

(90321)

Medical Benefit		Effective Date: 04/01/20	Next Review Date: 01/23
Preauthorization	No	Review Dates: 03/10, 03/11, 07/11, 01/12, 09/12, 01/13, 01/14, 11/14, 11/15, 11/16, 11/17, 07/18, 01/19, 01/20, 01/21, 01/22	

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.

RELATED PROTOCOL

Viscocanalostomy and Canaloplasty

Populations	Interventions	Comparators	Outcomes
Individuals: • With refractory open-angle glaucoma	Interventions of interest are: • Ab externo aqueous shunts	Comparators of interest are: • Ocular medication • Trabeculectomy	Relevant outcomes include: • Change in disease status • Functional outcomes • Medication use • Treatment-related morbidity
Individuals: • With refractory open-angle glaucoma	Interventions of interest are: • Ab interno aqueous stents	Comparators of interest are: • Ocular medication • Trabeculectomy	Relevant outcomes include: • Change in disease status • Functional outcomes • Medication use • Treatment-related morbidity
Individuals: • With mild-to-moderate open-angle glaucoma who are undergoing cataract surgery	Interventions of interest are: • Aqueous microstents	Comparators of interest are: • Cataract surgery alone	Relevant outcomes include: • Change in disease status • Functional outcomes • Medication use • Treatment-related morbidity
Individuals: • With mild-to-moderate open-angle glaucoma who are not undergoing cataract surgery	Interventions of interest are: • Aqueous microstents as a stand-alone procedure	Comparators of interest are: • Standard of care	Relevant outcomes include: • Change in disease status • Functional outcomes • Medication use • Treatment-related morbidity

DESCRIPTION

Glaucoma surgery is intended to reduce intraocular pressure (IOP) when the target IOP cannot be reached using medications. Due to complications with established surgical approaches (e.g., trabeculectomy), a variety of shunts are being evaluated as alternative surgical treatments for patients with inadequately controlled glauco-

ma. Microstents are also being evaluated in patients with mild-to-moderate open-angle glaucoma (OAG) currently treated with ocular hypotensive medication.

SUMMARY OF EVIDENCE

For individuals who have refractory OAG who receive ab externo aqueous shunts, the evidence includes randomized controlled trials (RCTs), retrospective studies, and systematic reviews. Relevant outcomes are a 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 IOP to slightly less than standard filtering surgery (trabeculectomy). Reported shunt success rates show that these devices are noninferior to trabeculectomy in the long term. The FDA-approved shunts have different adverse event profiles and avoid some of the most problematic complications of trabeculectomy. Two trials have compared the Ahmed and Baerveldt shunts. Both found that eyes treated with the Baerveldt shunt had slightly lower average IOP at 5 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 an improvement in the net health outcome.

For individuals who have refractory OAG who receive ab interno aqueous stents, the evidence includes a non-randomized retrospective comparative study and several single-arm studies. Relevant outcomes are a change in disease status, functional outcomes, medication use, and treatment-related morbidity. The comparative study reported that patients receiving the stent experienced similar reductions in IOP and medication use as patients undergoing trabeculectomy. The single-arm studies, with 12-month follow-up results, consistently showed that patients receiving the stents experienced reductions in IOP and medication use. Reductions in IOP ranged from 4 mm Hg to over 15 mm Hg. In addition, the FDA has given clearance to a gel stent based on equivalent IOP and medication use reductions as seen with ab externo shunts. Clearance for the stent was based on a review in which the FDA concluded that while there were technical differences between the stent and predicate devices (shunts), the differences did not affect safety and effectiveness in lowering IOP and medication use. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have mild-to-moderate OAG who are undergoing cataract surgery who receive aqueous microstents, the evidence includes RCTs and meta-analyses of RCTs. Relevant outcomes are a change in disease status, functional outcomes, medication use, and treatment-related morbidity. Implantation of 1 or 2 microstents has received the FDA approval for use in conjunction with cataract surgery for reduction of IOP in adults with mild-to-moderate OAG currently treated with ocular hypotensive medication. When compared to cataract surgery alone, the studies showed modest but statistically significant decreases in IOP and medication use through the first 2 years when stents were implanted in conjunction with cataract surgery. A decrease in topical medication application is considered to be an important outcome for patients and reduces the problem of non-compliance that can affect visual outcomes. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

