Schlemm's canal without external access or creation of a subconjunctival bleb. IOP with this ab interno procedure is typically higher than the pressure achieved with standard filtering trabeculectomy. Canaloplasty involves dilation and tension of Schlemm's canal with a suture loop between the inner wall of the canal and the trabecular meshwork. This ab externo procedure uses the iTrack™‡ illuminated microcatheter (iScience Interventional) to access and dilate the entire length of Schlemm's canal and to pass the suture loop through the canal.

Aqueous shunts may also be placed in the anterior or posterior chamber to facilitate drainage of aqueous humor. Established shunts include the Ahmed™‡ (New World Medical), Baerveldt®‡ (Advanced Medical Optics), Molteno®‡ (IOP), EX-PRESS®‡ mini-shunt (Alcon); and the SOLX®‡ DeepLight®‡ Gold Micro-Shunt (SOLX), which shunts aqueous humor between the anterior chamber and the suprachoroidal space. These devices differ depending on explant surface areas, shape, plate thickness, the presence or absence of a valve, and details of surgical installation. Generally, the risk of hypotony (low pressure) is reduced with aqueous shunts in comparison with trabeculectomy, but IOP outcomes are higher 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 less than after trabeculectomy, and failure rates are similar, with about 10% of devices failing each year. The primary indication for aqueous shunts is when prior medical or surgical therapy has failed, 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.

Other aqueous stents are being developed as minimally penetrating methods to drain aqueous humor from the anterior chamber into the Schlemm canal or the suprachoroidal space. These include the iStent®‡ (Glaukos), which is a 1-mm long stent inserted into the end of the Schlemm canal by an internal approach through the cornea and anterior chamber; the second generation iStent *inject*®‡ the third generation iStent

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supra®‡, which is designed for ab interno implantation into the suprachoroidal space; and the CyPass®‡ (Transcend Medical) suprachoroidal stent.

Since aqueous humor outflow is pressure-dependent, the pressure in the reservoir and venous system are critical for reaching the target IOP. Therefore, some devices may be unable to reduce IOP below the pressure of the distal outflow system used, eg, below 15 mm Hg, and are not indicated for patients for whom very low IOP is desired (eg, 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 for patients with glaucoma who require cataract surgery. An advantage of ab interno shunts is that they may be inserted into the same incision and at the same time as cataract surgery. In addition, most devices do not preclude subsequent trabeculectomy if needed. It may also be possible to insert more than 1 shunt to achieve the desired IOP. Therefore, health outcomes of interest are the IOP achieved, reduction in medications, ability to convert to trabeculectomy, complications, and durability of the device.

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration

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 FDA through the 510(k) process between 1989 and 1993; modified Ahmed and Molteno devices were cleared in 2006. Their indication for use is "in patients with intractable glaucoma to reduce intraocular pressure where medical and conventional surgical treatments have failed." The AquaFlow™‡ Collagen Glaucoma Drainage Device was approved by FDA through the premarket approval process for the maintenance of the subscleral space following nonpenetrating deep sclerectomy. The EX-PRESS Mini Glaucoma Shunt was cleared for marketing by FDA through the 510(k) process in 2003. 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.

Table 1. Regulatory Status of Aqueous Shunts and Stents

Device	Manufacturer	Type	FDA Status	Date
AquaFlow	Staar Surgical	Drainage device	PMA	2001
Trabectome	NeoMedix	Electrocautery device	510(k)	2006
Ahmed	New World Medical	Aqueous glaucoma shunt	510(k)	<1993
Baerveldt	Advanced Medical Optics	Aqueous glaucoma shunt	510(k)	<1993
Krupin	Eagle Vision	Aqueous glaucoma shunt	510(k)	<1993
Molteno	Molteno Ophthalmic	Aqueous glaucoma shunt	510(k)	<1993
EX-PRESS	Alcon	Mini-glaucoma shunt	510(k)	2003
iStent	Glaukos	Microstent	PMA	2012
CyPass	Transcend Medical	Suprachoroidal stent	PMA	2016
Hydrus	Ivantis	Microstent	Not approved	
SOLX Gold	SOLX	Micro-Shunt	Not approved	
iStent *inject*	Glaukos	Suprachoroidal stent	Not approved	
iStent *supra*	Glaukos	Suprachoroidal stent	Not approved	

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XEN Gel Stent	AqueSys	Subconjunctival	Not approved

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

In 2012, FDA approved the iStent Trabecular Micro-Bypass Stent through the premarket approval process 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 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 intraocular lens (IOL)
   - 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 circumstances 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.

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Centers for Medicare and Medicaid Services (CMS)
There is no national coverage determination (NCD) for aqueous shunts and stents for glaucoma. In the absence of an NCD, coverage decisions are left to the discretion of local Medicare carriers.

