Glaucoma Surgery

Number: 0484

Policy

*Please see amendment for Pennsylvania Medicaid at the end of this CPB.*

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 one or two iStent Trabecular Micro-Bypass Stents per eye 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.
Aetna considers the iStent Trabecular Micro-Bypass Stent System contraindicated and experimental and investigational for persons with primary angle-closure glaucoma, secondary angle-closure glaucoma (including neovascular glaucoma), retrobulbar tumor, thyroid eye disease, Sturge-Weber Syndrome or any other type of condition that may cause elevated episcleral venous pressure.

Aetna considers more than 2 iStents per eye experimental and investigational because their safety and effectiveness has not been established.

III. Aetna considers the Hydrus Microstent 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.

Aetna considers the Hydrus Microstent contraindicated and experimental and investigational for persons with birth defects of the anterior chamber angle of the eye, primary angle-closure glaucoma, secondary angle-closure glaucoma (including neovascular glaucoma), malignant glaucoma, traumatic glaucoma, and uveitic glaucoma.

Aetna considers more than 1 Hydrus Microstent per eye experimental and investigational because its safety and effectiveness has not been established.

IV. Aetna considers the XEN Glaucoma Treatment System medically necessary for the management of refractory glaucoma, including cases where previous surgical treatment has failed, cases of primary open angle glaucoma, and pseudoexfoliative or pigmentary glaucoma with open angles that are unresponsive to maximum tolerated medical therapy.
V. 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.

VI. 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.

VII. Aetna considers the CyPass Micro-Stent, and the iStent G3 Supra experimental and investigational because their safety and effectiveness have not been established.

VIII. Aetna considers the adjunctive use of anti-fibrotic agents (e.g., mitomycin C) medically necessary for use with the ExPRESS 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.

IX. 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.

X. Aetna considers beta radiation experimental and investigational for the treatment of glaucoma because its effectiveness has not been established for that indication.
XI. Aetna considers ab interno trabeculectomy (trabectome) experimental and investigational for the treatment of glaucoma because its effectiveness has not been established.

XII. Aetna considers combined glaucoma and cataract surgery medically necessary for persons with a visually significant cataract with uncontrolled glaucoma despite maximal medical therapy and/or laser trabeculoplasty.

XIII. Aetna considers sub-conjunctival injection of anti-vascular endothelial growth factor agent (e.g., bevacizumab, ranibizumab) for control of wound healing in glaucoma surgery experimental and investigational because the effectiveness of this approach has not been established.

See also CPB 0435 - Viscocanalostomy and Canaloplasty (0435.html).

Background

Glaucoma is an irreversible group of conditions/diseases involving death of the nerve cells in front of the optic nerve. It was once thought that glaucoma was generally due to increased intraocular pressure (IOP); however, the condition is also found in individuals with normal or low eye pressure. Therefore, diagnosis of glaucoma does not rely on increased IOP and may be related to optic nerve damage. Glaucoma is one of the leading causes of blindness with loss of peripheral vision being a hallmark sign of glaucoma.

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.

Medication, in the form of eye drops, pills or both, is the most common early treatment for glaucoma. There are numerous medications available for treating glaucoma; all of which must be taken regularly. If medication fails, other interventions may be recommended.

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. Laser Trabeculoplasty is a surgical procedure in which a sharply focused beam of light is used to treat the drainage angle of the eye, enabling fluid to flow out of the front part, decreasing pressure. Although this procedure is frequently used and well-tolerated, there are some concerns regarding its long-term effectiveness. 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 American Academy of Ophthalmology (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).

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).
Trabeculectomy is a surgical procedure used in the treatment of glaucoma to relieve intraocular pressure by removing part of the eye's trabecular meshwork and adjacent structures; the most common glaucoma surgery performed, it allows drainage of aqueous humor from within the eye to underneath the conjunctiva where it is absorbed.

The term aqueous drainage device refers to a broad class of tools used to facilitate aqueous flow out of the anterior chamber to control IOP. They may also be referred to as glaucoma drainage devices, tubes or shunts and may be valved or nonvalved. Such drainage devices may be placed in individuals with advanced disease in whom medical and laser therapies are inadequate and who have an underlying diagnosis that increases the risk of failure of conventional surgery. Examples of U.S. Food and Drug Administration (FDA) approved standard aqueous drainage devices include Ahmed glaucoma valve, Baerveldt seton, Schocket shunt, Krupin-Denver valve implant, Molteno implant, and the Glaucoma pressure regulator. These aqueous drainage/shunt devices are 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 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."

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
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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 antifibrotic 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 AAO (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).

The ExPress glaucoma filtration device, a stainless steel nonvalved shunt, is inserted through a conjunctival flap to drain aqueous from the anterior chamber without removal of any scleral or iris tissue. 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.

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 (RCTs) 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.

Transciliary fistulization (transciliary filtration, Singh filtration) uses a thermo-cauterization device called the Fugo Blade to create a filter track from the sclera through the ciliary body to allow aqueous fluid to drain from the posterior chamber of the eye. This differs from conventional filtering surgeries in which aqueous fluid is filtered from the anterior chamber. Transciliary filtration (TCF) (Singh filtration, Fugo Blade transciliary filtration) was 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.

Trabectome is the name of the device and procedure during which a strip of tissue along the edge of the iris is removed in an attempt to reestablish normal pressure and drainage in affected eyes.

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. Intraocular 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 % confidence interval [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.

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.

Bussel et al (2015) evaluated outcomes of ab interno trabeculectomy (AIT) with the trabectome following failed trabeculectomy. The indication for AIT was IOP above target on maximally tolerated therapy, and for phaco-AIT a visually significant cataract and need to lower IOP or glaucoma medications.

Outcomes included IOP, medications, complications, secondary procedures and success, defined as IOP of less than 21 mm Hg and a greater than 20 % reduction from baseline without further surgery. Exclusion criteria were trabeculectomy less than 3 months prior to AIT or follow-up under 1 year. A total of 73 eyes of 73 patients with 1 year follow-up were identified. At 1 year, mean IOP in AIT significantly decreased by 28 % from 23.7 ± 5.5 mm Hg, and medications from 2.8 ± 1.2 to 2 ± 1.3 (n = 58). In phaco-AIT, the
mean IOP decreased 19 % from 20 ± 5.9 mm Hg and medications from 2.5 ± 1.5 to 1.6 ± 1.4 (n = 15). Transient hypotony occurred in 7 %, and further surgery was necessary in 18 %. For AIT and phaco-AIT, the 1-year cumulative probability of success was 81 % and 87 %, respectively. The authors concluded that both AIT and phaco-AIT showed a reduction in IOP and medication use after 1 year, suggesting that AIT with or without cataract surgery is a safe and effective option following failed trabeculectomy.

Kaplowitz et al (2016) analyzed all of the PubMed publications on AIT with the Trabectome to determine the reduction in IOP and medications following the procedure. For IOP outcomes, PubMed was searched for “trabectome”, “ab interno trabeculotomy” and “ab interno trabeculectomy” and all available papers retrieved. The meta-analysis used a random-effects model to achieve conservative estimates and assess statistical heterogeneity. To investigate complications, these researchers included all abstracts from the American Glaucoma Society, AAO, American Society of Cataract and Refractive Surgery and the Association for Research in Vision and Ophthalmology. The overall arithmetic mean baseline IOP for stand-alone Trabectome was 26.71 ± 1.34 mm Hg and decreased by 10.5 ± 1.9 mm Hg (39 % decrease) on 0.99 ± 0.54 fewer medications. Defining success as IOP less than or equal to 21 with a 20 % decrease while avoiding re-operation, the overall average success rate after 2 years was 46 ± 34 %. For combined phacoemulsification-Trabectome, the baseline IOP of 21 ± 1.31 mm Hg decreased by 6.24 ± 1.98 mm Hg (27 % decrease) on 0.76 ± 0.35 fewer medications. The success rate using the same definition at 2 years was 85 ± 7 %. The weighted mean IOP difference from baseline to study end-point was 9.77 mm Hg (95 % CI: 8.90 to 10.64) stand-alone and 6.04 mm Hg (95 % CI: 4.95 to 7.13) for combined cases. Despite heterogeneity, meta-analysis showed significant and consistent decrease in IOP and medications from baseline to end-point in AIT and phaco-AIT. The rate of visually threatening complications was less than 1 %. On average, trabectome lowered the IOP by approximately 31 % to a final IOP near 15 mm Hg while decreasing the number of medications by less than 1, with a low rate of serious complications. After 2 years, the overall average success rate is 66 %.
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
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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.

Iridotomy, iridectomy or iridoplasty may be necessary for angle-closure glaucoma. 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. Iridectomy involves surgical removal of part of the iris of the eye. Iridoplasty is a procedure using laser energy to shrink the peripheral iris; also called goniodoplasty. Iridotomy is a surgical procedure in which a laser is used to cut into the iris.
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), ClinicalTrials.gov and the WHO International Clinical Trials Registry Platform (ICTRP). 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 colleagues (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 (trabecular bypass device or microbypass implant) is a small heparin-coated, titanium implant, placed into Schlemm's canal, intended to restore more normal fluid drainage and reduce IOP in individuals who are also undergoing cataract surgery. Schlemm's Canal is a circular channel in the eye that collects aqueous humor from the anterior chamber and delivers it into the bloodstream. CyPass Micro-Stent is a small drainage device inserted under gonioscopic view through a clear corneal incision using a retractable guidewire. Once in place, it is designed to directly connect the anterior chamber to the suprachoroidal space (between the sclera and choroid) to increase uveoscleral outflow, thereby purportedly decreasing IOP. The iStent G3 Supra is a third generation iStent device under development and is similar in design to the CyPass Micro-Stent. The device is inserted under
goinioscopic view through a clear corneal incision into the
suprachoroidal space and is proposed for use alone or at the time
of cataract surgery.