For individuals with mild-to-moderate OAG who are not undergoing cataract surgery who receive aqueous microstents as a stand-alone procedure, the evidence includes RCTs and a systematic review of 3 heterogeneous RCTs. Relevant outcomes are a change in disease status, functional outcomes, medication use, and treatment-related morbidity. Several RCTs have evaluated the use of multiple microstents but comparators differed. Two RCTs indicate that implantation of a microstent can reduce IOP at a level similar to ocular medications at 12-month follow-up. Reduction in medications is an important outcome for patients with glaucoma. Whether microstents remain patent after 12 months is uncertain, and whether additional stents can subsequently be safely implanted is unknown. Some evidence on longer-term outcomes is provided by an RCT that compared implantation of a single iStent to implantation of multiple iStents. At longer-term (42-month) follow-up, the need for additional medication increased in eyes implanted with a single microstent but not with multiple microstents. The

durability of multiple iStents is unknown. A fourth RCT compared implantation of the Hydrus microstent to 2 iStents. Outcomes from the Hydrus microstent were significantly better than 2 iStents, both statistically and clinically, for all outcome measures. The primary limitation of this study is that the duration of follow-up in the present publication is limited to 12 months. Longer-term follow-up from this study is continuing and will answer important questions on the durability of the procedure. Corroboration in an independent study and comparison with a medical therapy control group would also increase confidence in the results. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

POLICY

Insertion of ab externo aqueous shunts approved by the U.S. Food and Drug Administration (FDA) may be considered **medically necessary** as a method to reduce intraocular pressure in patients with glaucoma where medical therapy has failed to adequately control intraocular pressure.

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

Insertion of ab interno aqueous stents approved by the FDA as a method to reduce intraocular pressure in patients with glaucoma where medical therapy has failed to adequately control intraocular pressure, is considered **medically necessary**.

Implantation of one or two FDA-approved ab interno stents in conjunction with cataract surgery may be considered **medically necessary** in patients with mild to moderate open-angle glaucoma treated with ocular hypotensive medication.

Use of ab interno stents for all other indications is considered **investigational**.

POLICY GUIDELINES

Shunts and stents are only able to reduce intraocular pressure to the mid-teens, and may be inadequate when very low intraocular pressure is needed to reduce glaucoma damage.

MEDICARE ADVANTAGE

For Medicare Advantage, the above statements apply, except for the following:

One XEN45 device per eye may be considered **medically necessary** for the management of refractory glaucoma, defined as prior failure of filtering/cilioablative procedure and/or uncontrolled IOP (progressive damage and mean diurnal medicated IOP ≥ 20 mm Hg) on maximally tolerated medical therapy (i.e., four classes or more of topical IOP-lowering medications, or fewer in the case of tolerability or efficacy issues).

One iStent, Hydrus or CyPass device per eye may be considered **medically necessary** for the treatment of adults with mild or moderate open-angle glaucoma and a cataract when the individual is currently being treated with an ocular hypotensive medication and the procedure is being performed in conjunction with cataract surgery.

For Medicare Advantage, the following procedures are considered **not medically necessary**:

- insertion of an anterior segment aqueous drainage device, without extraocular reservoir, internal approach, suprachoroidal space;
- insertion of an anterior segment aqueous drainage device, without extraocular reservoir, internal approach, into the trabecular meshwork; each additional device insertion;

- insertion of an aqueous drainage device, without extraocular reservoir, internal approach into the subconjunctival space; each additional device.

