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Policy

I. Aetna considers laser trabeculoplasty or Food and Drug Administration (FDA)-approved aqueous drainage/shunt implants medically necessary for the treatment of members with refractory primary open-angle glaucoma when first-line drugs (e.g., latanoprost or timolol) and second-line drugs (e.g., brimonidine or dorzolamide) have failed to control intra-ocular pressure (IOP). Currently available implants include:
   A. Ahmed glaucoma implant
   B. Baerveldt seton
   C. Ex-PRESS mini glaucoma shunt
   D. Glaucoma pressure regulator
   E. Krupin-Denver valve implant
   F. Molteno implant
   G. Schocket shunt

II. Aetna considers transciliary filtration (Fugo Blade transciliary filtration, Singh filtration) experimental and investigational for the treatment of glaucoma or any other indications because its effectiveness has not been established.

III. Aetna considers suprachoroidal drainage of aqueous humor (suprachoroidal shunt), anterior segment aqueous drainage devices without extra-ocular reservoir inserted by an internal approach, and other shunts (e.g., the DeepLight Gold Micro-Shunt (SOLX, Boston, MA), Eyepass Glaucoma Implant (GMP Companies, Inc., Fort Lauderdale, FL) that have not been approved by the FDA as experimental and investigational for the treatment of glaucoma because their effectiveness has not been established.

IV. Aetna considers iStent Trabecular Micro-Bypass Stent System medically necessary for the treatment of adults with mild or moderate open-angle glaucoma and a cataract when medication therapies have failed to control IOP.
V. Aetna considers the adjunctive use of anti-fibrotic agents (e.g., mitomycin C) medically necessary for use with the Ex-PRESS mini glaucoma shunt. Aetna considers the adjunctive use of anti-fibrotic agents (e.g., mitomycin C) or systemic corticosteroids with other shunt implants experimental and investigational because there are no advantages to the adjunctive use of these agents with currently available shunts.

VI. Aetna considers insertion of a drug-eluting implant, including punctal dilation and implant removal when performed, into the lacrimal canaliculus experimental and investigational for the treatment of glaucoma or ocular hypertension because its effectiveness has not been established.

VII. Aetna considers beta radiation experimental and investigational for the treatment of glaucoma because its effectiveness has not been established for that indication.

VIII. Aetna considers ab interno trabeculectomy (trabectome) experimental and investigational for the treatment of glaucoma because its effectiveness has not been established.

See also CPB 0435 - Viscocanalostomy and Canaloplasty.

Background

Glaucoma is associated with increased intra-ocular pressure (IOP). The majority (about 90%) of patients with glaucoma have primary open-angle glaucoma (POAG) that is defined as a chronic condition in which the IOP is elevated beyond a level compatible with the continued health and function of the eye, with a gonioscopically open angle, and a decreased facility of outflow. It is a slow progressive, insidious optic neuropathy. Primary open-angle glaucoma is also known as chronic open-angle glaucoma and chronic simple glaucoma. Another form of glaucoma is acute angle-closure glaucoma (AACG), which occurs as a dramatic, violent attack with closure of the entire angle. In contrast to POAG, AACG manifests with symptoms of blurred vision with colored halos around lights, pain, redness, and often nausea and vomiting related to the pain. In AACG, the IOP can rise precipitously to more than 50 mm Hg.

Acute angle-closure glaucoma is treated with oral or intravenous carbonic anhydrase inhibitors (e.g., acetazolamide), topical beta-blockers (e.g., timolol), and miotics (e.g., pilocarpine) to induce miosis. If pharmacotherapies fail, laser iridotomy can be performed to create an opening in the peripheral iris to relieve pupillary block.

Primary open-angle glaucoma is usually treated with ophthalmic medications. The first-line drugs include timolol (a non-specific beta blocker) and latanoprost (a prostaglandin F2a agonist). The second-line drugs entail brimonidine (an alpha agonist) and dorzolamide (a topical carbonic anhydrase inhibitor). The third-line drugs include apraclonidine (an alpha agonist), pilocarpine (a cholinergic agonist), acetazolamide (an oral carbonic anhydrase inhibitor), and epinephrine (a non-specific adrenergic agonist). In a randomized controlled study, Doi et al (2005) concluded that the combination of bimatoprost and latanoprost in POAG increases IOP and should not be considered as a therapeutic option. An alternative to pharmacotherapies for the treatment of POAG is argon laser trabeculoplasty. Although this procedure is frequently used and well-tolerated, there are some concerns regarding its long-term effectiveness.

When medications and/or laser trabeculoplasty have failed to reduce IOP, the most commonly used surgical intervention for POAG in adults is known as a filtering procedure. In general, there are 4 techniques for filtering surgery: (i) full-thickness fistulas (e.g., thermal sclerostomy), (ii) partial-thickness fistulas (e.g., trabeculectomy), (iii) tubes and setons (e.g., Molteno implant, Krupin-Denver valve...
implant, or Ahmed glaucoma implant), and (iv) cyclodestructive procedures (e.g., cyclophotocoagulation or cyclocryotherapy).

Molteno implant, Krupin-Denver valve implant, Ahmed glaucoma implant, Baerveldt seton, Schocket shunt, and Glaucoma pressure regulator are examples of aqueous drainage/shunt devices implanted to reduce IOP in the anterior chamber of the eye. The basic design of these devices is similar -- a silicone tube shunts aqueous humor from the anterior chamber to a fibrous capsule surrounding a synthetic plate or band positioned at the equatorial region of the globe. The capsule serves as a reservoir for aqueous drainage. Many studies have demonstrated that these devices are comparable and are effective in treating patients with POAG.