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. 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,
pseudoexfoliative, 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.

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 pseudoexfoliative and pigmentary) and cataract underwent phaco-emulsification and intra-ocular 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

Proprietary
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.

Drug-eluting punctual plugs made of resorbable material are inserted into the lacrimal punctum (tear duct) and purportedly emit sustained release medications for a 30 - 60 day period until degrading and exiting via the nasolacrimal system. These devices are currently being studied but have not received FDA approval.

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.
Munoz-Negrete et al (2015) evaluated the safety and effectiveness of non-penetrating deep sclerectomy (NPDS) in 3 consecutive eyes with pre-existing and uncontrolled glaucoma after Descemet stripping with automated endothelial keratoplasty (DSAEK). Non-penetrating deep sclerectomy with intra-scleral implant and topical adjunctive intra-operative mitomycin C (0.2 mg/ml 1 minute) was performed. Intra-ocular pressure and number of glaucoma medication were registered before and after NPDS with at least 1-year follow-up. Intra-operative and post-operative complications were also registered. Before NPDS, IOP was 18 mm Hg in 1 patient and 32 mm Hg in the other 2 patients. Four anti-glaucoma drugs were used in 2 cases and 3 in the other one. At 1 year after NPDS, all the patients had an IOP less than or equal to 18 mm Hg. Two patients required post-operative anti-glaucoma medications (1 drug in 1 case and 2 drugs in the other one). Neodymium-doped yttrium aluminum garnet laser goniopuncture was needed in 2 patients and it had to be repeated in 1 of them. No complications related to NPDS were observed. A corneal graft rejection was observed 5 months after NPDS in 1 case that resolved without sequelae with intensive corticosteroid eye-drop therapy. The authors concluded that NPDS could be a safe and successful alternative to conventional filtration surgery after DSAEK in eyes with uncontrolled glaucoma. They stated that larger series and a longer follow-up would be needed to set the actual role of surgery in DSAEK patients.

An UpToDate review on "Open-angle glaucoma: Treatment" (Jacobs, 2016) states that "Filtration surgery not uncommonly fails due to excessive scar tissue formation. There are reports of the use of adjuncts before, during, or after surgery, such as beta irradiation and antimetabolites (5-fluorouracil and mitomycin C), to increase the rate of surgical success. There is great variation in use and choice of adjuncts worldwide, and adjuncts can be associated with a higher complication rate. For example, beta irradiation at the time of trabeculectomy can minimize scar tissue formation and increase the likelihood that surgery will effectively lower the IOP, but increases the risk of cataract formation."

Two iStents for the Treatment of Open-Angle Glaucoma
Myers and associates (2018) evaluated long-term outcomes of 2 trabecular micro-bypass stents, 1 suprachoroidal stent, and post-operative prostaglandin in eyes with refractory OAG. Prospective, ongoing 5-year study of 80 eligible subjects (70 with 4-year follow-up) with OAG and IOP of greater than or equal to 18 mmHg after prior trabeculectomy and while taking 1 to 3 glaucoma medications. Subjects received 2 iStent trabecular micro-bypass stents, 1 iStent Supra suprachoroidal stent, and post-operative travoprost. Post-operative IOP was measured with medication and annually following medication wash-outs. Performance was measured by the proportion of eyes with greater than or equal to 20 % IOP reduction on 1 medication (the protocol-specified prostaglandin) versus pre-operative medicated IOP (primary outcome); and the proportion of eyes with post-operative IOP of less than or equal to 15 and less than or equal to 18 mmHg on 1 medication (secondary outcome). Additional clinical and safety data included medications, visual field, pachymetry, gonioscopy, AEs, VA, and slit-lamp and fundus examinations. Pre-operatively, mean medicated IOP was 22.0 ± 3.1 mmHg on 1.2 ± 0.4 medications, and mean unmedicated IOP was 26.4 ± 2.4 mmHg. Post-operatively, among eyes without later cataract surgery, mean medicated IOP at all visits through 48 months was less than or equal to 13.7 mmHg (greater than or equal to 37 % reduction), and annual unmedicated IOP was less than or equal to 18.4 mmHg (reductions of greater than or equal to 30 % versus pre-operative unmedicated IOP and greater than or equal to 16 % versus pre-operative medicated IOP). At all post-operative visits among eyes without additional surgery or medication, greater than or equal to 91 % of eyes had greater than or equal to 20 % IOP reduction on 1 medication versus pre-operative medicated IOP. At month 48, 97 and 98 % of eyes achieved IOP of less than or equal to 15 and less than or equal to 18 mmHg, respectively, on 1 medication; 6 eyes required additional medication, no eyes required additional glaucoma surgery, and safety measurements were favorable throughout follow-up. The authors concluded that IOP control was achieved safely with 2 trabecular micro-bypass stents, 1 suprachoroidal stent, and post-operative prostaglandin; this micro-invasive, ab interno approach introduced a possible new treatment option for refractory disease.
In a prospective, randomized, single-masked, concurrently controlled, multi-center clinical trial, Samuelson and colleagues (2019) examined the safety and effectiveness of the iStent inject Trabecular Micro-Bypass System (Glaukos Corporation, San Clemente, CA) in combination with cataract surgery in subjects with mild-to-moderate POAG. Subject were individuals with eyes with mild-to-moderate POAG and pre-operative IOP of less than or equal to 24 mmHg on 1 to 3 medications, unmedicated diurnal IOP (DIOP) 21 to 36 mmHg, and cataract requiring surgery. After uncomplicated cataract surgery, eyes were randomized 3:1 intra-operatively to ab interno implantation of iStent inject (Model G2-M-IS; treatment group, n = 387) or no stent implantation (control group, n = 118). Subjects were followed through 2 years post-operatively. Annual wash-out of ocular hypotensive medication was performed. Effectiveness end-points were greater than or equal to 20 % reduction from baseline in month 24 unmedicated DIOP and change in unmedicated month 24 DIOP from baseline. Safety measures included best spectacle-corrected visual acuity (BSCVA), slit-lamp and fundus examinations, gonioscopy, pachymetry, specular microscopy, visual fields, complications, and AEs. The groups were well balanced pre-operatively, including medicated IOP (17.5 mmHg in both groups) and unmedicated DIOP (24.8 ± 3.3 mmHg versus 24.5 ± 3.1 mmHg in the treatment and control groups, respectively, p = 0.33). At 24 months, 75.8 % of treatment eyes versus 61.9 % of control eyes experienced greater than or equal to 20 % reduction from baseline in unmedicated DIOP (p = 0.005), and mean reduction in unmedicated DIOP from baseline was greater in treatment eyes (7.0 ± 4.0 mmHg) than in control eyes (5.4 ± 3.7 mmHg; p < 0.001). Of the responders, 84 % of treatment eyes and 67 % of control eyes were not receiving ocular hypotensive medication at 23 months. Furthermore, 63.2 % of treatment eyes versus 50.0 % of control eyes had month 24 medication-free DIOP of less than or equal to 18 mmHg (difference 13.2 %; 95 % CI: 2.9 to 23.4). The overall safety profile of the treatment group was favorable and similar to that in the control group throughout the 2-year follow-up. The authors concluded that clinically and statistically greater reductions in IOP without medication were achieved after iStent inject implantation with cataract surgery versus cataract surgery alone, with excellent safety through 2 years.
Combined Glaucoma and Cataract Surgery