BACKGROUND

GLAUCOMA

Glaucoma is characterized by elevated intraocular pressure (IOP), which results in visual field loss and irreversible blindness if left untreated. 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

Ocular Medication

First-line treatment typically involves pharmacologic therapy. Topical medications either increase the aqueous outflow (prostaglandins, alpha-adrenergic agonists, cholinergic agonists, Rho-kinase inhibitors) or decrease aqueous production (alpha-adrenergic agonists, beta-blockers, carbonic anhydrase inhibitors). Pharmacologic therapy may involve multiple medications, have potential side effects, and may be inconvenient for older adults or incapacitated patients.

Surgery

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

Insertion of shunts from outside the eye (ab externo) is another surgical option to lower IOP. Examples of ab externo devices cleared by the U.S. Food and Drug Administration (FDA) include the Ahmed, Baerveldt, Molteno, and EX-PRESS mini-shunt, which shunt aqueous humor between the anterior chamber and the suprachoroidal space. These devices differ by explant surface areas, shape, plate thickness, presence or absence of a valve, and details of surgical installation. Generally, the risk of hypotony (low pressure) is reduced with aqueous shunts compared with trabeculectomy, but IOP outcomes are worse than after standard guarded filtration surgery. 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.

Minimally Invasive Glaucoma Surgeries

Minimally invasive glaucoma surgeries (MIGS) are alternative, less invasive techniques that are being developed and evaluated. MIGS, which use microscopic-sized equipment and smaller incisions, involves less surgical manipulation of the sclera and the conjunctiva compared with other surgical techniques. There are several categories of MIGS: miniaturized trabeculectomy, trabecular bypass, milder laser photocoagulation, and totally internal or suprachoroidal stents. Shunts and stents can be administered through an external flap of the conjunctiva and sclera (ab externo) or in a small incision in the cornea with the devices inserted through the anterior chamber of the eye (ab interno). Some ab interno microstents may be inserted with injectors.

Examples of ab externo devices are the Ahmed, Baerveldt, and EX-PRESS shunts. Examples of ab interno devices either approved or given marketing clearance by the FDA include the iStent, which is a 1-mm long stent inserted into the end of the Schlemm canal through the cornea and anterior chamber, iStent inject, and XEN gelatin stent.

Because aqueous humor outflow is pressure-dependent, the pressure in the reservoir and venous system is critical for reaching the target IOP. Therefore, some devices may be unable to reduce IOP below the pressure of the distal outflow system used (e.g., <15 mm Hg) and are not indicated for patients for whom very low IOP is desired (e.g., those with advanced glaucoma). It has been proposed that stents such as the iStent, iStent inject, and Hydrus Microstent may be useful in patients with early-stage glaucoma to reduce the burden of medications and problems with compliance. One area of investigation is patients with glaucoma who require cataract surgery. An advantage of ab interno stents is that they may be inserted into the same incision and at the same time as cataract surgery. Also, most devices do not preclude subsequent trabeculectomy if needed. It may also be possible to insert more than 1 stent to achieve desired IOP.

REGULATORY STATUS

The regulatory status of the various ab externo and ab interno aqueous shunts and microstents are summarized in Table 1.

The first-generation Ahmed™ (New World Medical), Baerveldt® (Advanced Medical Optics), Krupin (Eagle Vision), and Molteno® (Molteno Ophthalmic) ab externo aqueous shunts were cleared for marketing by the FDA through the 510(k) process between 1989 and 1993; modified Ahmed and Molteno devices were cleared in 2006. They are indicated for use “in patients with intractable glaucoma to reduce IOP where medical and conventional surgical treatments have failed.” The AquaFlow™ Collagen Glaucoma Drainage Device (STAAR Surgical) was approved by the FDA through the premarket approval process for the maintenance of the subscleral space following nonpenetrating deep sclerectomy. In 2003, the ab externo EX-PRESS® Mini Glaucoma Shunt was cleared for marketing by the FDA through the 510(k) process.

