# Protocol

# Aqueous Shunts and Stents for Glaucoma

(90321)

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| **Medical Benefit** | | **Effective Date**: 04/01/15 | **Next Review Date**: 11/18 |
| **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 | |

***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.*

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

## Description

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.

## Summary of Evidence

For individuals who have refractory open-angle glaucoma who receive aqueous shunts, the evidence includes randomized controlled trials (RCTs) and single-arm studies. 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 reduces intra-

ocular pressure (IOP) to slightly less than standard filtering surgery (trabeculectomy). Reported shunt success rates are as good as trabeculectomy in the long term. FDA-approved shunts have different adverse event profiles and avoid some of the most problematic complications of trabeculectomy. Two trials have compared the Ahmed and Baerveldt shunts. Both found that eyes treated with the Baerveldt shunt had slightly lower average IOP at five years than eyes treated with the Ahmed but the Baerveldt also had a higher rate of serious hypotony-related complications. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals who have mild-to-moderate open-angle glaucoma who receive aqueous microstents during cataract surgery, the evidence includes RCTs and safety data from case series. Relevant outcomes are change in disease status, functional outcomes, medication use, and treatment-related morbidity. Two microstents have received FDA approval for use in conjunction with cataract surgery for reduction of IOP in adults with mild-to-moderate open-angle glaucoma currently treated with ocular hypotensive medication. RCTs have been conducted in patients with cataracts and less advanced glaucoma, where IOP is at least partially controlled with medication. Trial results have shown that IOP may be lowered below baseline with 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 are treated with aqueous shunts or microstents, the evidence includes RCTs. Relevant outcomes are change in disease status, functional outcomes, medication use, and treatment-related morbidity. 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 multiple microstent group. One RCT compared two iStents to travoprost. The study did not report statistical comparisons. The evidence is insufficient to determine the effects of the technology on health outcomes.

## Policy

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**.

Implantation of a single FDA-approved micro-stent in conjunction with cataract surgery may be considered **medically necessary** in patients with mild to moderate open-angle glaucoma currently treated with ocular hypotensive medication.

Use of a micro-stent 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:

An anterior segment aqueous drainage device, without extraocular reservoir, performed with cataract surgery

(internal approach) may be **medically necessary** for Medicare Advantage members with mild to moderate glaucoma on medication.

**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, 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., 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).

The Trabectome, an electrocautery device with irrigation and aspiration, has been used to selectively ablate the trabecular meshwork and inner wall of the Schlemm 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 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 illuminated 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).

Aqueous shunts may also be placed in the anterior or posterior chamber to facilitate drainage of aqueous humor. Examples of ab externo shunts cleared by the FDA include the Ahmed (New World Medical), Baerveldt (Advanced Medical Optics), Molteno (IOP), and EX-Press mini-shunt (Alcon), 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 to 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.

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. They include the iStent (Glaukos), which is a one 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 *supra*, which is designed

for ab interno implantation into the suprachoroidal space; and the CyPass (Transcend Medical) suprachoroidal stent.

Because aqueous humor outflow is pressure-dependent, 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., less than 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 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 one shunt 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 was approved by FDA through the premarket approval (PMA) process for the maintenance of the subscleral space following nonpenetrating deep sclerectomy. In 2003, the ab externo EX-PRESS® Mini Glaucoma Shunt was cleared for marketing by 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 FDA through the 510(k) process as an ab interno aqueous shunt for management of refractory glaucoma. 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

| Device | Manufacturer | Type | FDA Status | Date |
|---|---|---|---|---|
| AquaFlow™ | Staar Surgical | Drainage device | PMA | 2001 |
| Trabectome™ | NeoMedix | Electrocautery device, ab interno | 510(k) | 2006 |
| Ahmed™ | New World Medical | Aqueous glaucoma shunt, ab externo | 510(k) | < 1993 |
| Baerveldt® | Advanced Medical Optics | Aqueous glaucoma shunt, ab externo | 510(k) | < 1993 |
| Krupin | Eagle Vision | Aqueous glaucoma shunt, ab externo | 510(k) | < 1993 |
| Molteno® | Molteno Ophthalmic | Aqueous glaucoma shunt, ab externo | 510(k) | < 1993 |
| EX-PRESS® | Alcon | Mini-glaucoma shunt, ab externo | 510(k) | 2003 |
| XEN® Gel Stent | AqueSys/Allergan | Aqueous glaucoma shunt, ab interno | 510(k) | 2016 |
| iStent® | Glaukos | Microstent, ab interno | PMA | 2012 |
| CyPass® | Transcend Medical | Suprachoroidal stent, ab interno | 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 | |

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

In 2012, the iStent® Trabecular Micro-Bypass Stent (Glaukos) was approved by 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 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 IOL [intraocular lens]
    - When implantation has been without concomitant cataract surgery with IOL implantation for visually significant cataract.