Zhang and colleagues (2015) stated that cataract and glaucoma are leading causes of blindness worldwide, and their co-existence is common in elderly people. Glaucoma surgery can accelerate cataract progression, and performing both surgeries may increase the rate of post-operative complications and compromise the success of either surgery. However, cataract surgery may independently lower intraocular pressure (IOP), which may allow for greater IOP control among patients with co-existing cataract and glaucoma. The decision between undergoing combined glaucoma and cataract surgery versus cataract surgery alone is complex. Therefore, it is important to compare the effectiveness of these 2 interventions to aid clinicians and patients in choosing the better treatment approach. In a Cochrane review, these investigators evaluated the relative safety and effectiveness of combined surgery versus cataract surgery (phacoemulsification) alone for co-existing cataract and glaucoma. The secondary objectives included cost-analyses for different surgical techniques for co-existing cataract and glaucoma. These investigators searched CENTRAL (which contains the Cochrane Eyes and Vision Group Trials Register) (2014, Issue 10), Ovid MEDLINE, Ovid MEDLINE In-Process and Other Non-Indexed Citations, Ovid MEDLINE Daily, Ovid OLDMEDLINE (January 1946 to October 2014), EMBASE (January 1980 to October 2014), PubMed (January 1948 to October 2014), Latin American and Caribbean Health Sciences Literature Database (LILACS) (January 1982 to October 2014), the metaRegister of Controlled Trials (mRCT), ClinicalTrials.gov, and the World Health Organization (WHO) International Clinical Trials Registry Platform (ICTRP). They did not use any date or language restrictions in the electronic searches for trials. They last searched the electronic databases on October 3, 2014. They checked the reference lists of the included trials to identify further relevant trials. These researchers used the Science Citation Index to search for references to publications that cited the studies included in the review. They also contacted investigators and experts in the field to identify additional trials. The authors included RCTs of participants who had open-angle, pseudoexfoliative, or pigmentary glaucoma and age-related cataract. The comparison of interest was combined cataract surgery (phacoemulsification) and any type of glaucoma surgery versus cataract surgery (phacoemulsification)
alone. Two review authors independently assessed study eligibility, collected data, and judged risk of bias for included studies. They used standard methodological procedures expected by the Cochrane Collaboration. These investigators included 9 RCTs, with a total of 655 participants (657 eyes), and follow-up periods ranging from 12 to 30 months; 7 trials were conducted in Europe, 1 in Canada and South Africa, and 1 in the United States. These researchers graded the overall quality of the evidence as low due to observed inconsistency in study results, imprecision in effect estimates, and risks of bias in the included studies. Glaucoma surgery type varied among the studies: 3 studies used trabeculectomy, 3 studies used iStent implants, 1 study used trabeculotomy, and 2 studies used trabecular aspiration. All of these studies found a statistically significant greater decrease in mean IOP post-operatively in the combined surgery group compared with cataract surgery alone; the MD was -1.62 mmHg (95 % CI: -2.61 to -0.64; 489 eyes) among 6 studies with data at 1 year follow-up. No study reported the proportion of participants with a reduction in the number of medications used after surgery, but 2 studies found the mean number of medications used post-operatively at 1 year was about 1 less in the combined surgery group than the cataract surgery alone group (MD -0.69, 95 % CI: -1.28 to -0.10; 301 eyes); 5 studies showed that participants in the combined surgery group were about 50 % less likely compared with the cataract surgery alone group to use 1 or more IOP-lowering medications 1 year post-operatively (RR 0.47, 95 % CI: 0.28 to 0.80; 453 eyes). None of the studies reported the mean change in visual acuity or visual fields. However, 6 studies reported no significant differences in visual acuity and 2 studies reported no significant differences in visual fields between the 2 intervention groups post-operatively (data not analyzable). The effect of combined surgery versus cataract surgery alone on the need for re-operation to control IOP at 1 year was uncertain (RR 1.13, 95 % CI: 0.15 to 8.25; 382 eyes). Also uncertain was whether eyes in the combined surgery group required more interventions for surgical complications than those in the cataract surgery alone group (RR 1.06, 95 % CI: 0.34 to 3.35; 382 eyes). No study reported any vision-related quality of life data or cost outcome. Complications were reported at 12 months (2 studies), 12 to 18 months (1 study), and 2 years (4 studies) after surgery. Due to the small number of
events reported across studies and treatment groups, the difference between groups was uncertain for all reported adverse events. The authors concluded that there is low quality evidence that combined cataract and glaucoma surgery may result in better IOP control at 1 year compared with cataract surgery alone. The evidence was uncertain in terms of complications from the surgeries. Furthermore, this Cochrane review has highlighted the lack of data regarding important measures of the patient experience, such as visual field tests, quality of life measurements, and economic outcomes after surgery, and long-term outcomes (5 years or more). They stated that additional high-quality RCTs measuring clinically meaningful and patient-important outcomes are needed to provide evidence to support treatment recommendations.

CyPass Micro-Stent

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.

Saheb and associates (2014) evaluated the supra-ciliary space (SCS) with anterior segment optical coherence tomography (OCT) imaging after CyPass Micro-Stent implantation. The SCS was imaged with OCT after micro-stent implantation at 1, 6 months, and 1 year. Images were graded on a scale of 0 to 4 for morphological features indicative of fluid presence within, or drainage through, the SCS. A total of 35 patients underwent ab-interno micro-stent implantation. Mean age was 68.6 ± 10.2 years. Baseline mean IOP was 21.9 ± 6.1 mm Hg on average of 3.0 topical medications. At 1 month, the fluid space grade was greater than or equal to 1 for 96 % (24/25) of patients for tenting, 79 % (15/19) for fluid posterior to the micro-stent, and 89 % (8/9) for fluid surrounding the micro-stent. The mean (composite) score for all features was 2.5 ± 0.99. The majority of patients maintained aqueous fluid through 12 months. The authors concluded that OCT imaging provided adequate visualization of the angle, the SCS and aqueous fluid drainage after implantation of a suprachoroidal micro-stent into the SCS.

The drawbacks of this study included its retrospective nature and short-term follow-up (12 months). Furthermore, while standardized for the purposes of this study, the grading of OCT images did not follow a validated systematic approach due to the lack of such grading scales. There is a paucity of OCT grading systems in general, and none available for the SCS. The authors used the size of the micro-stent as a standard measure, since its size was consistent across all subjects and independent of OCT software or print-outs. The individual measuring the images was masked as to the post-operative time of the image, however, there may have been a bias toward larger measures when the micro-stent was fully visible. Finally, images were not available for all subjects, with a gradual decrease in available images at later time-points. There could have been some selection bias in this study for imaging of
patients with poorer post-operative outcomes. This bias needs to be considered as researchers evaluate the grades of the available images, especially at later time-points.

In a multi-center, prospective, consecutive case-series study, Hoh and co-workers (2014) evaluated through 2 post-operative years the clinical outcomes associated with a novel SCS micro-stent for the surgical treatment of OAG when implanted in conjunction with cataract surgery. A total of 136 subjects (136 eyes) with OAG and requiring cataract surgery with 24-month post-operative data were included. A combined phacoemulsification procedure, with intraocular lens insertion and CyPass Micro-Stent implantation into the SCS of the study eye, was performed. At baseline, all subjects were on glaucoma medication with either uncontrolled IOP (greater than or equal to 21 mmHg, Cohort 1, n = 51) or controlled IOP (less than 21 mmHg, Cohort 2, n = 85). Glaucoma medications were stopped post-operatively, but could be re-started if needed, at the investigator's discretion. Device-related adverse events (AEs), post-operative IOP, best corrected distance visual acuity (BCDVA), and number of IOP-lowering medications were recorded. The micro-stent was successfully implanted in all eyes. At 24 months, 82 subjects remained in the study. No sight-threatening AEs occurred. The most common AEs were transient hypotony (15.4 %) and micro-stent obstruction (8.8 %), typically due to iris tissue overgrowth; 15 subjects (11 %) required secondary incisional glaucoma surgery. For Cohort 1 (n = 23), mean ± SD IOP was 15.8 ± 3.8 mmHg after 24 months (change, -37 % ± 19 %). Mean IOP decrease from baseline was statistically significant (p < 0.0001) at months 6, 12, and 24. For Cohort 2 (n = 59), mean ± SD IOP at 24 months was 16.1 ± 3.2 mmHg (change, 0 % ± 28 %). Mean decrease from baseline was statistically significant at months 6 (p = 0.0188) and 12 (p = 0.0356). At 24 months, the mean ± SD number of medications was 1.0 ± 1.1 in Cohort 1 and 1.1 ± 1.1 in Cohort 2. Mean decrease from baseline medication use was statistically significant at months 6 (p < 0.001), 12 (p < 0.001), and 24 (p = 0.0265) in Cohort 1, and at months 6, 12, and 24 (all p < 0.0001) in Cohort 2. The authors concluded that CyPass Micro-Stent implantation, in combination with cataract surgery, was associated with minimal complications while substantially lowering IOP and/or use of IOP-lowering medications.
In a multi-center RCT, Void and colleagues (2016) evaluated 2-year safety and effectiveness of SCS micro-stenting for treating mild-to-moderate POAG in patients undergoing cataract surgery. Subjects were enrolled beginning July 2011, with study completion in March 2015. Subjects had POAG with mean diurnal un-medicated IOP 21 to 33 mmHg and were undergoing phacoemulsification cataract surgery. After completing cataract surgery, subjects were intra-operatively randomized to phacoemulsification only (control) or SCS micro-stenting with phacoemulsification (micro-stent) groups (1:3 ratio). Micro-stent implantation via an ab interno approach to the SCS allowed concomitant cataract and glaucoma surgery. Outcome measures included percentage of subjects achieving greater than or equal to 20% un-medicated diurnal IOP lowering versus baseline, mean IOP change and glaucoma medication use, and ocular AE incidence through 24 months. Of 505 subjects, 131 were randomized to the control group and 374 were randomized to the micro-stent group. Baseline mean IOPs in the control and micro-stent groups were similar: 24.5 ± 3.0 and 24.4 ± 2.8 mmHg, respectively (p > 0.05); mean medications were 1.3 ± 1.0 and 1.4 ± 0.9, respectively (p > 0.05). There was early and sustained IOP reduction, with 60% of controls versus 77% of micro-stent subjects achieving greater than or equal to 20% un-medicated IOP lowering versus baseline at 24 months (p = 0.001; per-protocol analysis). Mean IOP reduction was a decrease of 7.4 mmHg for the micro-stent group versus a decrease of 5.4 mmHg in controls (p < 0.001), with 85% of micro-stent subjects not requiring IOP medications at 24 months. Mean 24-month medication use was 67% lower in micro-stent subjects (p < 0.001); 59% of control versus 85% of micro-stent subjects were medication free. Mean medication use in controls decreased from 1.3 ± 1.0 drugs at baseline to 0.7 ± 0.9 and 0.6 ± 0.8 drugs at 12 and 24 months, respectively, and in the micro-stent group from 1.4 ± 0.9 to 0.2 ± 0.6 drugs at both 12 and 24 months (p < 0.001 for reductions in both groups at both follow-ups versus baseline). No vision-threatening micro-stent-related AEs occurred; VA was high in both groups through 24 months; greater than 98% of all subjects achieved 20/40 BCVA or better. The authors concluded that the findings of this RCT demonstrated safe and sustained 2-year reduction in IOP and glaucoma medication use after micro-stent surgical treatment for mild-to-moderate POAG.
The authors stated that findings from this study were generalizable to men and women aged over 45 years, with Shaffer grade greater than or equal to 3 POAG and baseline un-medicated IOP 21 to 33 mmHg, and demographics typical of the enrolled US subpopulation. They noted that the Latino/Hispanic ethnicity category constituted only 4% of the cohort and may be under-represented. These investigators also noted that another drawback of this study was that the principal investigator at each study site was not masked to treatment randomization during patient follow-up examinations.