Guidelines from the American Academy of Ophthalmology (AAO, 2003) stated that “[t]he use of drainage devices (such as those described by Molteno, Ahmed, Krupin, Baerveldt, and others) is generally reserved for patients who have failed filtering surgery with antimetabolites or for patients whose conjunctiva is so scarred from previous surgery that filtering surgery with antimetabolites is at high risk for failure.”

Optinol (Kansas City, KS) introduced the Ex-PRESS mini glaucoma shunt in an attempt to simplify the glaucoma drainage device implantation. This device is a single-piece, stainless steel, translimbal implant that is placed using an inserter. Although its ease of implantation is greatly desired, its long-term efficacy and risk of complications have yet to be determined. The Ex-PRESS mini glaucoma shunt is a 400-micron diameter tube made from implantable stainless steel that is less than 3 mm long, and is loaded on a specially designed disposable inserter. The device reduces IOP by diverting excess aqueous humor from the anterior chamber to a subconjunctival bleb. The Ex-PRESS shunt has an advantage over conventional filtering surgery in that it is minimally invasive. Originally, the Ex-PRESS was designed for a direct limbus insertion through the irido-corneal angle under a conjunctival flap to drain aqueous from the anterior chamber to the subconjunctival space. However, because of long-term complications, including conjunctival erosions, hypotony, tube dislocation, conjunctival scarring or fibrosis within the tube, the device was re-designed. The new device is inserted via an external approach in the superficial scleral flap through the trabeculum into the anterior chamber.

In a multi-center study evaluating the safety and effectiveness of the Ex-PRESS R-50 mini glaucoma shunt, researchers found the device effective in reducing IOP. The success rate of the Ex-PRESS in lowering IOP to less than 21 mm Hg was 69 % after 1 year without medications. This represented a 30 to 40 % IOP reduction. The overall average number of glaucoma medications dropped significantly from 1.65 to 0.38 at 1 year (Optonol, Inc., 2002).

In a retrospective comparative series of 100 eyes, Maris et al (2007) compared the Ex-PRESS mini implant (Model R 50) placed under a partial-thickness scleral flap with standard trabeculectomy. Success was defined as IOP greater than or equal to 5 mm Hg and less than or equal to 21 mm Hg, with or without glaucoma medications, without further glaucoma surgery or removal of implant. Early post-operative hypotony was defined as IOP less than 5 mm Hg during the first post-operative week. The average follow-up was 10.8 months (range of 3.5 to 18) for the Ex-PRESS group and 11.2 months (range of 3 to 15) for the trabeculectomy group. Although the mean IOP was significantly higher in the early post-operative period in the Ex-PRESS group compared with the trabeculectomy group, the reduction of IOP was similar in both groups after 3 months. The number of post-operative glaucoma medications in both groups was not significantly different. Kaplan-Meier survival curve analysis showed no significant difference in the success between the 2 groups (p = 0.594). Early post-operative hypotony and choroidal effusion were significantly more frequent after trabeculectomy compared with the Ex-PRESS implant under scleral flap (p < 0.001). The authors concluded that the Ex-PRESS implant under a scleral flap had similar IOP lowering efficacy with a lower rate of early hypotony compared with trabeculectomy.
Transciliary filtration (TCF) (Singh filtration, Fugo Blade transciliary filtration) is a procedure developed by Daljit Singh, M.D., Amistar, India for advanced glaucoma cases in which conventional surgery has failed or is most likely to fail. Transciliary filtration creates an opening in the region of the pars plana of the ciliary body, the least vascularized part of the uveal tract and very close to the site of aqueous formation. An opening in this region provides almost direct passage outwards without risking uveal tissue prolapse. Currently, the literature is limited to case series reports by the same author on the technical feasibility of the procedure (Singh et al, 1979, 1981, 2002). Singh and Singh (2002) described the procedure using a new thermo-cauterization device called the Fugo Blade™ (plasma blade) (Medisurg Ltd., Norristown, PA). The Fugo Blade, which is also used in anterior capsulotomies, received 510(k) marketing clearance from the FDA for sclerostomy in the treatment of POAG where maximum tolerated medical therapy and trabeculoplasty have failed. However, the manufacturer was not required to submit to the FDA the evidence of efficacy that is necessary to support a premarket approval application (PMA). The Fugo Blade utilizes plasma energy surrounding a thin, blunt ablation filament about as thick as a human hair to dissolve tissue bonds. The blade generates a cloud of plasma, which produces a microablation path comparable to the effect of a miniature excimer laser. The proposed benefit of the Fugo Blade is that there is very little bleeding, and compared with traditional trabeculectomy, Fugo Blade TCF is quicker to perform and eliminates the risk of anterior chamber collapse, since aqueous fluid drains from behind rather than from in front of the iris. However, at the present time, there is insufficient evidence in the peer-reviewed medical literature on the TCF procedure. Randomized controlled studies are needed to determine whether TCF is an effective procedure for glaucoma compared to other traditional forms of filtering techniques, and which glaucoma patients, if any, would benefit.

An AAO's technology assessment on "Novel glaucoma procedures" (Francis et al, 2011) noted that the disadvantages of FUGO Blade TCF are that it is an external filtration procedure with bleb formation, risk of over-filtration, and hypotony.