In 2016, the XEN® Glaucoma Treatment System (Allergan), which consists of the XEN45 Gel Stent preloaded into the XEN Injector, was cleared for marketing by the FDA through the 510(k) process as an ab interno aqueous stent for management of refractory glaucoma. The approval was for patients with refractory glaucoma who failed previous surgical treatment or for patients with primary open-angle glaucoma unresponsive to maximum tolerated medical therapy. The FDA determined that this device was substantially equivalent to existing devices, specifically the Ahmed™ Glaucoma Valve and the EX-PRESS® Glaucoma Filtration Device.

In 2018, the first microstent, the iStent® Trabecular Micro-Bypass Stent preloaded into the iStent *inject* device (Glaukos) was approved by the FDA through the 515(d) process for use in conjunction with cataract surgery for the reduction of IOP in adults with mild-to-moderate OAG currently treated with ocular hypotensive medication.

In August 2018, Alcon announced an immediate voluntary recall of the CyPass microstent, which had been approved by the FDA in 2016 for use in conjunction with cataract surgery in adults with mild-to-moderate OAG.

The recall was based on 5 year postsurgery data from the COMPASS-XT long-term safety study. Results showed a statistically significant increase in endothelial cell loss among patients receiving the CyPass microstent compared with patients receiving cataract surgery alone.

Table 1. Regulatory Status of Aqueous Shunts and Stents

Device	Manufacturer	Type	FDA Status	Date
AquaFlow™	STAAR Surgical	Drainage device	PMA	2001
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; XEN injector	AqueSys/Allergan	Aqueous glaucoma stent, ab interno	510(k)	2016
iStent®; iStent inject®	Glaukos	Microstent, ab interno	515(d) in conjunction with cataract surgery	2018
iStent <i>supra</i> ®	Glaukos	Suprachoroidal stent	Not approved; in clinical trial	
CyPass®	Alcon	Suprachoroidal stent, ab interno	Company voluntarily recalled	2018
Hydrus™	Ivantis	Microstent, ab interno	PMA approval	2018
SOLX® Gold	SOLX	Micro-Shunt, ab externo	Not approved; in clinical trial	
Beacon Aqueous Microshunt	MicroOptx	Micro-Shunt, ab externo	Not approved; in clinical trial	
PRESERFLO® MicroShunt	Santan	Micro-Shunt, ab externo	Not approved; in clinical trial	
iStent Infinite	Glaukos	Micro-Shunt, ab externo	Not approved; in clinical trial	

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

FDA product codes: OGO, KYF.

