For dates of service on or after August 1, 2022, refer to LCD L37531.

BlueCross BlueShield of Alabama

Name of Blue Advantage Policy:

Aqueous Shunts and Stents for Glaucoma

Policy #: 324
Latest Review Date: September 2022
Category: Surgery

BACKGROUND:

Blue Advantage *medical policy does not conflict with Local Coverage Determinations (LCDs), Local Medical Review Policies (LMRPs) or National Coverage Determinations (NCDs) or with coverage provisions in Medicare manuals, instructions or operational policy letters. In order to be covered by Blue Advantage the service shall be reasonable and necessary under Title XVIII of the Social Security Act, Section 1862(a)(1)(A). The service is considered reasonable and necessary if it is determined that the service is:*

1. *Safe and effective;*
2. *Not experimental or investigational*;*
3. *Appropriate, including duration and frequency that is considered appropriate for the service, in terms of whether it is:*
   - *Furnished in accordance with accepted standards of medical practice for the diagnosis or treatment of the patient's condition or to improve the function of a malformed body member;*
   - *Furnished in a setting appropriate to the patient's medical needs and condition;*
   - *Ordered and furnished by qualified personnel;*
   - *One that meets, but does not exceed, the patient's medical need; and*
   - *At least as beneficial as an existing and available medically appropriate alternative.*

Routine costs of qualifying clinical trial services with dates of service on or after September 19, 2000 which meet the requirements of the Clinical Trials NCD are considered reasonable and necessary by Medicare. Providers should bill* ***Original Medicare* *for covered services that are related to* ***clinical trials*** *that meet Medicare requirements (Refer to Medicare National Coverage Determinations Manual, Chapter 1, Section 310 and Medicare Claims Processing Manual Chapter 32, Sections 69.0-69.11).*

POLICY:

For dates of service on or after August 1, 2022:
Refer to LCD L37531.

Effective for dates of service March 24, 2020, through July 31, 2022:
For **0191T, 0376T, 0449T and 0450T**, refer to Local Coverage Determination (LCD): Micro-Invasive Glaucoma Surgery (MIGS) (L37531)

For **0253T and 0474T**, refer to criteria below:

Blue Advantage will treat **insertion of ab externo aqueous shunts approved by the U.S. Food and Drug Administration (FDA)** as a **covered benefit** as a method to reduce intraocular pressure in individuals with glaucoma where medical therapy has failed to adequately control intraocular pressure.

Blue Advantage will treat **use of an ab externo aqueous shunt for all other conditions,** including in individuals with glaucoma when intraocular pressure is adequately controlled by medications, as a **non-covered benefit** and **investigational**.

Blue Advantage will treat **insertion of ab interno aqueous stents approved by the Food and Drug Administration** as a method to reduce intraocular pressure in individuals with glaucoma, where medical therapy has failed to adequately control intraocular pressure, as a **covered benefit**.

Blue Advantage will treat **implantation of 1 or 2 FDA-approved ab interno stents in conjunction with cataract surgery** as a **covered benefit** in individuals with mild to moderate open-angle glaucoma currently treated with ocular hypotensive medication.

Blue Advantage will treat use of **ab interno stents for all other conditions** as a **non-covered benefit** and as **investigational**.

Effective for dates of service prior to March 24, 2020:
For 0191T, 0376T, 0449T and 0450T, refer to Local Coverage Determination (LCD): Micro-Invasive Glaucoma Surgery (MIGS) (L37531)

For 0253T and 0474T, refer to LCD for Non-covered Category III CPT Codes (L34555)

Blue Advantage does not approve or deny procedures, services, testing, or equipment for our members. Our decisions concern coverage only. The decision of whether or not to have a certain test, treatment or procedure is one made between the physician and his/her patient. Blue Advantage administers benefits based on the members' contract and medical policies. Physicians should always exercise their best medical judgment in providing the care they feel is most

appropriate for their patients. Needed care should not be delayed or refused because of a coverage determination.

DESCRIPTION OF PROCEDURE OR SERVICE:

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 and stents are being evaluated as alternative surgical treatments for patients with inadequately controlled glaucoma. Micro stents are also being evaluated in patients with mild-to-moderate open-angle glaucoma (OAG) currently treated with ocular hypotensive medication.

Glaucoma

Glaucoma is the leading cause of irreversible blindness worldwide and is characterized by elevated intraocular pressure (IOP). In 2020, glaucoma affected approximately 52.7 million individuals globally, with a projected increase to 79.8 million in 2040. Glaucoma has been reported to be seven times more likely to cause blindness and 15 times more likely to cause visual impairment in Black individuals as compared to White individuals. In the U.S. in 2010, Black individuals had the highest prevalence rate of primary open angle glaucoma at 3.4% compared to 1.7% among White individuals.

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 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 intraocular pressure (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 sub-conjunctival space. This procedure creates a sub-conjunctival 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 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 the

Schlemm canal and excises deep sclera and peripheral cornea), and viscocanalostomy, (which removes 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 micro-catheter (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 supra-choroidal 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 micro stents 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 FDA include the iStent, which is a one mm long stent inserted into the end of the Schlemm canal through the cornea and anterior chamber, iStent inject, and XEN gelatin stent.