Rationale/Source

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), with a total of 1153 participants, on the Ahmed, Baerveldt, Molteno, and Schocket shunts. Trabeculectomy was found to result in a lower mean 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 1 shunt over another.

A technology assessment 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. It indicated that the IOP will generally settle at higher levels (approximately 18 mm Hg) with aqueous shunts than after standard trabeculectomy (14-16 mm Hg) or after trabeculectomy with antifibrotic agents 5-fluorouacil or mitomycin C (8-10 mm Hg). In 1 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 2 procedures were found to be similar (50%). The assessment concluded that based on level 1 evidence, 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 on glaucoma treatments, prepared for the Agency for Healthcare Research and Quality, found that available data 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 versus 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. The study included 212 eyes of 212 patients (18-85 years) who had previous trabeculectomy and/or cataract extraction with IOL 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 intention-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). 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 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 (N=63) and Wagschal et al (N=64). 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. 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. 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, 73 years) with cataracts and mild to moderate open-angle glaucoma (IOP ≤ 24 mm Hg controlled on 1-3 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 intention-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 end point. The proportion of patients achieving the secondary efficacy end point 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 (eg, 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, 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 end point, 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. Twenty-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 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. 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 the FDA
iStent inject
An industry-sponsored multicenter unblinded randomized trial compared implantation of 2 iStent *inject* devices versus 2 ocular hypotensive agents. 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 versus cataract surgery alone. 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. The group with the Hydrus Microstent was using significantly fewer medications (0.5 vs 1.0, $p=0.019$) and proportion of patients using no hypotensive medications was higher when the Hydrus Microstent was inserted at the time of cataract surgery (73% vs 38%, $p=0.001$).

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Other
Case series have been identified on the EyePass and CyPass microstent. The CyPass has not received FDA approval/clearance at this time. The EyePass is no longer being developed.

Ongoing and Unpublished Clinical Trials
Some currently unpublished trials that might influence this policy are listed in Table 2.

Table 2. Summary of Key Trials

NCT No.	Trial Name	Planned Enrollment	Completion Date
Ongoing			
NCT01282346[a]	Clinical Evaluation of the SOLX Gold Shunt for the Reduction of Intraocular Pressure (IOP) in Refractory Glaucoma	60	Dec 2015 (ongoing)
NCT02024464[a]	A Prospective, Multicenter, Randomized Comparison of the Hydrus Microstent to the iStent for Lowering Intraocular Pressure in Glaucoma Patients Undergoing Cataract Surgery	300	Jan 2017
NCT01444040[a]	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%	200	April 2017
NCT01456390	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	80	Apr 2017
NCT02023242[a]	A Prospective, Multicenter, Randomized Comparison of the Hydrus to the iStent® for Lowering Intraocular Pressure in Primary Open Angle Glaucoma	100	Jan 2018
NCT01461291[a]	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	1200	Oct 2018
NCT01461278[a]	A Prospective, Randomized, Single-Masked, Controlled, Parallel Groups, Multicenter Clinical Investigation of the Glaukos® Suprachoroidal Stent Model G3 In Conjunction With Cataract Surgery	1200	Apr 2019

NCT: national clinical trial.
[a] Denotes industry-sponsored or cosponsored trial.

Clinical Input Received Through Physician Specialty Societies and Academic Medical Centers
While the various physician specialty societies and academic medical centers may collaborate with and make recommendations during this process through the provision of appropriate reviewers, input received does not represent an endorsement or position statement by the physician specialty societies or academic medical centers, unless otherwise noted.

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In response to requests, input was received from 1 physician specialty societies and 2 academic medical centers while this policy was under review in 2013. The input supported use of aqueous shunts in patients with moderate to severe glaucoma uncontrolled by medication. Input supported use of a single microstent in patients with mild to-moderate glaucoma undergoing cataract surgery to reduce side effects of medications and to avoid noncompliance.

Summary
The evidence for aqueous shunts in individuals who have open-angle glaucoma includes RCTs. Relevant outcomes are change in disease status, functional outcomes, medication use, and treatment-related morbidity. RCTs assessing 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 qualitatively 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.