The AAO Preferred Practice Pattern Glaucoma Panel (Prum et al, 2015) stated that “Several other glaucoma surgeries exist as alternatives to trabeculectomy and aqueous shunt implantation. The precise role of these procedures in the surgical management of glaucoma remains to be determined”. Trabecular micro-bypass stent (or iStent) is listed as one of these procedures.

The XEN Glaucoma Treatment System (XEN45 Gel Stent and XEN Injector)

In a pilot, non-randomized, prospective clinical trial, Sheybani and colleagues (2015) examined the effect on IOP of implanting a new gelatin stent at the time of cataract surgery in the treatment of OAG. The implantation of 2 models of a gelatin stent (Xen140 and Xen63) was performed at the time of cataract surgery without mitomycin-C. Complete success was defined as a post-operative IOP of less than 18 mm Hg and more than a 20 % reduction in IOP at 12 months without glaucoma medication. Failure was defined as loss of light perception vision or worse, a need for additional glaucoma surgery, or less than a 20 % reduction in the IOP from baseline. The study included 37 eyes of 37 patients. The mean pre-operative IOP was 22.4 mm Hg ± 4.2 (SD) on 2.5 ± 1.4 medication classes. The mean IOP was reduced to 15.4 ± 3.0 mm Hg on 0.9 ± 1.0 medication classes (p < 0.0001) 12 months post-operatively. This resulted in a qualified success of 85.3 % and a complete success rate off medications of 47.1 %. There were no failures. The authors concluded that cataract surgery combined with implantation of the gelatin stent resulted in a significant reduction in IOP in eyes with OAG.
Sheybani and associates (2016) evaluated the IOP-lowering effect of the XEN140 micro-fistula gel stent implant for the surgical treatment of OAG. A total of 49 eyes (49 patients) with an IOP of greater than 18 mm Hg and less than or equal to 35 mm Hg were studied in a prospective non-randomized multi-center cohort trial of the surgical implantation of the XEN140 implant in patients with OAG. Complete success was defined as a post-operative IOP less than or equal to 18 mm Hg with greater than or equal to 20 % reduction in IOP at 12 months without any glaucoma medications. Failure was defined as vision loss of light perceptions vision or worse, need for additional glaucoma surgery, or less than 20 % reduction of IOP from baseline. The average age was 64.3 (28.1 to 86.9) years old; 21 eyes had prior failed trabeculectomy with mitomycin C surgery; IOP at 12 months decreased from a mean of 23.1 (± 4.1) mm Hg to 14.7 (± 3.7) mm Hg for a 36.4 % reduction in IOP from baseline. The number of patients at 12 months who achieved an IOP of less than or equal to 18 mm Hg and greater than or equal to 20 % reduction in IOP was 40 (89 %). The number of patients who achieved an IOP of less than or equal to 18 mm Hg and greater than or equal to 20 % reduction in IOP without anti-glaucoma medications was 18 (40 %). The authors concluded that XEN140 gel stent lowered IOP with few complications when implanted for the surgical treatment of OAG.

Dupont and Collignon (2016) noted that POAG is a progressive ocular disease affecting adults and associated with visual field defect. The aim of its treatment is to lower the IOP by means of ocular drops, laser or surgery. To-date, traditional surgical techniques still remain quite invasive, but recent research efforts have been made with a view to develop minimally invasive techniques. The XEN Gel Stent is one of them. It allows a safe and efficient lowering of IOP by creating a sub-conjunctival flow, following an ab interno procedure that highly preserves the architecture of the treated eye.

On November 21, 2016, the FDA cleared the XEN Glaucoma Treatment System for the management of refractory glaucoma, including cases where previous surgical treatment has failed, cases of POAG, and pseudoexfoliative glaucoma (PXG) or pigmentary glaucoma with open angles that are unresponsive to maximum
tolerated medical therapy. In the U.S. pivotal trial conducted in refractory glaucoma patients, XEN reduced IOP from a mean medicated baseline of 25.1 (+ 3.7) mmHg to 15.9 (+ 5.2) mmHg at the 12 month visit (n=52). The mean baseline number of IOP-lowering medications was 3.5 (± 1.0) versus an average use of 1.7 (± 1.5) medications at 12 months. The most common postoperative adverse events included BCVA loss of > 2 lines (< 30 days 15.4%; > 30 days 10.8%; 12 months 6.2%), hypotony IOP < 6 mm Hg at any time (24.6%; no clinically significant consequences were associated, no cases of persistent hypotony, and no surgical intervention was required), IOP increase > 10 mm Hg from baseline (21.5%), and needling procedure (32.3%).

XEN Gel Stent is contraindicated in angle-closure glaucoma where angle has not been surgically opened, previous glaucoma shunt/valve or conjunctival scarring/pathologies in the target quadrant, active iris neovascularization, anterior chamber IOL, intraocular silicone oil, and vitreous in the anterior chamber.

XEN Gel Stent complications may include choroidal effusion, hyphema, hypotony, implant migration, implant exposure, wound leak, need for secondary surgical intervention, and intraocular surgery complications. Safety and effectiveness in neovascular, congenital, and infantile glaucoma has not been established. The product labeling recommends avoiding digital pressure following implantation of the XEN Gel Stent to avoid implant damage.

Kerr and associates (2017) stated that recently, many new devices and procedures have been developed to lower IOP in a less invasive and purportedly safer manner than traditional glaucoma surgery. These new devices might encourage an earlier transition to surgery and reduce the long-term commitment to topical glaucoma medications with their associated compliance and intolerance issues. Although often seen as an adjunct to cataract surgery, a growing body of evidence suggested that primary MIGS may be a viable initial treatment option. New studies have shown that primary ab interno trabeculectomy (Trabectome, NeoMedix Inc., Tustin, CA), trabecular micro-bypass stent insertion (iStent and iStent Inject, Glaukos Corporation, Laguna Hills, CA), canalicular scaffolding (Hydrus, Invantis Inc., Irvine CA), the ab interno gel
Implant (XEN, Allergan, Dublin, Ireland) or SC stenting (CyPass Micro-Stent, Alcon, Fort Worth, TX) may lower the lowering IOP and/or topical medication burden in phakic or pseudophakic patients with glaucoma. This effect appeared to last at least 12 months, but reliable cost-effectiveness and quality of life (QOL) indicators have not yet been established by investigator-initiated randomized trials of sufficient size and duration.

Richter and Coleman (2016) stated that MIGS aims to provide a medication-sparing, conjunctival-sparing, ab interno approach to IOP reduction for patients with mild-to-moderate glaucoma that is safer than traditional incisional glaucoma surgery. The current approaches include: increasing trabecular outflow (Trabectome, iStent, Hydrus stent, gonioscopy-assisted transluminal trabeculotomy [GATT], Excimer laser trabeculotomy); suprachoroidal shunts (Cypass micro-stent); reducing aqueous production (endocyclophotocoagulation); and subconjunctival filtration (XEN gel stent).

These investigators noted that MIGS technology has the potential to solve a variety of problems in current glaucoma management. These include minimizing patient adherence problems, increasing QOL for patients with ocular toxicity, and potentially reducing lifetime costs of expensive glaucoma medications, all while preserving the conjunctiva if additional, more invasive glaucoma surgeries are necessary in the future. Non-adherence rates in glaucoma have been reported to vary from 24% to 59%, and patient reasons for non-adherence include forgetfulness, side effects, lack of affordability, difficulty administering drops, complicated medication schedules, poor understanding of the disease, and poor patient-doctor communication. Moderate-to-severe ocular surface disease is present in 71% of patients receiving triple-drop therapy, and in these patients, implementing preservative-free alternatives may help but present additional cost and/or logistical insurance coverage barriers. Stein et al recently reported that laser trabeculoplasty is more cost-effective than a prostaglandin analog for newly diagnosed POAG when taking into account realistic patient adherence rates. Meanwhile, Kaplan et al recently reported that both Baerveldt implant and trabeculectomy with mitomycin C are more cost-effective than maximal medical...
treatment. While there are no data on cost-effectiveness of MIGS yet, if long-term efficacy of MIGS is demonstrated in future clinical studies, MIGS may also prove more cost-effective than medical treatment.