Stein and Challa (2007) stated that laser trabeculoplasty has been reported to be an effective method to lower IOP in patients with primary or secondary OAG, both as an initial therapy or in conjunction with hypotensive medications. These investigators described the proposed mechanisms of action of argon laser trabeculoplasty and selective laser trabeculoplasty, as well as reviewed current studies of the therapeutic effect of these interventions. The exact mechanisms by which argon laser and selective laser trabeculoplasty lower IOP are unclear; the authors discussed the 3 most common theories: (i) the mechanical theory, (ii) the cellular (biologic) theory, and (iii) the cell division theory. Since both lasers are applied to the same tissue and produce similar results, they most likely produce their effects in comparable ways. These researchers also described the results of several studies comparing these devices. Most show them to be equally effective at lowering IOP; however, there are a few circumstances when selective laser trabeculoplasty may be a better option than argon laser trabeculoplasty. The authors concluded that argon laser and selective laser trabeculoplasty are safe and effective procedures for lowering IOP. They noted that results of ongoing clinical trials will help further define their role in the management of patients with OAG.

The American Optometric Association's guideline on care of the patient with OAG (AOA, 2002; reviewed 2007) listed argon laser trabeculoplasty as an alternative to drug therapy for the management of patients with POAG. The Singapore Ministry of Health's guideline on glaucoma stated that laser trabeculoplasty may be used as an adjunct to medical therapy. Furthermore, the AAO's guideline on POAG (2005) stated that laser trabeculoplasty is an appropriate initial therapeutic alternative (e.g., patients with memory problems or are intolerant to the medication).

In a report on aqueous shunts in glaucoma by the AAO, Minckler et al (2008) provided an evidence-based summary of commercially available aqueous shunts currently used in substantial numbers
(Ahmed [New World Medical, Inc., Rancho Cucamonga, CA], Baerveldt [Advanced Medical Optics, Inc., Santa Ana, CA], Krupin [Eagle Vision, Inc, Memphis, TN], Molteno [Molteno Ophthalmic Ltd., Dunedin, New Zealand]) to control IOP in various glaucomas. A total of 17 previously published randomized trials, 1 prospective non-randomized comparative trial, 1 retrospective case-control study, 2 comprehensive literature reviews, and published English language, non-comparative case series and case reports were reviewed and graded for methodologic quality. Aqueous shunts are used primarily after failure of medical, laser, and conventional filtering surgery to treat glaucoma and have been successful in controlling IOP in a variety of glaucomas. The principal long-term complication of anterior chamber tubes is corneal endothelial failure. The most shunt-specific delayed complication is erosion of the tube through overlying conjunctiva. There is a low incidence of this occurring with all shunts currently available, and it occurs most frequently within a few millimeters of the corneo-scleral junction after anterior chamber insertion. Erosion of the equatorial plate through the conjunctival surface occurs less frequently. Clinical failure of the various devices over time occurs at a rate of approximately 10 % per year, which is approximately the same as the failure rate for trabeculectomy. The authors concluded that based on level I evidence, aqueous shunts seem to have benefits (IOP control, duration of benefit) comparable with those of trabeculectomy in the management of complex glaucomas (phakic or pseudophakic eyes after prior failed trabeculectomies). Level I evidence indicates that there are no advantages to the adjunctive use of anti-fibrotic agents or systemic corticosteroids with currently available shunts. Too few high-quality direct comparisons of various available shunts have been published to assess the relative efficacy or complication rates of specific devices beyond the implication that larger-surface-area explants provide more enduring and better IOP control. Long-term follow-up and comparative studies are encouraged.

A review by the American Academy of Ophthalmology (Minckler, et al., 2008) concluded that Level I evidence indicates that there are no advantages to the adjunctive use of antifibrotic agents with currently available shunts. The AAO assessment stated that two of three randomized controlled trials concluded that antifibrotic agents have no beneficial long-term outcome effect when used with aqueous shunts (citing Cantor, et al., 1998, Costa, et al., 2004). The AAO assessment stated that, among published randomized controlled trials, only the study of Duan, et al. (2003) concluded that adjunctive mitomycin C was helpful to promote bleb formation and duration. The AAO assessment noted that, as pointed out in the Cochrane Review on aqueous shunts (citing Minckler, et al., 2006), this study had several methodologic flaws. The AAO assessment (Minckler, et al., 2008) concluded: “Thus, there is sufficient level I evidence that demonstrates no benefit in using antifibrotic agents as adjuncts to aqueous shunt procedures.” This conclusion was reaffirmed in an AAO Preferred Practice Pattern on primary open-angle glaucoma (AAO, 2010).

Filippopoulos and Rhee (2008) reviewed recent advances in penetrating glaucoma surgery with particular attention paid to 2 novel surgical approaches: (i) ab interno trabeculectomy with the Trabectome, and (ii) implantation of the Ex-PRESS shunt. Ab interno trabeculectomy (Trabectome) achieves a sustained 30 % reduction in IOP by focally ablating and cauterizing the trabecular meshwork/inner wall of Schlemm's canal. It has a remarkable safety profile with respect to early hypotonous or infectious complications as it does not generate a bleb, but it can be associated with early post-operative IOP spikes that may necessitate additional glaucoma surgery. The Ex-PRESS shunt is more commonly implanted under a partial thickness scleral flap, and appears to have similar efficacy to standard trabeculectomy offering some advantages with respect to the rate of early complications related to hypotony. The authors concluded that penetrating glaucoma surgery will continue to evolve. The findings of randomized clinical trials will determine the exact role of these surgical techniques in the glaucoma surgical armamentarium.