References

1. Blue Cross and Blue Shield Association, Medical Policy Reference Manual, "Aqueous Shunts and Stents for Glaucoma", 9.03.21, 3:2016.
2. Minckler DS, Vedula SS, Li TJ, et al. Aqueous shunts for glaucoma. *Cochrane Database Syst Rev.* 2006(2):CD004918. PMID 16625616
3. Minckler DS, Francis BA, Hodapp EA, et al. Aqueous shunts in glaucoma: a report by the American Academy of Ophthalmology. *Ophthalmology.* Jun 2008;115(6):1089-1098. PMID 18519069
4. Boland MV, Ervin AM, Friedman D, et al. *Treatment for Glaucoma: Comparative Effectiveness. Comparative Effectiveness Review No. 60. (Prepared by the Johns Hopkins University Evidence-based Practice Center under Contract No. HHSA 290-2007-10061-I.) AHRQ Publication No. 12-EHC038-EF.* Rockville, MD: Agency for Healthcare Research and Quality; 2012.
5. Gedde SJ, Schiffman JC, Feuer WJ, et al. Treatment outcomes in the Tube Versus Trabeculectomy (TVT) study after five years of follow-up. *Am J Ophthalmol.* May 2012;153(5):789-803 e782. PMID 22245458
6. Netland PA, Sarkisian SR, Jr., Moster MR, et al. Randomized, prospective, comparative trial of EX-PRESS glaucoma filtration device versus trabeculectomy (XVT study). *Am J Ophthalmol.* Feb 2014;157(2):433-440 e433. PMID 24210765
7. de Jong LA. The Ex-PRESS glaucoma shunt versus trabeculectomy in open-angle glaucoma: a prospective randomized study. *Adv Ther.* Mar 2009;26(3):336-345. PMID 19337705
8. de Jong L, Lafuma A, Aguade AS, et al. Five-year extension of a clinical trial comparing the EX-PRESS glaucoma filtration device and trabeculectomy in primary open-angle glaucoma. *Clin Ophthalmol.* 2011;5:527-533. PMID 21607021

9. Gonzalez-Rodriguez JM, Trope GE, Drori-Wagschal L, et al. Comparison of trabeculectomy versus Ex-PRESS: 3-year follow-up. Br J Ophthalmol. Dec 16 2015. PMID 26674779
10. Wagschal LD, Trope GE, Jinapriya D, et al. Prospective randomized study comparing Ex-PRESS to trabeculectomy: 1-year results. J Glaucoma. Oct-Nov 2015;24(8):624-629. PMID 24247999
11. Wang X, Khan R, Coleman A. Device-modified trabeculectomy for glaucoma. Cochrane Database Syst Rev. 2015;12:CD010472. PMID 26625212
12. U.S. Food and Drug Administration. FDA Executive Summary, Glaucos, Inc. iStent Trabecular Micro-Bypass Stent. 2010; http://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/MedicalDevices/MedicalDevicesAdvisoryCommittee/OphthalmicDevicesPanel/UCM220398.pdf.
13. Samuelson TW, Katz LJ, Wells JM, et al. Randomized evaluation of the trabecular micro-bypass stent with phacoemulsification in patients with glaucoma and cataract. *Ophthalmology.* Mar 2011;118(3):459-467. PMID 20828829
14. Craven ER, Katz LJ, Wells JM, et al. Cataract surgery with trabecular micro-bypass stent implantation in patients with mild-to-moderate open-angle glaucoma and cataract: Two-year follow-up. *J Cataract Refract Surg.* Aug 2012;38(8):1339-1345. PMID 22814041
15. Fea AM. Phacoemulsification versus phacoemulsification with micro-bypass stent implantation in primary open-angle glaucoma: randomized double-masked clinical trial. *J Cataract Refract Surg.* Mar 2010;36(3):407-412. PMID 20202537
16. Fea AM, Consolandi G, Zola M, et al. Micro-bypass implantation for primary open-angle glaucoma combined with phacoemulsification: 4-year follow-up. J Ophthalmol. 2015;2015:795357. PMID 26587282
17. Katz LJ, Erb C, Carceller GA, et al. Prospective, randomized study of one, two, or three trabecular bypass stents in open-angle glaucoma subjects on topical hypotensive medication. Clin Ophthalmol. 2015;9:2313-2320. PMID 26715834
18. Belovay GW, Naqi A, Chan BJ, et al. Using multiple trabecular micro-bypass stents in cataract patients to treat open-angle glaucoma. *J Cataract Refract Surg.* Nov 2012;38(11):1911-1917. PMID 22980724
19. Donnenfeld ED, Solomon KD, Voskanyan L, et al. A prospective 3-year follow-up trial of implantation of two trabecular microbypass stents in open-angle glaucoma. Clin Ophthalmol. 2015;9:2057-2065. PMID 26604675
20. Fea AM, Belda JI, Rekas M, et al. Prospective unmasked randomized evaluation of the iStent inject ((R)) versus two ocular hypotensive agents in patients with primary open-angle glaucoma. Clin Ophthalmol. 2014;8:875-882. PMID 24855336
21. Pfeiffer N, Garcia-Feijoo J, Martinez-de-la-Casa JM, et al. A Randomized Trial of a Schlemm's Canal Microstent with Phacoemulsification for Reducing Intraocular Pressure in Open-Angle Glaucoma. Ophthalmology. Jul 2015;122(7):1283-1293. PMID 25972254
22. Dietlein TS, Jordan JF, Schild A, et al. Combined cataract-glaucoma surgery using the intracanalicular Eyepass glaucoma implant: first clinical results of a prospective pilot study. *J Cataract Refract Surg.* Feb 2008;34(2):247-252. PMID 18242448
23. Hoeh H, Ahmed, II, Grisanti S, et al. Early postoperative safety and surgical outcomes after implantation of a suprachoroidal micro-stent for the treatment of open-angle glaucoma concomitant with cataract surgery. *J Cataract Refract Surg.* Mar 2013;39(3):431-437. PMID 23506920
24. American Glaucoma Society. Position statement on new glaucoma surgical procedures. 2012; http://www.americanglaucomasociety.net/professionals/policy_statements/new_glaucoma_surgical_procedures. Accessed July 7, 2015.
25. American Academy of Ophthalmology. Preferred practice pattern: Primary open-angle glaucoma 2010; http://one.aao.org/preferred-practice-pattern/primary-openangle-glaucoma-ppp--october-2010. Accessed July 7, 2015.
26. Francis BA, Singh K, Lin SC, et al. Novel glaucoma procedures: a report by the American Academy of Ophthalmology. Ophthalmology. Jul 2011;118(7):1466-1480. PMID 21724045
27. National Institute for Health and Clinical Evidence (NICE). Trabecular stent bypass microsurgery for open angle glaucoma. 2011; http://www.nice.org.uk/guidance/ipg396. Accessed July 7, 2015.