Nonetheless, there are several limitations to the current state of MIGS. These include limited quality and duration of evidence, lack of study standardization, lack of cost-effectiveness data, and incomplete knowledge of ideal patient selection. MIGS evidence is currently limited by the retrospective and non-masked nature in the majority of cases. Directly comparing the evidence of each MIGS type is difficult due to the varied study designs, patient populations, and outcome measures. Long-term outcomes over several years are mostly unknown. In evaluating current MIGS data, because most trials have included cataract surgery, it is important for clinicians to recognize the IOP-lowering ability of cataract surgery alone. According to a recent review by the AAO, cataract surgery results in a small, moderate, and marked reduction in IOP and medications for POAG, PXG, and PACG, respectively. In studies where MIGS surgery has only been reported in combination with cataract surgery, clinicians cannot assume that IOP-lowering abilities will be similar when cataract surgery is not also performed. Additionally, nearly all of the current MIGS procedures have the potential risk of late failure due to scarring, and longer follow-up periods in future studies are needed to determine how the longevity of these MIGS procedures compares to the less than ideal longevity of selective laser trabeculoplasty.

While the current MIGS procedures are generally designed to treat patients with mild-to-moderate OAG, clinicians will need to learn which specific patients will or will not benefit from a particular MIGS procedure. The specific clinical indications that have been learned to-date were discussed under the "Adverse events and clinical considerations" sections for each procedure. In general, the trabecular procedures will not benefit patients with elevated episcleral venous pressure. Patients with a bleeding predisposition are less ideal for GATT and possibly for Trabectome as well. It is also interesting to note that in the trabecular procedures, patients with higher baseline IOPs appeared to demonstrate the greatest IOP-lowering effects. These data are not yet available for the non-
trabecular procedures. Future data will also help clinicians to individualize their management strategy for each patient. Advances in aqueous angiography imaging will allow clinicians to localize the most active collector channels pre-operatively, before deciding where to place a particular trabecular stent. Such imaging modalities may also assess the activity of uveo-scleral flow, thus informing placement location for uveo-scleral stents. Perhaps in the future, these diagnostic studies will determine which class of MIGS procedure would be most effective for a particular patient. Because future trials will follow more standardized clinical trial protocols, the ability to select appropriate patients for each MIGS type will become more optimized. Future-generation MIGS devices will aim to surpass current MIGS outcomes, and these devices have the ever-increasing potential to improve the lives of patients with glaucoma worldwide.

Hohberger and co-workers (2017) stated that treatment of glaucoma eyes with irido-corneal endothelial syndrome is complex; MIGS, such as one that implements a novel, micro-invasive device, known as XEN gel stents, has shown promise in surgical glaucoma treatment and offers a new therapeutic option. In a case report, these investigators reported the successful implantation of XEN45 gel stent in a woman with secondary glaucoma due to unilateral irido-corneal endothelial syndrome after descemnet membrane endothelial keratoplasty (DMEK) operation, and the follow-up were presented. The authors concluded that implantation of XEN gel stents may be a promising option for minimally invasive glaucoma surgery in difficult situations, as low adverse events (AEs), good post-surgery VA and sufficient regulation of IOP can be seen.

Pinto Ferreira and colleagues (2017) noted that MIGS aims to provide a safer and less-invasive means of reducing IOP compared with traditional surgery, with the goal of reducing the need for topical medications. The XEN gel stent is an ab-interno minimally invasive glaucoma surgery device that approaches IOP reduction by creating a sub-conjunctival drainage pathway. As with any new device there is lack of experience and knowledge about its long-term results in terms of effectiveness, technique, and complications. These investigators reported a clinical case of a
XEN blood clot internal ostium obstruction and how it was managed. The ab-interno approach with micro-forceps appeared a minimally invasive, safe, and effective procedure.

Vinod and Gedde (2017) reviewed recent studies evaluating the effectiveness and complication profiles of novel glaucoma procedures promoting aqueous outflow. Literature from the 2015 to 2016 review period included abundant data regarding new and emerging glaucoma procedures. Notable findings from recent RCTs include titratability of IOP with multiple trabecular micro-bypass stents (iStent; Glaukos, Laguna Hills, CA) and greater reduction in IOP and medication usage following intra-canalicular scaffolding (Hydrus Microstent; Ivantis Inc., Irvine, CA) combined with phacoemulsification versus phacoemulsification alone. A SC micro-stent (CyPass Micro-Stent; Transcend Medical, Inc., Menlo Park, CA) received approval from the FDA after a pivotal trial demonstrated its safety and effectiveness. Early studies of investigational sub-conjunctival filtering devices (XEN Gel Stent; AqueSys, Inc., Aliso Viejo, CA and InnFocus MicroShunt; InnFocus Inc., Miami, FL) offer promising evidence, but late complications are as yet unknown. The authors concluded that newer glaucoma procedures targeting different aqueous outflow pathways have improved the safety profile of glaucoma surgery while preserving modest effectiveness. Most can be combined with phacoemulsification, allowing for simultaneous treatment of co-morbid cataract and glaucoma. Moreover, they stated that well-designed RCTs with extended follow-up are needed to evaluate the long-term effectiveness and late complications of these novel procedures.

Furthermore, UpToDate reviews on “Open-angle glaucoma: Treatment” (Jacobs, 2017) and “Angle-closure glaucoma” (Weizer, 2017) do not mention stenting as a therapeutic option.

In a prospective 12-month study on patients with POAG, Fea and colleagues (2017a) evaluate the safety and efficacy of the Xen Gel Stent and provided a macroscopic as well as microscopic analyses of bleb morphology. Patients underwent implantation of the XEN Gel Stent (Allergan INC, Dublin, Ireland) either alone or combined with a cataract surgery (CS). Biomicroscopy, in-vivo confocal...
microscopy (IVCM), and anterior segment-optical coherence tomography (AS-OCT) were used to assess bleb morphology. Safety parameters were AEs, BCVA, visual field, and corneal endothelial cell loss. A post-operative IOP less than or equal to 18 mmHg without or on medications was respectively defined as complete and qualified success while an IOP greater than or equal to 18 mmHg was defined as failure. A total of 12 eyes of 11 patients were evaluated. At 1 year, 5 out of 10 patients available achieved a complete success while 5 were qualified success; AS-OCT showed that bleb wall reflectivity was significantly higher in the failure group; IVCM revealed that stromal density was significantly lower in the success group. No safety issues were recorded. The authors concluded that these findings showed that there were statistically significant reductions in both IOP and medication use following implantation of the XEN Gel Stent in this group of POAG patients, and no safety issues related to the procedure or to the study device were observed. They stated that implantation of the XEN Gel Stent appeared to be a safe and effective procedure for the treatment of POAG. It is unclear whether these results provided clinically significant health outcomes.

The authors noted that this study had several drawbacks. It had a small sample size (n = 12 eyes), had a relatively short follow-up (12 months), and lacked an early post-operative evaluation to more stringently monitor the bleb development. A more standardized approach in bleb evaluation with imaging techniques was also needed. The presence of inflammatory cells, indicators of inflammation, and subsequent fibrosis in the conjunctival epithelium was not methodically investigated; however, it could provide a valuable predictive tool and deserved further investigations. It was also possible that AS-OCT may mis-represent bleb structure and artifacts. These researchers stated that larger scale studies with longer follow-up are needed.

In a prospective, interventional study, Galal and associates (2017) evaluated gel microstent (XEN, AqueSys, Inc.) for treatment of POAG. A total of 13 eyes with POAG underwent XEN implantation with subconjunctival mitomycin-C. Of those eyes, 3 were pseudophakic and 10 underwent simultaneous phacoemulsification and XEN. Patients had uncontrolled IOP, had intolerance to
therapy, or had maximal therapy but undergoing cataract extraction. Follow-up visits included IOP, number of medications, vision, and complications and lasted for 1 year. Complete success was defined as IOP reduction greater than or equal to 20 % from pre-operative baseline at 1 year without any glaucoma medications while partial success as IOP reduction of greater than or equal to 20 % at 1 year with medications. IOP dropped from 16 ± 4 mmHg pre-op to 9 ± 5, 11 ± 6, 12 ± 5, 12 ± 4, and 12 ± 3 mmHg at 1 week, 1, 3, 6, and 12 months (p = 0.004, 0.026, 0.034, 0.01, and 0.01, Wilcoxon Signed Ranks) consecutively. BCVA (LogMAR) was 0.33 ± 0.34 and improved to 0.13 ± 0.11 at 1 year. Mean number of medications dropped from 1.9 ± 1 pre-operatively to 0.3 ± 0.49 (p = 0.003) at 1 year; 42 % of eyes achieved complete success and 66 % qualified success. Complications included choroidal detachment in 2 eyes, and implant extrusion in 1 eye, and 2 eyes underwent trabeculectomy. The authors concluded that XEN implant was an effective surgical treatment for POAG, with significant reduction in IOP and glaucoma medications at 1 year follow-up. Moreover, they stated that this new technique needed further assessment for longer follow-up survival.