In a review on the use of novel devices for control of IOP, Minckler and Hill (2009) noted that Trabectome, Glaukos iStent, iScience (canaloplasty), and SOLX (suprachoroidal shunt) are newly
developed surgical technologies for the treatment of OAG. These new approaches to angle surgery have been demonstrated in preliminary case series to safely lower IOP in the mid-teens with far fewer complications than expected with trabeculectomy and without anti-fibrotics. Trabectome and iStent are relatively non-invasive, aim to improve access of aqueous to collector channels and do not preclude subsequent standard surgery. SOLX potentially offers an adjustable aqueous outflow from the anterior chamber into the suprachoroidal space.

An AAO's technology assessment on "Novel glaucoma procedures" (Francis et al, 2011) noted that the SOLX gold shunt is limited to investigational use in the U.S. The disadvantages of the SOLX gold shunt are the presence of a permanent implant in the anterior chamber and suprachoroidal space with the risk of erosion or exposure, and that the mechanism of action is not well-delineated. The assessment also stated that randomized controlled trials (RCTs) are needed to ascertain the effectiveness of procedures (including FUGO Blade goniotomy, iStent, and the SOLX gold shunt) compared with trabeculectomy, with one another, and with phacoemulsification alone (in the case of combined procedures).

In a Cochrane review, Kirwan and colleagues (2009) evaluated the effectiveness of beta radiation during glaucoma surgery (trabeculectomy). These investigators searched the Cochrane Central Register of Controlled Trials (CENTRAL) in The Cochrane Library (which includes the Cochrane Eyes and Vision Group Trials Register) (Issue 4 2008), MEDLINE (January 1966 to October 2008) and EMBASE (January 1980 to October 2008). The databases were last searched on 24 October 2008. They included randomized controlled trials comparing trabeculectomy with beta radiation to trabeculectomy without beta radiation. Data on surgical failure (IOP greater than 21 mm Hg), IOP, and adverse effects of glaucoma surgery were collected. Data were pooled using a fixed-effect model. These researchers found 4 trials that randomized 551 people to trabeculectomy with beta irradiation versus trabeculectomy alone -- 2 studies were in Caucasian people (n = 126), 1 study in black African people (n = 320), and 1 study in Chinese people (n = 105). People who had trabeculectomy with beta irradiation had a lower risk of surgical failure compared to people who had trabeculectomy alone (pooled risk ratio (RR) 0.23 (95 % confidence interval [CI]: 0.14 to 0.40). Beta irradiation was associated with an increased risk of cataract (RR 2.89, 95 % CI: 1.39 to 6.0). The authors concluded that trabeculectomy with beta irradiation has a lower risk of surgical failure compared to trabeculectomy alone. They stated that a trial of beta irradiation versus anti-metabolite is needed.

Current guidelines (AAO, 2010) describe the indication for laser peripheral iridoplasty in the treatment of acute angle closure crisis (AACC) when laser iridotomy is not possible or if the AACC cannot be medically broken.

However, there is insufficient evidence for the use of laser peripheral iridoplasty in the nonacute setting. In a Cochrane review, Ng and colleagues (2012) evaluated the effectiveness of laser peripheral iridoplasty in the treatment of narrow angles (i.e., primary angle-closure suspect), primary angle-closure (PAC) or primary angle-closure glaucoma (PACG) in non-acute situations when compared with any other intervention. In this review, angle-closure will refer to patients with narrow angles (PACs), PAC and PACG. These investigators searched CENTRAL (which contains the Cochrane Eyes and Vision Group Trials Register) (The Cochrane Library 2011, Issue 12), MEDLINE (January 1950 to January 2012), EMBASE (January 1980 to January 2012), Latin American and Caribbean Literature on Health Sciences (LILACS) (January 1982 to January 2012), the metaRegister of Controlled Trials (mRCT) (www.controlled-trials.com), ClinicalTrials.gov (www.clinicaltrials.gov) and the WHO International Clinical Trials Registry Platform (ICTRP) (www.who.int/ictrp/search/en). There were no date or language restrictions in the electronic searches for trials. The electronic databases were last searched on January 5, 2012. These researchers included only RCTs in this review. Patients with narrow angles, PAC or PACG were eligible. They excluded studies that included only patients with acute presentations, using laser peripheral iridoplasty to break acute crisis. No analysis was carried out as...
only 1 trial (n = 158) was included in the review. The trial reported laser peripheral iridoplasty as an adjunct to laser peripheral iridotomy compared to iridotomy alone. The study reported no superiority in using iridoplasty as an adjunct to iridotomy for IOP, number of medications or need for surgery. The authors concluded that there is currently no strong evidence for laser peripheral iridoplasty’s use in treating angle-closure.

On behalf of the AAO, Francis and cooleagues (2011) reviewed the published literature and summarized clinically relevant information about novel, or emerging, surgical techniques for the treatment of open-angle glaucoma and described the devices and procedures in proper context of the appropriate patient population, theoretic effects, advantages, and disadvantages. Devices and procedures that have FDA clearance or are currently in phase III clinical trials in the United States were included: the Fugo blade (Medisurg Ltd., Norristown, PA), Ex-PRESS mini glaucoma shunt (Alcon, Inc., Hunenberg, Switzerland), SOLX Gold Shunt (SOLX Ltd., Boston, MA), excimer laser trabeculotomy (AIDA, Glautec AG, Nurnberg, Germany), canaloplasty (iScience Interventional Corp., Menlo Park, CA), trabeculotomy by internal approach (Trabectome, NeoMedix, Inc., Tustin, CA), and trabecular micro- bypass stent (iStent, Glaukos Corporation, Laguna Hills, CA). Literature searches of the PubMed and the Cochrane Library databases were conducted up to October 2009 with no date or language restrictions. These searches retrieved 192 citations, of which 23 were deemed topically relevant and rated for quality of evidence by the panel methodologist. All studies but 1, which was rated as level II evidence, were rated as level III evidence. All of the devices studied showed a statistically significant reduction in IOP and, in some cases, glaucoma medication use. The success and failure definitions varied among studies, as did the calculated rates. Various types and rates of complications were reported depending on the surgical technique. On the basis of the review of the literature and mechanism of action, the authors also summarized theoretic advantages and disadvantages of each surgery. The authors concluded that the novel glaucoma surgeries studied all show some promise as alternative treatments to lower IOP in the treatment of open-angle glaucoma. It is not possible to conclude whether these novel procedures are superior, equal to, or inferior to surgery such as trabeculectomy or to one another. The studies provide the basis for future comparative or randomized trials of existing glaucoma surgical techniques and other novel procedures.