Because 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, (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 Micro stent may be useful to lower IOP in patients with early-stage glaucoma to reduce the burden of medications and problems with compliance. One area of investigation are 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. In addition, most devices do not preclude subsequent trabeculectomy if needed. It may also be possible to insert more than one stent to achieve the desired IOP.

KEY POINTS:

The most recent literature review was updated through July 29, 2022.

Summary of Evidence

For individuals who have refractory OAG who receive ab externo aqueous shunts, the evidence includes RCTs, retrospective studies, and systematic reviews. Relevant outcomes are a change in disease status, functional outcomes, medication use, and treatment-related morbidity. Randomized controlled trials assessing FDA-approved shunts have shown 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 non-inferior 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 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 an improvement in the net health outcome.

For individuals who have refractory OAG who receive ab interno aqueous stents, the evidence includes systematic reviews, a nonrandomized 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 four 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 micro stents, 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 one or two micro stents has received 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 two 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 micro stents as a stand-alone procedure, the evidence includes RCTs and a systematic review of three 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 micro stents, but comparators differed. Two RCTs indicate that implantation of a micro stent 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 micro stents 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 micro stent but not with multiple micro stents. The durability of multiple iStents is unknown. A fourth RCT compared implantation of the Hydrus micro stent to two iStents. Outcomes from the Hydrus micro stent were significantly better than two iStents, both statistically and clinically, for all outcome measures. The primary limitation of this study is that the duration of follow-up in the 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.

Practice Guidelines and Position Statements
The purpose of the following information is to provide reference material. Inclusion does not imply endorsement or alignment with the evidence review conclusions.

Guidelines or position statements will be considered for inclusion in ‘Supplemental Information' if they were issued by, or jointly by, a US professional society, an international society with US representation, or National Institute for Health and Care Excellence (NICE). Priority will be given to guidelines that are informed by a systematic review, include strength of evidence ratings, and include a description of management of conflict of interest.

American Academy of Ophthalmology (AAO)
The American Academy of Ophthalmology (AAO, 2008) published a technology assessment on commercially available aqueous shunts, including the Ahmed, Baerveldt, Krupin, and Molteno devices, which was last reviewed for currency in 2014. The assessment indicated that, in general, intraocular pressure (IOP) would settle at higher levels (approximately 18 mm Hg) with shunts than after standard trabeculectomy (14 to 16 mm Hg). Five-year success rates of 50% have been found for the two procedures, indicating that aqueous shunts are comparable with trabeculectomy for IOP control and duration of benefit (based on Level I evidence; well-designed randomized controlled trials). The assessment indicated that although aqueous shunts have been generally reserved for intractable glaucoma when prior medical or surgical therapy has failed, indications for shunts have broadened (based on Level III evidence; case series, case reports, and poor-quality case-control or cohort studies). The AAO concluded that, based on Level I evidence, aqueous shunts offer a valuable alternative to standard filtering surgery or to cyclodestructive therapy for many patients with refractory glaucoma.

In 2020, the AAO updated its preferred practice pattern on primary open-angle glaucoma (POAG). The document notes that aqueous shunts have traditionally been used to manage medically uncontrolled glaucoma when trabeculectomy has failed to control IOP or is deemed unlikely to succeed; however, the indications for using aqueous shunts have been broadening, and these devices are being increasingly used in the surgical management of glaucoma. The preferred practice pattern notes that "several studies have compared aqueous shunts with trabeculectomy" and that the "selection of aqueous shunts or trabeculectomy should be left to the discretion of the treating ophthalmologist, in consultation with the individual patient."

American Glaucoma Society
In 2020, the American Glaucoma Society published a position paper on micro invasive glaucoma surgery. The Society supports efforts that facilitate patient access to these procedures, including more flexible regulatory pathways for new devices, expansion of the indications for already approved devices, and greater availability of information obtained by regulatory authorities.

National Institute for Health and Care Excellence
The National Institute for Health and Care Excellence (2017) updated guidance on trabecular stent by-pass microsurgery for open-angle glaucoma (OAG). The guidance stated that “Current evidence on trabecular stent bypass microsurgery for open-angle glaucoma raises no major safety concerns. Evidence of efficacy is adequate in quality and quantity.

The National Institute for Health and Care Excellence (2018) published a guidance entitled "Micro invasive Sub-conjunctival Insertion of a Trans-scleral Gelatin Stent for POAG". The guidance states that evidence is limited in quantity and quality and therefore, the procedure should only be used with special arrangements and that patients should be informed of the uncertainty of the procedure.

U.S. Preventative Services Task Force Recommendations
Not applicable.

KEY WORDS:
Eyepass, Hydrus Micro stent, iStent, trabecular shunt, Trabectome, Solx gold shunt, SOLX Gold Shunt, Ex-PRESS®, AquaFlow™, Ahmed™, Baerveldt, Krupin, Molteno®, iStent supra, Cy Pass, aqueous shunt, trabecular stent, micro-stent, iStent® Trabecular Micro-Bypass Stent, XEN Ab interno, ab externo, Hydrus, iStent inject

APPROVED BY GOVERNING BODIES:
The regulatory status of the various aqueous shunts and micro stents is summarized in the table below.