Services that are the subject of a clinical trial do not meet our Technology Assessment and Medically Necessary Services Protocol criteria and are considered investigational. *For explanation of experimental and investigational, please refer to the Technology Assessment and Medically Necessary Services 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.* Apr 19 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):1089-98. 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.e2. PMID 22245458
5. Kotecha A, Feuer WJ, Barton K, et al. Quality of Life in the Tube Versus Trabeculectomy Study. *Am J Ophthalmol*. Apr 2017;176:228-235. PMID 28161049
6. Swaminathan SS, Jammal AA, Kornmann HL, et al. Visual Field Outcomes in the Tube Versus Trabeculectomy Study. *Ophthalmology*. Sep 2020;127(9):1162-1169. PMID 32327255
7. Wang X, Khan R, Coleman A. Device-modified trabeculectomy for glaucoma. *Cochrane Database Syst Rev*. Dec 01 2015;(12):CD010472. PMID 26625212
8. Netland PA, Sarkisian SR, 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.e3. PMID 24210765
9. de Jong LA. The Ex-PRESS glaucoma shunt versus trabeculectomy in open-angle glaucoma: a prospective randomized study. *Adv Ther*. Mar 2009;26(3):336-45. PMID 19337705
10. 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;5:527-33. PMID 21607021
11. 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):624-9. PMID 24247999
12. 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):1269-73. PMID 26674779
13. Konopinska J, Byszewska A, Saeed E, et al. Phacotrabeculectomy versus Phaco with Implantation of the Ex-PRESS Device: Surgical and Refractive Outcomes-A Randomized Controlled Trial. *J Clin Med*. Jan 22 2021; 10(3). PMID 33499300
14. Budenz DL, Barton K, Gedde SJ, et al. Five-year treatment outcomes in the Ahmed Baerveldt comparison study. *Ophthalmology*. Feb 2015;122(2):308-16. PMID 25439606
15. 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.e3. PMID 26596400
16. Christakis PG, Kalenak JW, Tsai JC, et al. The Ahmed Versus Baerveldt Study: Five-Year Treatment Outcomes. *Ophthalmology*. Oct 2016;123(10):2093-102. PMID 27544023
17. Christakis PG, Zhang D, Budenz DL, et al. Five-Year Pooled Data Analysis of the Ahmed Baerveldt Comparison Study and the Ahmed Versus Baerveldt Study. *Am J Ophthalmol*. Apr 2017;176:118-126. PMID 28104418
18. Schlenker MB, Gulamhusein H, Conrad-Hengerer I, et al. Efficacy, Safety, and Risk Factors for Failure of Stand alone Ab Interno Gelatin Microstent Implantation versus Standalone Trabeculectomy. *Ophthalmology*. Nov 2017;124(11):1579-1588. PMID 28601250
19. Wagner FM, Schuster AK, Emmerich J, et al. Efficacy and safety of XEN(R)-Implantation vs. trabeculectomy: Data of a "real-world" setting. *PLoS One*. 2020;15(4):e0231614. PMID 32310972
20. Stoner AM, Capitena Young CE, SooHoo JR, et al. A Comparison of Clinical Outcomes After XEN Gel Stent and EX-PRESS Glaucoma Drainage Device Implantation. *J Glaucoma*. Jun 01 2021;30(6):481-488. PMID 34060508
21. Gabbay IE, Goldberg M, Allen F, et al. Efficacy and safety data for the Ab interno XEN45 gel stent implant at 3 Years: A retrospective analysis. *Eur J Ophthalmol*. May 02 2021;11206721211014381. PMID 33938304
22. Le JT, Bicket AK, Wang L, et al. Ab interno trabecular bypass surgery with iStent for open-angle glaucoma. *Cochrane Database Syst Rev*. Mar 28 2019;3:CD012743. PMID 30919929
23. Healey PR, Clement CI, Kerr NM, et al. Standalone iStent Trabecular Micro-bypass Glaucoma Surgery: A Systematic Review and Meta-Analysis. *J Glaucoma*. Jul 01 2021;30(7):606-620. PMID 33596009