The iStent, an anterior segment aqueous drainage device, is a small (approximately 1 mm by 0.5 mm) L-shaped titanium device that is inserted into the trabecular meshwork through the cornea and is designed to create a bypass between the anterior chamber and Schlemm's canal for aqueous humor to flow directly into the canal toward the episcleral drainage system.

In a prospective, non-randomized, interventional case-series study, Buchacra et al (2011) evaluated the mid-term safety and effectiveness of the iStent glaucoma device in patients with secondary open-angle glaucoma. A total of 10 patients with secondary open-angle glaucoma (traumatic, steroid, pseudoxfoliative, and pigmentary glaucoma) of recent onset who underwent ab interno implantation iStent were included in this analysis. Patients were assessed following the procedure on days 1, 7, and 15 and months 1, 3, 6, and 12, and examinations included visual acuity, IOP measurement using Goldmann tonometry, number of glaucoma medications, and complications. Wilcoxon rank-test for data with abnormal distribution was used for the analysis of IOP and glaucoma medications at baseline versus 3, 6, and 12 months following the procedure. The mean baseline IOP was 26.5 ± 7.9 (range of 18 to 40) mm Hg, and significantly decreased in 10.4 ± 9.2 mm Hg at 3 months (p < 0.05), in 7.4 ± 4.9 mm Hg at 6 months (p < 0.05), and in 6.6 ± 5.4 mm Hg at 12 months (p < 0.05) following iStent implantation. The mean number of hypotensive medications at baseline was 2.9 ± 0.7 (range of 2 to 4). Statistically significant reductions in the number of medications of 1.1 ± 1.1 were observed at 3 months (p < 0.05), 1.0 ± 0.7 at 6 months (p < 0.05), and 1.1 ± 0.6 at 12 months (p < 0.05). No significant changes in visual acuity were noted. The most common complications comprised mild hyphema in 7 eyes and transient IOP greater than or equal to 30 mm Hg in 3 eyes on post-operative
day 1. Obstruction of the lumen of the stent with a blood clot was seen in 3 eyes, and all instances resolved spontaneously. The authors concluded that the iStent is a safe and effective treatment option in patients with secondary open-angle glaucoma, and reduces the topical treatment burden in one hypotensive medication.

Francis and Winarko (2012) stated that in POAG, the site of greatest resistance to aqueous outflow is thought to be the trabecular meshwork. Augmentation of the conventional (trabecular) outflow pathway would facilitate physiologic outflow and subsequently lower IOP. Ab interno Schlemm's canal surgery including 2 novel surgical modalities, Trabectome (trabeculotomy internal approach) and Trabecular Micro-bypass Stent (iStent), is designed to reduce IOP by this approach. In contrast to external filtration surgeries such as trabeculectomy and aqueous tube shunt, these procedures are categorized as internal filtration surgeries and are both performed from an internal approach via gonioscopic guidance. Published results suggest that these surgical procedures are both safe and efficacious for the treatment of open-angle glaucoma.

Augustinus and Zeyen (2012) reviewed the different aspects that influence the choice and sequence of surgical treatment in patients with co-existing open-angle glaucoma and cataract. The effect of phaco-emulsification on IOP and on a pre-existing bleb was discussed and phaco-trabeculectomy and trabeculectomy were compared. Moreover, the most recent surgical pressure lowering techniques in combination with phaco-emulsification were reviewed: iStent, Trabectome, Hydrus, Cypass and Canaloplasty. Medline database was used to search for relevant, recent articles. The authors concluded that a sustained IOP decrease of 1.5 mm Hg can be expected after a phaco-emulsification in patients with open-angle glaucoma. The higher the pre-operative pressure, the greater the IOP lowering will be. A phaco-emulsification on a trabeculectomized eye will often lead to reduced bleb function and an IOP rise of on average 2 mm Hg after 12 months. Compared to a trabeculectomy, phaco-trabeculectomy will have a less IOP lowering effect and a higher complication rate. iStent and Trabectome combined with phaco-emulsification can decrease the IOP with 3 to 5 mm Hg, with a low complication rate. The combination of Cypass and Hydrus with phaco-surgery may have a more significant IOP lowering effect but long-term results are not yet published. Combining Canaloplasty with phaco-emulsification is a more challenging surgery but if a tension suture can be placed, an IOP decrease around 10 mm Hg might be expected.