The first generation Ahmed™ (New World Medical), Baerveldt® (Advanced Medial Optics), Krupin (Eagle Vision), and Molteno® (Molteno Ophthalmic) ab externo aqueous shunts were cleared for marketing by the U.S. Food and Drug Administration (FDA) through the 510(k)

process between 1989 and 1993; modified Ahmed and Molteno devices were most recently 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 (STARR Surgical) was approved by FDA through the premarket approval process for the maintenance of the subscleral space following non-penetrating deep sclerectomy. In 2003, the ab externo EX-PRESS® Mini Glaucoma Shunt was cleared for marketing by 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 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 micro stent, the iStent® Trabecular Micro-Bypass Stent preloaded into the iStent inject device (Glaukos) was approved by FDA through the 515(d) 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.

In August 2018, Alcon announced an immediate voluntary recall of the CyPass micro stent, which had been approved by the FDA in 2016 for use in conjunction with cataract surgery in adults with mild to moderate open angle glaucoma (OAG). The recall was based on five-year post-surgery data from the COMPASS- XT long-term safety study. Results showed a statistically significant increase in endothelial cell loss among patients receiving the CyPass micro stent compared with patients receiving cataract surgery alone.

Table. 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®	Molento 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	Micro sent, ab interno	515(d) in conjunction with cataract surgery	2018
iStent supra®	Glaukos	Suprachoroidal stent	Not Approved; in clinical trial	
CyPass®	Alcon	Suprachoroidal stent, ab interno	Company voluntarily recalled	2018
Hydrus™	Ivantis	Micro stent, ab interno	PMA approval, in conjunction with cataract surgery	2018
Beacon Aqueous Microshunt	MicroOptx	Micro-Shunt, ab externo	Not approved; in clinical trial	
PRESERFLO® Microshunt (previously InFocus)	Santan	Micro-Shunt, ab externo	Not approved; in clinical trial	
iStent Infinate	Glaukos	Micro stent, ab interno	Not approved; in clinical trial	

FDA: Food and Drug Administration; PMA: premarket approval.
FDA product codes: OGO, KYF.

BENEFIT APPLICATION:

Coverage is subject to member's specific benefits. Group specific policy will supersede this policy when applicable.

CURRENT CODING:

CPT Codes:

66183	Insertion of anterior segment aqueous drainage device, without extraocular reservoir, external approach
66989	Complex extracapsular cataract removal with insertion of intraocular lens prosthesis requiring devices or techniques not generally used in routine cataract surgery or performed on patients in the amblyogenic developmental stage; including drainage device insertion, one or more (Effective 01/01/22)
66991	Extracapsular cataract removal with insertion of intraocular lens prosthesis with drainage device insertion, one or more (Effective 01/01/22)
0253T	Insertion of anterior segment aqueous drainage device, without extraocular reservoir; internal approach, into the suprachoroidal space
0449T	Insertion of aqueous drainage device, without extraocular reservoir, internal approach, into the sub-conjunctival space; initial device
0450T	; each additional device
0474T	Insertion of anterior segment aqueous drainage device, with creation of intraocular reservoir, internal approach, into the supraciliary space
0671T	Insertion of anterior segment aqueous drainage device into the trabecular meshwork, without external reservoir, and without concomitant cataract removal, one or more (Effective 01/01/22)

HCPCS Codes:

L8612	Aqueous Shunt

PREVIOUS CODING:

CPT Codes:

0191T	Insertion of anterior segment aqueous drainage device, without extraocular reservoir; internal approach, into the trabecular meshwork; initial insertion (Deleted 12/31/21)
0376T	Insertion of anterior segment aqueous drainage device, without extraocular reservoir,

	internal approach, into the trabecular meshwork; each additional device insertion (List separately in addition to code for primary procedure) (Deleted 12/31/21)

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POLICY HISTORY:

Adopted for Blue Advantage, July 2008
Available for comment August 2-September 15, 2008
Policy replaced by LCD L32569 effective June 15, 2010
Policy replaced by Article A48165 effective January 1, 2011
Medical Policy Group, January 2018
Available for comment January 25 through March 10, 2018
Medical Policy Group, April 2018
Available for comment April 12 through May 25, 2018
Medical Policy Group, June 2018 **(6)**: Updates to Description, Policy statement updated to distinguish ab interno vs ab externo, Key Points, Governing Bodies, Key words added (Ab interno, ab externo, Hydrus), L8612 added to Coding and References.
Medical Policy Group, April 2019
Medical Policy Group, September 2019
Medical Policy Group, September 2020
Medical Policy Group, September 2021
Medical Policy Group, November 2021
Medical Policy Group, September 2022

common medical practices in the treatment and diagnosis of disease as of the date hereof. Physicians and other providers are solely responsible for all aspects of medical care and treatment, including the type, quality, and levels of care and treatment.

This policy is intended to be used for adjudication of claims (including pre-admission certification, pre-determinations, and pre-procedure review)in Blue Cross and Blue Shield's administration of plans contracts.