In a single-arm, open-label, multi-center clinical study, Grover and co-workers (2017) evaluated the IOP-lowering performance and safety of an ab interno gelatin stent (XEN 45 Gel Stent, Allergan plc, Irvine, CA) in refractory glaucoma. Following mitomycin C pre-treatment, the stent was placed ab interno in patients who failed prior filtering/cilio-ablative procedure or had uncontrolled IOP on maximum-tolerated medical therapy, with medicated IOP greater than or equal to 20 and less than or equal to 35 mm Hg and visual field mean deviation less than or equal to -3 dB. Primary performance outcomes: patients (%) achieving greater than or equal to 20 % IOP reduction from baseline on the same or fewer medications and mean IOP change from baseline at month 12. Procedure-related complications and ocular AEs were assessed. A total of 65 patients were implanted (intent-to-treat/safety population). At 12 months, 75.4 % (46/61; observed data) reported greater than or equal to 20 % IOP lowering from baseline on the same or fewer medications. Mean IOP change from baseline was -9.1 mm Hg (95 % CI: -10.7 to -7.5) (n = 52; observed data) at 12 months, excluding patients with missing data (n = 4) and those
requiring a glaucoma-related secondary surgical intervention (n = 9). Mean medication count decreased from 3.5 (baseline) to 1.7 (12 months). No intra-operative complications or unexpected post-operative AEs were reported. Most AEs were mild/moderate; common AEs included needling (without sight-threatening complications), non-persistent loss of BCVA, and transient hypotony (requiring no surgical intervention). The authors concluded that the gelatin stent reduced IOP and medication use without raising unexpected safety concerns, offering a minimally invasive surgical option for refractory glaucoma patients.

The authors stated that potential study limitations included the absence of comparator and open-label study design, which could have impacted the outcomes. As mentioned in the key studies of the supra-ciliary microstent and trabecular micro-bypass, however, investigator masking was not feasible with this type of treatment. It was also worth noting that potential effects on the study eye of changes in the fellow eye were not considered. In addition, the study population included less than or equal to 5% Asian patients and less than or equal to 13% patients with pseudo-exfoliation, pigmentary, or mixed-mechanism glaucoma. Nonetheless, they stated that these findings were generalizable to men and women with refractory glaucoma characterized by uncontrolled IOP on maximum-tolerated medical therapy and open angles.

Lavia and colleagues (2017) analyzed the change in IOP and glaucoma medications using different MIGS devices (Trabectome, iStent, Excimer Laser Trabeculotomy (ELT), iStent Supra, CyPass, XEN, Hydrus, Fugo Blade, Ab interno canaloplasty, Goniscopy-assisted transluminal trabeculotomy) as a solo procedure or in association with phacoemulsification; RCTs and non-RCTs (non-randomized comparative studies, non-randomized studies [NRS], and before-after studies) were included. Studies with at least 1 year of follow-up in patients affected by POAG, pseudo-exfoliative glaucoma or pigmentary glaucoma were considered. Risk of bias assessment was performed using the Cochrane Risk of Bias and the ROBINS-I tools. The main outcome was the effect of MIGS devices compared to medical therapy, CS, other glaucoma surgeries and other MIGS on both IOP and use of glaucoma medications 12 months after surgery. Outcomes measures were
the MD in the change of IOP and glaucoma medication compared to baseline at 1 and 2 years and all ocular AEs. Over a total of 3,069 studies, 9 RCTs and 21 case series with a total of 2,928 eyes were included. Main concerns about risk of bias in RCTs were lack of blinding, allocation concealment and attrition bias while in non-RCTs they were represented by patients’ selection, masking of participants and co-intervention management. Limited evidence was found based on both RCTs and non-RCTs that compared MIGS surgery with medical therapy or other MIGS. In before-after series, MIGS surgery appeared effective in lowering both IOP and glaucoma drug use; MIGS showed a good safety profile: IOP spikes were the most frequent complications and no cases of infection or BCVA loss due to glaucoma were reported. The authors concluded that although MIGS appeared efficient in the reduction of the IOP and glaucoma medication and showed good safety profile, this evidence was mainly derived from non-comparative studies and further, good quality RCTs are needed. They suggested that future research should be comparative, ideally randomized, including patients and alternative treatments that are relevant to clinical settings.

Ozal and co-workers (2017) reported follow-up data for patients who underwent XEN45 gel stent implantation. A total of 15 eyes in 15 patients who underwent XEN45 gel stent implantation surgery were examined in the study. All patients were examined pre-operatively and at the following post-operative time points: 1 day; 1 and 2 weeks; and 1, 2, 3, 6, and 12 months; IOP was measured via Goldmann applanation tonometry. Combined surgical procedures (XEN45 + phacoemulsification + intraocular lens) were performed in patients who had cataracts in addition to glaucoma. The mean IOP values were significantly lower than the pre-operative values at all post-operative visits (p < 0.001). In 2 patients, the IOP exceeded 20 mmHg 12 months after surgery. These IOP increases were controlled by medical therapy, and none of the patients needed another surgical procedure. The authors concluded that the results of this study were promising, and XEN45 gel stent implantation presented a valuable contribution to glaucoma surgery. Using XEN45 gel stents, these investigators reduced IOP and medication use without significant complications in patients with different forms of glaucoma. They believed that this new surgical procedure would
play an important role in glaucoma surgery in the future. Moreover, they stated that further studies with greater numbers of patients and longer follow-up periods are needed to clarify certain points.

The authors stated that this study had several drawbacks; in particular, the small number of patients (n = 15) and the lack of control group limited their comparisons. Thus, it has not been evaluated whether the efficacy of XEN45 gel implantation differs between patients according to prior glaucoma surgery. Furthermore, the mild IOP-reducing effect of phacoemulsification alone was not evaluated. In addition, these researchers could not evaluate in which glaucoma type this surgical method is most effective. They noted that clinical trials (NCT02006693, NCT02036541) are ongoing for XEN gel stents; these researchers think that after the results of these studies have been published, new aspects of XEN gel stent implantation will be revealed.

Sng and associates (2018) noted that the XEN-45 implant (a hydrophilic collagen implant that drains aqueous to the subconjunctival space) has not been studied in the context of uveitic glaucoma. In an exploratory, prospective, case-series study, these researchers determined the safety and efficacy of the XEN-45 collagen implant in eyes with uveitic glaucoma. A total of 24 consecutive patients with medically uncontrolled uveitic glaucoma (mean age ± standard deviation [SD] = 45.3 ± 18.1 years) were implanted with the XEN-45 implant. The primary outcome measure was IOP reduction at 12 months as compared to baseline. Secondary outcome measures included ocular hypotensive medication use at 12 months, the requirement for further glaucoma surgery and failure. Intra-operative and post-operative complications were documented. The baseline mean ± SD IOP was 30.5 ± 9.8 mmHg and the mean ± SD number of glaucoma medications required was 3.3 ± 0.8. In 20 eyes (83.3 %) in whom conventional glaucoma surgery was originally perceived to be inevitable, further surgery was not required after XEN-45 implantation. The mean IOP was reduced by 60.2 % from baseline to 12.2 ± 3.1 mmHg and mean medication usage was reduced to 0.4 ± 0.9 at 12 months (both p < 0.001); 1 patient had hypotony persisting beyond 2 months that required surgical revision, and 1 patient developed blebitis. The 12-month cumulative Kaplan-Meier
survival probability was 79.2%. The authors concluded that the XEN-45 implant was effective for the treatment of patients with medically uncontrolled uveitic glaucoma. Moreover, they stated that potentially sight-threatening complications, including bleb-related ocular infection and persistent hypotony, may occur. These researchers noted that these preliminary findings from an exploratory study need to be validated by well-designed studies.

In an international, multi-center, retrospective, interventional cohort study, Schlenker and colleagues (2017) compared the safety, efficacy, and risk factors for failure of standalone ab interno gelatin microstent implantation with mitomycin C (MMC) versus trabeculectomy with MMC. A total of 354 eyes of 293 patients (185 microstent and 169 trabeculectomy) with no prior incisional surgery were included in this trial. Consecutive eyes with uncontrolled glaucoma underwent microstent or trabeculectomy surgery from January 1, 2011 through July 31, 2015 at 4 academic ophthalmology centers. Primary outcome measure was HR of failure, with failure defined as 2 consecutive IOP readings of less than 6 mmHg with vision loss or greater than 17 mmHg without glaucoma medications (complete success) at least 1 month after surgery despite in-clinic interventions (including needling).