Saheb and Ahmed (2012) noted that there is an increasing interest and availability of micro-invasive glaucoma surgery (MIGS) procedures. It is important that this increase is supported by sound, peer-reviewed evidence. These researchers defined MIGS, reviewed relevant publications in the period of annual review and discussed future directions. The results of the pivotal trial comparing iStent combined with phaco-emulsification to phacoemulsification alone showed a significantly higher percentage of patients with unmedicated IOP of less than or equal to 21 mm Hg, and a comparable safety profile. Initial results were published regarding a second-generation micro-bypass stent (iStent inject, Glaukos Corporation, Laguna Hills, CA), a canalicular scaffold (Hydrus, Ivantis Inc., Irvine, CA) and an ab interno suprachoroidal micro-stent (CyPass, Transcend Medical, Menlo Park, CA), showing a decrease in mean post-operative IOP. Phaco-Trabectome (Ab interno trabeculectomy Trabectome, NeoMedix Inc., Tustin, CA) was compared to phaco-trabeculectomy and showed less IOP reduction, less post-operative complications, and a similar success rate. Similar success rates were found with the comparison of excimer laser trabeculostomy (ELT, AIDA, Glautec AG, Nurnberg, Germany) and selective laser trabeculoplasty. A number of publications reviewed the importance of the location of implantable devices, intra-operative gonioscopy, cost-effectiveness and quality-of-life studies, and randomized clinical trials. The authors concluded that MIGS procedures offer reduction in IOP, decrease in dependence on glaucoma medications and an excellent safety profile. Their role within the glaucoma treatment algorithm continues to be clarified and differs from the role of more invasive glaucoma surgeries such as trabeculectomy or glaucoma drainage devices.
In a prospective, non-comparative, uncontrolled, non-randomized, interventional case series study, Arriola-Villalobos and associates (2012) evaluated the long-term safety and effectiveness of combined cataract surgery and Glaukos iStent implantation for co-existent open-angle glaucoma and cataract. Subjects older than 18 years with co-existent uncontrolled mild or moderate open-angle glaucoma (including pseudoxfoliative and pigmentary) and cataract underwent phaco-emulsification and intracocular lens implantation along with ab-interno gonioscopically guided implantation of 1 Glaukos iStent. The variables recorded during a minimum of 3 years of follow-up were: IOP, number of anti-glaucoma medications and best-corrected visual acuity (BCVA). The 19 patients enrolled were 58 to 88 years old (mean age of 74.6 ± 8.44 years). Mean follow-up was 53.68 ± 9.26 months. Mean IOP was reduced from 19.42 ± 1.89 mm Hg to 16.26 ± 4.23 mm Hg (p = 0.002) at the end of follow-up, indicating a 16.33 % decrease in IOP. The mean number of pressure-lowering medications used by the patients fell from 1.32 ± 0.48 to 0.84 ± 0.89 (p = 0.046). In 42 % of patients, no anti-glaucoma medications were used at the end of follow-up. Mean BCVA significantly improved from 0.29 ± 0.13 to 0.62 ± 0.3 (p < 0.001). No complications of surgery were observed. The authors concluded that combined cataract surgery and Glaukos iStent implantation seems to be an effective and safe procedure to treat co-existent open-angle glaucoma and cataract.

In a prospective randomized controlled multi-center (29 sites) clinical trial, Craven et al (2012) evaluated the long-term safety and effectiveness of a single trabecular micro-bypass stent with concomitant cataract surgery versus cataract surgery alone for mild-to-moderate open-angle glaucoma. Eyes with mild-to-moderate glaucoma with an unmedicated IOP of 22 mm Hg or higher and 36 mm Hg or lower were randomly assigned to have cataract surgery with iStent trabecular micro-bypass stent implantation (stent group) or cataract surgery alone (control group). Patients were followed for 24 months post-operatively. The incidence of adverse events was low in both groups through 24 months of follow-up. At 24 months, the proportion of patients with an IOP of 21 mm Hg or lower without ocular hypotensive medications was significantly higher in the stent group than in the control group (p = 0.036). Overall, the mean IOP was stable between 12 months and 24 months (17.0 mm Hg ± 2.8 [SD] and 17.1 ± 2.9 mm Hg, respectively) in the stent group but increased (17.0 ± 3.1 mm Hg to 17.8 ± 3.3 mm Hg, respectively) in the control group. Ocular hypotensive medication was statistically significantly lower in the stent group at 12 months; it was also lower at 24 months, although the difference was no longer statistically significant. The authors concluded that patients with combined single trabecular micro-bypass stent and cataract surgery had significantly better IOP control on no medication through 24 months than patients having cataract surgery alone. Both groups had a similar favorable long-term safety profile.

On June 25, 2012, the FDA approved the iStent Trabecular Micro-Bypass Stent System, Model GTS100R/L. This is the first device approved for use in combination with cataract surgery to reduce IOP in adult patients with mild or moderate open-angle glaucoma and a cataract who are currently being treated with medication to reduce IOP.