Note that use of the iStent® has subsequently been reported for many of the circumstances or conditions listed above; most of the publications are case series.

In 2016, the CyPass® Micro-Stent (Alcon Laboratories) was approved by FDA through the PMA process for use in combination with cataract surgery in adults with mild-to-moderate primary open-angle glaucoma.

The SOLX® DeepLight® Gold Micro-Shunt and Hydrus™ Microstent 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.

**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.

1. Minckler DS, Vedula SS, Li TJ, et al. Aqueous shunts for glaucoma. Cochrane Database Syst Rev. 2006(2):CD004918. PMID 16625616
2. 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
3. Boland MV, Ervin AM, Friedman D, et al. Treatment for Glaucoma: Comparative Effectiveness. Comparative Effectiveness Review No. 60 (AHRQ Publication No. 12-EHC038-EF). Rockville, MD: Agency for Healthcare Research and Quality; 2012.
4. 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
5. 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
6. 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
7. 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
8. 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
9. Gonzalez-Rodriguez JM, Trope GE, Drori-Wagschal L, et al. Comparison of trabeculectomy versus Ex-PRESS: 3-year follow-up. Br J Ophthalmol. Sep 2016; 100(9):1269-1273. PMID 26674779
10. Wang X, Khan R, Coleman A. Device-modified trabeculectomy for glaucoma. Cochrane Database Syst Rev. 2015; 12:CD010472. PMID 26625212
11. Food and Drug Administration. Xen Glaucoma Treatment System 510(k). 2016; http://www.accessdata.fda.gov/cdrh_docs/pdf16/K161457.pdf. Accessed February 21, 2017.
12. Budenz DL, Barton K, Gedde SJ, et al. Five-year treatment outcomes in the Ahmed Baerveldt comparison study. Ophthalmology. Feb 2015; 122(2):308-316. PMID 25439606
13. Budenz DL, Feuer WJ, Barton K, et al. Postoperative complications in the Ahmed Baerveldt comparison study during five years of follow-up. Am J Ophthalmol. Mar 2016; 163:75-82 e73. PMID 26596400
14. Christakis PG, Kalenak JW, Tsai JC, et al. The Ahmed versus Baerveldt study: five-year treatment outcomes. Ophthalmology. Oct 2016; 123(10):2093-2102. PMID 27544023

15. 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. Accessed July 7, 2015.
16. 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
17. 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
18. 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
19. 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
20. Vold S, Ahmed, II, Craven ER, et al. Two-year COMPASS trial results: supraciliary microstenting with phaco-emulsification in patients with open-angle glaucoma and cataracts. Ophthalmology. Oct 2016; 123(10):2103-2112. PMID 27506486
21. Fernandez-Barrientos Y, Garcia-Feijoo J, Martinez-de-la-Casa JM, et al. Fluorophotometric study of the effect of the glaukos trabecular microbypass stent on aqueous humor dynamics. Invest Ophthalmol Vis Sci. Jul 2010; 51(7):3327-3332. PMID 20207977
22. 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
23. 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
24. 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
25. 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
26. 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
27. Vold SD, Voskanyan L, Tetz M, et al. Newly diagnosed primary open-angle glaucoma randomized to 2 trabecular bypass stents or prostaglandin: outcomes through 36 months. Ophthalmol Ther. Dec 2016; 5(2):161-172. PMID 27619225
28. 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.
29. Prum BE, Jr., Rosenberg LF, Gedde SJ, et al. Primary open-angle glaucoma Preferred Practice Pattern ((R)) guidelines. Ophthalmology. Jan 2016; 123(1):P41-p111. PMID 26581556
30. 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
31. National Institute for Health and Care Evidence (NICE). Trabecular stent bypass microsurgery for open angle glaucoma [IPG396]. 2011; http://www.nice.org.uk/guidance/ipg396. Accessed July 7, 2015.
32. National Institute for Health and Care Evidence (NICE). Trabecular stent bypass microsurgery for open-angle glaucoma [IPG575]. 2017; https://www.nice.org.uk/guidance/ipg575.

33. European Glaucoma Society. Terminology and Guidelines for Glaucoma. 4th ed. Savona, Italy: PubiComm; 2014.
34. National Government Services, Inc. (Primary Geographic Jurisdiction - Illinois, New York - Entire State, Connecticut, Massachusetts, Maine, New Hampshire, Rhode Island, Vermont, Wisconsin, Minnesota) Local Coverage Determination (LCD): Category III CPT® Codes (L33392), Revision Effective Date for services performed on or after 09/01/2017.