Secondary outcome measures included IOP thresholds of 6 to 14 mmHg and 6 to 21 mmHg and same thresholds allowing for medications (qualified success), interventions, complications, and re-operations. Baseline characteristics were similar, except more men (56% versus 43%), younger patients (average, by 3 years), better pre-operative VA (22% versus 32% with 0.4 logarithm of the minimum angle of resolution vision or worse), and more trabeculoplasty (52% versus 30%) among microstent eyes. The adjusted HR of failure of the microstent relative to trabeculectomy was 1.2 (95% CI: 0.7 to 2.0) for complete success and 1.3 (95% CI: 0.6 to 2.8) for qualified success, and similar for other outcomes. Time to 25% failure was 11.2 months (95% CI: 6.9 to 16.1 months) and 10.6 months (95% CI: 6.8 to 16.2 months) for complete success and 30.3 months (95% CI: 19.0 to infinity months) and 33.3 months (95% CI: 25.7 to 46.2 months) for qualified success. Overall, white ethnicity was associated with decreased risk of failure (adjusted HR, 0.49; 95% CI: 0.25 to 0.96), and diabetes was associated with increased risk of failure (adjusted HR, 4.21; 95% CI: 1.8 to 9.9).
CI: 2.10 to 8.45). There were 117 and 165 distinct interventions: 43 % and 31 % underwent needling, respectively, and 50 % of trabeculectomy eyes underwent laser suture lysis. There were 22 and 30 distinct complications, although most were transient; 10 % and 5 % underwent re-operation (p = 0.11). The authors concluded that there was no detectable difference in risk of failure and safety profiles between stand-alone ab interno microstent with MMC and trabeculectomy with MMC.

In a retrospective analysis, Hengerer and associates (2017) evaluated the IOP-lowering effects and complication management of an ab interno gel implant for the treatment of patients refractory to anti-glaucoma medication or glaucoma surgery. These investigators examined medical records of 242 consecutive eyes of 146 patients with uncontrolled IOP despite maximum tolerated medical therapy or prior surgical intervention that underwent XEN45 implantation (as sole procedure or in combination with CS) between March 2014 and June 2015. Data included IOP, number of glaucoma medications, the need for additional surgery, needling, and complications. During the study period, mean IOP had decreased by 54.1 % from 32.19 (± 9.1) mm Hg to 14.24 (± 4.0) mm Hg (p = 0.00; Wilcoxon test). The number of anti-glaucoma medications had decreased from a mean of 3.13 ± 1.0 to 0.3 ± 0.7 (p = 0.00; Wilcoxon test). Needling was required between week 1 and months 3 in 27.7 % of all eyes to enhance the outflow. Hypotony (IOP less than 6 mm Hg) was observed in 9 eyes (4.0 %) at 1 month but normalized in all eyes at 12 months post-operatively; 2 eyes experienced hypotony requiring the refill of the anterior chamber. The authors concluded that these findings indicated that the XEN45 gel implant had a favorable safety profile and was an effective therapeutic option for controlling IOP in glaucoma patients with unregulated IOP despite IOP-lowering medical therapy or prior surgical intervention. It offered an effective approach, both as sole procedure and in combination with CS.

In a prospective, non-randomized, clinical study, De Gregorio and co-workers (2018) examined the efficacy in IOP reduction and safety of the smallest gel stent (XEN 45 Gel Stent) micro-incisional glaucoma surgery combined with micro-incisional CS (MICS). A total of 41 eyes of 33 patients with OAG underwent a XEN 45 Gel
Stent implantation combined with MICS. Treatment outcomes analyzed included: IOP, medication use, intra- and post-operative complications. At the end of the follow-up, these researchers evaluated the complete success, defined as a post-operative IOP of greater than or equal to 6 and less than or equal to 17 mmHg without glaucoma medications and the qualified success defined as a post-operative IOP greater than or equal to 6 and less than or equal to 17 mmHg, with glaucoma medications. The mean pre-operative IOP was 22.5 ± 3.7 mmHg on 2.5 ± 0.9 medication classes. After 12 months, the mean post-operative IOP was 13.1 ± 2.4 mmHg (mean IOP reduction of 41.82 %) with a mean of 0.4 ± 0.8 medication classes (p < 0.05 for IOP and medications). The complete success rate was achieved in 80.4 % and a qualified success in 97.5 %. There were no major intra- and post-operative complications during the 1st year of follow-up. The authors concluded that this study demonstrated that the smaller diameter XEN 45 gel implant was statistically effective in reducing IOP and medications in glaucoma patients with a low rate of complications.

The main drawbacks of this study were its small sample size (n = 33 patients), relatively short-term follow-up (12 months), and its non-randomized design.

In a prospective, interventional study, Mansouri and colleagues (2018) evaluated the safety and efficacy of XEN gel implant as a stand-alone treatment versus combined XEN-phacoemulsification surgery (XEN + CS) in glaucoma patients. A total of 149 eyes (113 patients) with OAG and uncontrolled (IOP despite medical treatment were enrolled at a tertiary glaucoma center and followed-up for a minimum of 1 year. Approximately 2/3 of patients underwent combined XEN + CS, while the remainder had XEN alone surgery. Primary outcome was a 20 % or more decrease in IOP from medicated baseline at 1 year. Mean IOP, mean number of medications at last follow-up, and incidence of AEs were analyzed. Of 149 enrolled eyes, data of 87 (58 %) were available at 1 year. A total of 109 (73.2 %) eyes underwent XEN + CS and 40 (26.8 %) XEN alone surgery. Mean medicated IOP was 20.0 ± 7.1 at baseline and 13.9 ± 4.3 mm Hg at 1 year (p < 0.01), a 31 % IOP reduction. Mean medications dropped from 1.9 ± 1.3 pre-operatively to 0.5 ± 0.8 at 1 year (p < 0.001). In total, 62.1 % of patients achieved a greater than or equal to 20 % IOP reduction;
this proportion was higher in the XEN alone group; 57.7 % of eyes achieved complete success (without any anti-glaucoma medications) and 71.1 % qualified success (with or without medications) when IOP of less than 16 mm Hg was considered as the definition of success. In all, 37 % of patients required needling intervention; AEs included bleb revision in 5 eyes, choroidal detachment in 2 eyes, and 2nd glaucoma surgery in 9 eyes. The authors concluded that the XEN gel implant as a stand-alone procedure or combined with CS demonstrated safe and sustained IOP reduction after 1 year. This study had 2 main drawbacks: First, only 58 % (87) of the 149 enrolled eyes were available at 1 year follow-up; and second, follow-up was short-term (1 year).

Widder and colleagues (2018) examined the IOP-lowering potential, the risk profile, and the success rate of the XEN45 Gel Stent. A total of 261 eyes underwent surgery. The mean follow-up time was 8.5 months. The aim of the treatment was to achieve adequate IOP reduction without medication. Therefore, all patients who did not show sufficiently reduced IOP underwent a surgical revision with opening of the conjunctiva. To determine the success rate, these researchers performed 2 kinds of analysis: the primary success rate -- eyes with appropriate IOP control without medication or surgical revision, and overall success rate -- 1 surgical revision was allowed; IOP was lowered from 24.3 mmHg (SD 6.6) to 16.8 mmHg (SD 7.6), and the medication score was lowered from 2.6 (SD 1.1) to 0.2 (SD 0.7). Revisional surgery was performed in 80 eyes (34 %). After a 1st revision, IOP was lowered to 14.0 mmHg (SD 5.1), and the medication score was lowered to 0.2 (SD 0.6). The primary success rate was 66 % and the overall success rate 90 %. The primary success rate was higher in pseudophakic eyes (73 %) than in phakic eyes (53 %) or combined surgery (55 %). The authors concluded that the XEN45 Gel Stent had an IOP-lowering potential and few side-effects; pseudophakic eyes appeared to have a better primary prognosis compared to combined surgery or surgery in phakic eyes.

In a prospective, non-randomized, open-label, multi-center, 2-year study, Reitsamer and colleagues (2019) examined the effectiveness of an ab interno subconjunctival gelatin implant (the AqueSys XEN Implant) as primary surgical intervention in reducing IOP and IOP-
lowering medication count in medically uncontrolled moderate POAG. Eyes with medicated baseline IOP 18 to 33 mmHg on 1 to 4 topical medications were implanted with (phaco + implant) or without (implant alone) phacoemulsification. Changes in mean IOP and medication count at months 12 (primary outcomes) and 24, clinical success rate (eyes [%] achieving greater than or equal to 20 % IOP reduction from baseline on the same or fewer medications without glaucoma-related secondary surgical intervention), intra-operative complications, and post-operative AEs were assessed. The modified intent-to-treat population included 202 eyes (of 218 implanted). Changes (S.D.) in mean IOP and medication count from baseline were - 6.5 (5.3) mmHg and - 1.7 (1.3) at month 12 and - 6.2 (4.9) mmHg and - 1.5 (1.4) at month 24, respectively (all p <0.001). Mean medicated baseline IOP was reduced from 21.4 (3.6) to 14.9 (4.5) mmHg at 12 months and 15.2 (4.2) mmHg at 24 months, with similar results in both treatment groups. The clinical success rate was 67.6 % at 12 months and 65.8 % at 24 months. Overall, 51.1 (12 months) and 44.7 % (24 months) of eyes were medication-free. The implant safety profile compared favorably with that published for trabeculectomy and tube shunts. The authors concluded that the gelatin implant effectively reduced IOP and medication needs over 2 years in POAG uncontrolled medically, with an acceptable safety profile.

In summary, further investigation with RCTs are needed on the XEN Glaucoma Treatment System, especially with its long-term effectiveness as well as cost-effectiveness.