In a retrospective, cohort study, Jea and colleagues (2012) compared the effect of ab interno trabeculectomy with trabeculectomy. A total of 115 patients who underwent ab interno trabeculectomy (study group) were compared with 102 patients who underwent trabeculectomy with intra-operative mitomycin as an initial surgical procedure (trabeculectomy group). Inclusion criteria were open-angle glaucoma, aged greater than or equal to 40 years, and uncontrolled on maximally tolerated medical therapy. Exclusion criterion was concurrent surgery. Clinical variables were collected from patient medical records. Main outcome measures included IOP and Cox proportional hazard ratio (HR) and Kaplan-Meier survival analyses with failure defined as IOP greater than 21 mmHg or less than 20 % reduction below baseline on 2 consecutive follow-up visits after 1 month; IOP less than or equal to 5 mmHg on 2 consecutive follow-up visits after 1 month; additional glaucoma surgery; or loss of light
perception vision. Secondary outcome measures included number of glaucoma medications and occurrence of complications. Mean follow-up was 27.3 and 25.5 months for the study and trabeculectomy groups, respectively. Intra-ocular pressure decreased from 28.1 +/- 8.6 mmHg at baseline to 15.9 +/- 4.5 mmHg (43.5 % reduction) at month 24 in the study group, and from 26.3 +/- 10.9 mmHg at baseline to 10.2 +/- 4.1 mmHg (61.3 % reduction) at month 24 in the trabeculectomy group. The success rates at 2 years were 22.4 % and 76.1 % in the study and trabeculectomy groups, respectively (p < 0.001). Younger age (p = 0.037; adjusted HR, 0.98 per year; 95 % CI: 0.97 to 0.99) and lower baseline IOP (p = 0.016; adjusted HR, 0.96 per 1 mmHg; 95 % CI: 0.92 to 0.99) were significant risk factors for failure in the multi-variate analysis of the study group. With the exception of hyphema, the occurrence of post-operative complications was more frequent in the trabeculectomy group (p < 0.001). More additional glaucoma procedures were performed after ab interno trabeculectomy (43.5 %) than after trabeculectomy (10.8 %, p < 0.001). The authors concluded that ab interno trabeculectomy has a lower success rate than trabeculectomy.

Furthermore, a Cochrane review on “Medical versus surgical interventions for open angle glaucoma” (Burr et al, 2012), and a U.S. Preventive Services Task Force's review on “Comparative effectiveness of treatments for open-angle glaucoma” (Boland et al, 2013), as well as an UpToDate review on “Open-angle glaucoma: Treatment” (Jacobs, 2013) mentioned trabeculectomy, but not ab interno trabeculectomy.

Chen and colleagues (2014) evaluated the safety and effectiveness of Ex-PRESS implantation (Ex-PRESS) compared to trabeculectomy in the treatment of patients with OAG. A comprehensive literature search using the Cochrane Methodology Register to identify randomized controlled clinical trials (RCCTs) comparing Ex-PRESS to trabeculectomy in patients with OAG. Efficacy estimates were measured by weighted mean difference (WMD) for the percentage IOP reduction (IOPR%) from baseline to end-point, and odds ratios (OR) for the complete success rate and post-operative interventions. Safety estimates were measured by OR for post-operative complications. Statistical analysis was performed using the RevMan 5.1 software. A total of 4 RCCTs were selected for this meta-analysis, including 215 eyes of 200 patients (110 eyes in the Ex-PRESS group, 105 eyes in the trabeculectomy group). There was no significant difference between Ex-PRESS and trabeculectomy in the IOPR%. The pooled OR comparing Ex-PRESS to trabeculectomy for the complete success rate at 1 year after surgery were in favor of Ex-PRESS. The Ex-PRESS procedure was found to be associated with lower number of post-operative interventions and with a significantly lower frequency of hyphema than trabeculectomy, whereas other complications did not differ statistically. The authors concluded that in OAG, Ex-PRESS and trabeculectomy provided similar IOP control, but Ex-PRESS was more likely to achieve complete success, with fewer post-operative interventions. Complication rates were similar for the 2 types of surgery, except for a lower frequency of hyphema in the Ex-PRESS group.

In a retrospective, non-comparative cases-series study, Grover et al (2014) introduced a minimally invasive, ab interno approach to a circumferential 360-degree trabeculotomy and reported the preliminary results. A total of 85 eyes of 85 consecutive patients with uncontrolled OAG and underwent gonioscopy-assisted transluminal trabeculotomy (GATT) for whom there was at least 6 months of follow-up data were included in this analysis. These investigators performed retrospective chart review of patients who underwent GATT by 4 of the authors between October 2011 and October 2012. The surgery was performed in adults with various OAG. Main outcome measures included (IOP, glaucoma medications, visual acuity, and intra-operative as well as post-operative complications. Eighty-five patients with an age range of 24 to 88 years underwent GATT with at least 6 months of follow-up. In 57 patients with POAG, the IOP decreased by 7.7 mm Hg (standard deviation [SD], 6.2 mm Hg; 30.0 % [SD, 22.7 %]) with an average decrease in glaucoma medications of 0.9 (SD, 1.3) at 6 months. In this group, the IOP decreased by 11.1 mm Hg (SD, 6.1 mm Hg; 39.8 % [SD, 16.0 %]) with 1.1 fewer glaucoma medications at 12 months. In the secondary glaucoma group of 28 patients, IOP decreased
by 17.2 mm Hg (SD, 10.8 mm Hg; 52.7 % [SD, 15.8 %]) with an average of 2.2 fewer glaucoma medications at 6 months. In this group, the IOP decreased by 19.9 mm Hg (SD, 10.2 mm Hg; 56.8 % [SD, 17.4 %]) with an average of 1.9 fewer medications (SD, 2.1) at 12 months. Treatment was considered to have failed in 9 % (8/85) of patients because of the need for further glaucoma surgery. The cumulative proportion of failure at 1 year ranged from 0.1 to 0.32, depending on the group. Lens status or concurrent cataract surgery did not have a statistically significant effect on IOP in eyes that underwent GATT at either 6 or 12 months (p > 0.35). The most common complication was transient hyphema, seen in 30 % of patients at the 1-week visit. The authors concluded that the preliminary results and safety profile for GATT, a minimally invasive circumferential trabeculotomy, are promising and at least equivalent to previously published results for ab externo trabeculotomy.