24. 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):459-67. PMID 20828829
25. 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):1339-45. PMID 22814041
26. Samuelson TW, Sarkisian SR, Lubeck DM, et al. Prospective, Randomized, Controlled Pivotal Trial of an Ab Interno Implanted Trabecular Micro-Bypass in Primary Open-Angle Glaucoma and Cataract: Two-Year Results. *Ophthalmology*. Jun 2019;126(6):811-821. PMID 30880108
27. Hooshmand J, Rothschild P, Allen P, et al. Minimally invasive glaucoma surgery: Comparison of iStent with iStent inject in primary open angle glaucoma. *Clin Exp Ophthalmol*. Sep 2019;47(7):898-903. PMID 31034687
28. Al Yousef Y, Strzalkowska A, Hillenkamp J, et al. Comparison of a second-generation trabecular bypass (iStent inject) to ab interno trabeculectomy (Trabectome) by exact matching. *Graefes Arch Clin Exp Ophthalmol*. Dec 2020;258(12):2775-2780. PMID 32960322
29. Salimi A, Watt H, Harasymowycz P. Three-Year Outcomes of Second-generation Trabecular Micro-bypass Stents (iStent inject) With Phacoemulsification in Various Glaucoma Subtypes and Severities. *J Glaucoma*. Mar 01 2021;30(3):266-275. PMID 33105306
30. Otarola F, Virgili G, Shah A, et al. Ab interno trabecular bypass surgery with Schlemms canal microstent (Hydrus) for open angle glaucoma. *Cochrane Database Syst Rev*. Mar 09 2020;3:CD012740. PMID 32147807
31. 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):1283-93. PMID 25972254
32. Samuelson TW, Chang DF, Marquis R, et al. A Schlemm Canal Microstent for Intraocular Pressure Reduction in Primary Open-Angle Glaucoma and Cataract: The HORIZON Study. *Ophthalmology*. Jan 2019;126(1):29-37. PMID 29945799
33. Ahmed IK, Fea A, Au L, et al. A Prospective Randomized Trial Comparing Hydrus and iStent Microinvasive Glaucoma Surgery Implants for Standalone Treatment of Open-Angle Glaucoma: The COMPARE Study. *Ophthalmology*. Jan 2020;127(1):52-61. PMID 31034856
34. Fea AM, Ahmed II, Lavia C, et al. Hydrus microstent compared to selective laser trabeculoplasty in primary open angle glaucoma: one year results. *Clin Exp Ophthalmol*. Mar 2017;45(2):120-127. PMID 27449488
35. Fea AM, Belda JJ, 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; 8:875-82. PMID 24855336
36. 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
37. Berdahl J, Voskanyan L, Myers JS, et al. iStent inject trabecular micro-bypass stents with topical prostaglandin as standalone treatment for open-angle glaucoma: 4-year outcomes. *Clin Exp Ophthalmol*. Aug 2020; 48(6):767-774. PMID 32311201
38. Lindstrom R, Sarkisian SR, Lewis R, et al. Four-Year Outcomes of Two Second-Generation Trabecular Micro-Bypass Stents in Patients with Open-Angle Glaucoma on One Medication. *Clin Ophthalmol*. 2020;14:71-80. PMID 32021070
39. 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;9:2313-20. PMID 26715834
40. Katz LJ, Erb C, Carceller Guillamet A, et al. Long-term titrated IOP control with one, two, or three trabecular micro-bypass stents in open-angle glaucoma subjects on topical hypotensive medication: 42-month outcomes. *Clin Ophthalmol*. 2018;12:255-262. PMID 29440867

41. Prum BE, Rosenberg LF, Gedde SJ, et al. Primary Open-Angle Glaucoma Preferred Practice Pattern((R)) Guidelines. *Ophthalmology*. Jan 2016;123(1):P41-P111. PMID 26581556
42. Fellman RL, Mattox C, Singh K, et al. American Glaucoma Society Position Paper: Microinvasive Glaucoma Surgery. *Ophthalmol Glaucoma*. Jan 2020;3(1):1-6. PMID 32672638
43. 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>. Accessed August 5, 2021.
44. National Institute for Health and Care Excellence. Microinvasive subconjunctival insertion of a trans-scleral gelatin stent for primary open-angle glaucoma. [IPG612]. 2018; <https://www.nice.org.uk/guidance/ipg612/chapter/1-Recommendations>. Accessed August 5, 2021.
45. National Government Services, Inc. (Primary Geographic Jurisdiction 06 & K - Illinois, Minnesota, Wisconsin, Connecticut, New York - Entire State, Maine, Massachusetts, New Hampshire, Rhode Island, Vermont) Local Coverage Determination (LCD): Micro-Invasive Glaucoma Surgery (MIGS) (L37244), Revision Effective Date for services performed on or after 12/01/2019.
46. National Government Services, Inc. (Primary Geographic Jurisdiction 06 & K - Illinois, Minnesota, Wisconsin, Connecticut, New York - Entire State, Maine, Massachusetts, New Hampshire, Rhode Island, Vermont) Local Coverage Article: Billing and Coding: Micro-Invasive GLAUCOMA Surgery (MIGS) (A56588), Revision Effective Date 12/01/2019.