Policy History

Original Effective Date:	05/21/2014
Current Effective Date:	11/16/2016
05/01/2014	Medical Policy Committee review
05/21/2014	Medical Policy Implementation Committee approval. New policy.
09/04/2014	Medical Policy Committee review
09/17/2014	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
01/01/2015	Coding Update

Aqueous Shunts and Stents for Glaucoma

Policy # 00421
Original Effective Date: 05/21/2014
Current Effective Date: 11/16/2016

08/03/2015 Coding update: ICD10 Diagnosis code section added; ICD9 Procedure code section removed.
10/29/2016 Medical Policy Committee review
11/16/2015 Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
10/01/2016 Coding update
11/03/2016 Medical Policy Committee review
11/16/2016 Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
01/01/2017 Coding update: Removing ICD-9 Diagnosis Codes and CPT coding update
Next Scheduled Review Date: 11/2017

Coding

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Code Type	Code			
CPT	0191T, 0253T, 0376T, 66179, 66180, 66183, 66184, 66185, 66999 New codes eff 1/1/17: 0449T,0450T			
HCPCS	C1783			
ICD-10 Diagnosis	H40.001-H40.069	H40.10X0-H40.10X4	H40.1210-H40.1214	H40.1220-H40.1224
	H40.1230-H40.1234	H40.1290-H40.1294	H40.1310-H40.1314	H40.1320-H40.1324
	H40.1330-H40.1334	H40.1390-H40.1394	H40.1410-H40.1414	H40.1420-H40.1424
	H40.1430-H40.1434	H40.1490-H40.1494	H40.151-H40.159	H40.20X0-H40.20X4
	H40.211-H40.219	H40.2210-H40.2214	H40.2220-H40.2224	H40.2230-H40.2234
	H40.2290-H40.2294	H40.231-H40.239	H40.241-H40.249	H40.30X0-H40.30X4
	H40.31X0-H40.31X4	H40.32X0-H40.32X4	H40.33X0-H40.33X4	H40.40X0-H40.40X4
	H40.41X0-H40.41X4	H40.42X0-H40.42X4	H40.43X0-H40.43X4	H40.50X0-H40.50X4
	H40.51X0-H40.51X4	H40.52X0-H40.52X4	H40.53X0-H40.53X4	H40.60X0-H40.60X4

Aqueous Shunts and Stents for Glaucoma

Policy # 00421
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	H40.61X0-H40.61X4	H40.62X0-H40.62X4	H40.63X0-H40.63X4	H40.811-H40.819
	H40.821-H40.829	H40.831-H40.839	H40.89	H40.9
	H42	Q15.0		
	Codes deleted eff 10-1-16:	H40.11X0-H40.11X4		
	Codes added eff 10-1-16:	H40.111	H40.1110-H40.1114	H40.1120-H40.1124
		H40.1130-H40.1134	H40.1190-H40.1194	

*****Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

A. Whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. FDA and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or
B. Whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:
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    2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
    3. Reference to federal regulations.

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A. In accordance with nationally accepted standards of medical practice;
B. Clinically appropriate, in terms of type, frequency, extent, level of care, site and duration, and considered effective for the patient's illness, injury or disease; and
C. Not primarily for the personal comfort or convenience of the patient, physician or other health care provider, and not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.

For these purposes, "nationally accepted standards of medical practice" means standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, Physician Specialty Society recommendations and the views of Physicians practicing in relevant clinical areas and any other relevant factors.

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