Ocular Therapeutics is currently conducting clinical trials regarding the insertion of a drug-eluting implant, including punctual dilation and implant removal when performed, into the lacrimal canaliculus. The clinical trials are investigating the use of dexamethasone intracanalicular plugs for the treatment of post-operative inflammation and pain and travoprost intracanalicular plugs for reduction of intraocular pressure in patients with glaucoma or ocular hypertension. Ocular Therapeutix recently announced that the American Medical Association (AMA) approved a Category III CPT code for the insertion of a drug-eluting implant which could be used in clinical trials to establish use and provide a mechanism for reimbursement for insertion of these intracanalicular plugs following FDA approval.

CPT Codes / HCPCS Codes / ICD-9 Codes

Laser Trabeculoplasty or Food and Drug Administration (FDA)-approved aqueous drainage/shunt implants:

CPT codes covered if selection criteria are met:

65855
66180
66183
66185

CPT codes not covered for indications listed in the CPB:

0123T
0191T
0253T

Other CPT codes related to the CPB:

65855
66150
66155
66160
### HCPCS codes covered if selection criteria are met:

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>L8612</td>
<td>Aqueous shunt [covered if FDA approved] [DeepLight Gold Micro-Shunt and Eyepass Glaucoma Implant are not covered]</td>
</tr>
</tbody>
</table>

### HCPCS codes not covered for indications listed in the CPB:

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>J0702</td>
<td>Injection, betamethasone acetate and betamethasone sodium phosphate, per 3 mg</td>
</tr>
<tr>
<td>J1020</td>
<td>Injection, methylprednisolone acetate, 20 mg</td>
</tr>
<tr>
<td>J1030</td>
<td>Injection, methylprednisolone acetate, 40 mg</td>
</tr>
<tr>
<td>J1040</td>
<td>Injection, methylprednisolone acetate, 80 mg</td>
</tr>
<tr>
<td>J1094</td>
<td>Injection, dexamethasone acetate, 1 mg</td>
</tr>
<tr>
<td>J1100</td>
<td>Injection, dexamethasone sodium phosphate, 1mg</td>
</tr>
<tr>
<td>J1700</td>
<td>Injection, hydrocortisone acetate, up to 25 mg (i.e., Hydrocortone acetate)</td>
</tr>
<tr>
<td>J1710</td>
<td>Injection, hydrocortisone sodium phosphate, up to 50 mg (i.e., Hydrocortone phosphate)</td>
</tr>
<tr>
<td>J1720</td>
<td>Injection, hydrocortisone sodium succinate, up to 100 mg (i.e., Solu-Cortef)</td>
</tr>
<tr>
<td>J2650</td>
<td>Injection, prednisolone acetate, up to 1 ml (i.e., Key-Pred 25, Key-Pred 50, Predcor-25, Predcor-50, Predoject 50, Predalone-50, Predicort-50)</td>
</tr>
<tr>
<td>J2920</td>
<td>Injection, methylprednisolone sodium succinate, up to 40 mg (i.e., Solu-Medrol)</td>
</tr>
<tr>
<td>J2930</td>
<td>Injection, methylprednisolone sodium succinate, up to 125 mg (i.e., Solu-Medrol)</td>
</tr>
<tr>
<td>J3301</td>
<td>Injection, triamcinolone acetonide, not otherwise specified, per 10 mg (i.e., Kenalog)</td>
</tr>
<tr>
<td>J3302</td>
<td>Injection, triamcinolone diacetate, per 5 mg (i.e., Aristocort)</td>
</tr>
<tr>
<td>J3303</td>
<td>Injection, triamcinolone hexacetonide, per 5 mg (i.e., Aristospan)</td>
</tr>
<tr>
<td>J7315</td>
<td>Mitomycin, ophthalmic, 0.2 mg</td>
</tr>
<tr>
<td>J7506</td>
<td>Prednisone, oral, per 5 mg</td>
</tr>
<tr>
<td>J7509</td>
<td>Methylprednisolone, oral, per 4 mg</td>
</tr>
</tbody>
</table>
J7510  Prednisolone, oral, per 5 mg
J8540  Dexamethasone, oral, 0.25 mg
J9280  Injection, Mitomycin, 5 mg

Other HCPCS codes related to the CPB:
J0171  Injection, adrenaline, epinephrine, 0.1 mg
J1120  Injection, acetazolamide sodium, up to 500 mg

ICD-9 codes covered if selection criteria are met:
365.11  Primary open-angle glaucoma [must be reported with a code from 366.0-366.9]

iStent Trabecular Micro-Bypass Stent System:

CPT codes covered if selection criteria are met:
0191T  Insertion of anterior segment aqueous drainage device, without extraocular reservoir; internal approach, into the trabecular network

ICD-9 codes covered if selection criteria are met:
365.11  Primary open-angle glaucoma [must be reported with a code from 366.0-366.9]
366.00 - 366.9  Cataract [must be reported with 365.11]
743.30 - 743.39  Congenital cataract and lens anomalies

Beta radiation for glaucoma:

CPT codes not covered for indications listed in the CPB:
0190T
77401 - 77421

ICD-9 codes not covered for indications listed in the CPB:
365.00 - 365.9  Glaucoma
743.20 - 743.22  Bupthalmos

Drug-eluting implant into the lacrimal canaliculus:

CPT codes not covered for indications listed in the CPB:
0356T  Insertion of drug-eluting implant (including punctual dilation and implant removal when performed) into lacrimal canaliculus, each

ICD-9 codes not covered for indications listed in the CPB:
365.00 - 365.9  Glaucoma
The above policy is based on the following references:


85. Jacobs DS. Open-angle glaucoma: Treatment. UpToDate [online serial]. Waltham, MA: UpToDate; reviewed March 2013.