Drug-Eluting Ocular Insert

Bhagav et al (2011) stated that pathology of eye, especially in the case of glaucoma, requires optimal therapeutically effective concentration of the drug in the ocular tissues for prolonged period of time with decreased dosing frequency and improved patient compliance. In the present study, brimonidine tartrate (BRT) ocular inserts were designed based on hydrophilic and/or inert/zwitterionic polymer matrix to design muco-adhesive and extended release ocular inserts. Designed inserts were evaluated for their physicochemical properties such as crushing strength/hardness, friability, drug content and muco-adhesion, and erosion and in-vitro drug release characteristics. The selected optimized formulations
were compared with marketed preparation for in-vivo ocular irritation in healthy rabbits and for in-vivo pharmacodynamic efficacy on alpha-chymotrypsin-induced glaucomatous rabbits. The developed formulations showed good physicochemical properties and muco-adhesive strength, and a good correlation was seen between rate of erosion or swelling with drug release rate in case of formulations with higher proportion of polyethylene oxide (PEO). Modulation of drug release was achieved by incorporating Eudragit in PEO matrix. Addition of Eudragit resulted in shifting of drug release mechanism from erosion-controlled to diffusion-controlled mechanism. The authors concluded that in-vivo ocular irritation studies confirmed the absence of any irritation upon administration in rabbits; and intra-ocular pressure (IOP) measurement studies showed an improved IOP-lowering ability of ocular insert of BRT in comparison to eye drops.

Franca et al (2014) developed and evaluated a novel sustained-release drug delivery system of bimatoprost (BIM). Chitosan polymeric inserts were prepared using the solvent casting method and characterized by swelling studies, infrared spectroscopy, differential scanning calorimetry, drug content, scanning electron microscopy and in-vitro drug release. Bio-distribution of 99mTc-BIM eye drops and 99mTc-BIM-loaded inserts, after ocular administration in Wistar rats, was accessed by ex-vivo radiation counting. The inserts were evaluated for their therapeutic efficacy in glaucomatous Wistar rats. Glaucoma was induced by weekly intra-cameral injection of hyaluronic acid. BIM-loaded inserts (equivalent to 9.0 µg BIM) were administered once into conjunctival sac, after ocular hypertension (OHT) confirmation. BIM eye drop was topically instilled in a second group of glaucomatous rats for 15 days, while placebo inserts were administered once in a third group. An untreated glaucomatous group was used as control; IOP was monitored for 4 consecutive weeks after treatment began. At the end of the experiment, retinal ganglion cells and optic nerve head cupping were evaluated in the histological eye sections. Characterization results revealed that the drug physically interacted, but did not chemically react with the polymeric matrix. Inserts released continually BIM in-vitro during 8 hours. Bio-distribution studies showed that the amount of 99mTc-BIM that remained in the eye was significantly lower after eye drop instillation than after
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chitosan insert implantation. BIM-loaded inserts lowered IOP for 4 weeks, after 1 application, while IOP values remained significantly high for the placebo and untreated groups. Eye drops were only effective during the daily treatment period; IOP results were reflected in retinal ganglion cells counting and optic nerve head cupping damage. The authors concluded that BIM-loaded inserts provided sustained release of BIM and appeared to be a promising system for glaucoma management.

In a phase II, parallel-arm, multi-center, double-masked, randomized controlled trial (RCT), Brandt et al (2016) compared topical BIM ocular insert with twice-daily timolol (TIM) eye drops in patients with open-angle glaucoma (OAG) or OHT treated for 6 months. A total of 130 adult OAG or OHT patients were included in this study. Eligible patients were randomized 1:1 to receive a BIM insert plus artificial tears twice-daily or a placebo insert plus TIM (0.5 % solution) twice-daily for 6 months after a screening wash-out period. Diurnal IOP measurements (at 0, 2, and 8 hours) were obtained at baseline; weeks 2, 6, and 12; and months 4, 5, and 6. Key eligibility included wash-out IOP of 23 mmHg or more at time 0, IOP of 20 mmHg or more at 2 and 8 hours, and IOP of 34 mmHg or less at all time-points; no prior incisional surgery for OAG or OHT; and no known non-responders to prostaglandins. The primary efficacy end-point examined the difference in mean change from baseline in diurnal IOPs (point estimate, 95 % CI) across 9 co-primary end-points at weeks 2, 6, and 12 comparing the BIM-arm with the TIM-arm using a non-inferiority margin of 1.5 mmHg. Secondary end-points were diurnal IOP measurements at months 4, 5, and 6 and adverse events (AEs). A mean reduction from baseline IOP of -3.2 to -6.4 mmHg was observed for the BIM group compared with -4.2 to -6.4 mmHg for the TIM group over 6 months. The study met the non-inferiority definition at 2 of 9 time-points but was under-powered for the observed treatment effect. Adverse events were consistent with BIM or TIM exposure; no unexpected ocular AEs were observed. Primary retention rate of the insert was 88.5 % of patients at 6 months. The authors concluded that clinically relevant reduction in mean IOP was observed over 6 months with a BIM ocular insert and appeared to be safe and well-
tolerated. They stated that the topically applied BIM insert may provide an alternative to daily eye drops to improve adherence, consistency of delivery, and reduction of elevated IOP.

**Hydrus Microstent**

In a prospective, multi-center, single-masked RCT, Pfeiffer and co-workers (2015) evaluated the safety and effectiveness of the Hydrus Microstent (Ivantis, Inc., Irvine, CA) with concurrent cataract surgery (CS) for reducing IOP in OAG. A total of 100 eyes from 100 patients aged 21 to 80 years with OAG and cataract with IOP of 24 mmHg or less with 4 or fewer hypotensive medications and a washed-out diurnal IOP (DIOP) of 21 to 36 mmHg. On the day of surgery, patients were randomized 1:1 to undergo CS with the microstent or CS alone. Post-operative follow-up was at 1 day, 1 week, and 1, 3, 6, 12, 18, and 24 months. Washout of hypotensive medications was repeated at 12 and 24 months. Response to treatment was defined as a 20 % or more decrease in washed out DIOP at 12 and 24 months of follow-up compared with baseline. Mean DIOP at 12 and 24 months, the proportion of subjects requiring medications at follow-up, and the mean number of medications were analyzed. Safety measures included AEs, change in VA, and slit-lamp observations. The proportion of patients with a 20 % reduction in washed out DIOP was significantly higher in the Hydrus plus CS group at 24 months compared with the CS group (80 % versus 46 %; p = 0.0008). Washed out mean DIOP in the Hydrus plus CS group was significantly lower at 24 months compared with the CS group (16.9 ± 3.3 mmHg versus 19.2 ± 4.7 mmHg; p = 0.0093), and the proportion of patients using no hypotensive medications was significantly higher at 24 months in the Hydrus plus CS group (73 % versus 38 %; p = 0.0008). There were no differences in follow-up VA between groups. The only notable device-related AE was focal peripheral anterior synechiae (1 to 2 mm in length). Otherwise, AE frequency was similar in the 2 groups. The authors concluded that IOP was clinically and statistically significantly lower at 2 years in the Hydrus plus CS group compared with the CS alone group, with no differences in safety.
In a retrospective case-series study, Fea and associates (2017b) examined the safety and efficacy of a new Schlemm canal scaffold microstent (Hydrus) combined with CS in routine clinical practice. Clinical outcomes in patients with POAG who had combined phacoemulsification and microstent implantation were analyzed. Data (IOP, number of glaucoma medications, incidence of complications) were collected pre-operatively and post-operatively through 24 months. A total of 92 eyes were included; 6 patients had previous glaucoma surgeries; 67 patients completed a 2-year follow-up. The mean baseline IOP was 19.4 mm Hg ± 4.4 (SD). The mean IOP was 15.5 ± 2.7 mm Hg at 1 year and 15.7 ± 2.5 mm Hg at 2 years (p < 0.001). The IOP reduction was correlated with the baseline IOP (R² = 0.72). The mean number of glaucoma medications was 2.1 ± 1.0 pre-operatively, decreasing significantly at 1 year (0.6 ± 1.0) and 2 years (0.7 ± 1.0) (p < 0.001). At 2 years, 64% of patients were medication-free. In patients with an IOP of 18 mm Hg or higher pre-operatively, the reduction in IOP and in the number of medications was higher; 2 patients required microstent re-positioning intra-operatively; 1 patient was treated with an argon laser for microstent obstruction, and 1 patient had a trabeculectomy at 18 months. The authors concluded that this microstent combined with CS safely and effectively reduced the IOP and medication use in a routine clinical practice setting with results comparable to those in previously published controlled clinical trials.

In a prospective, interventional, case-series study, Fea and colleagues (2017c) compared the reduction of IOP and glaucoma medications following selective laser trabeculoplasty (SLT) versus stand-alone placement of the Hydrus microstent. This trial included a total of 56 eyes (56 patients) with uncontrolled POAG. Patients received either SLT (n = 25) or Hydrus implantation (n = 31) in 2 centers; they were evaluated at baseline and 1, 7 days, 1, 3, 6 and 12 months after surgery. Main outcome measures were IOP and number of glaucoma medications variations inter-groups and intra-groups. There were no significant differences at baseline between groups, but the mean deviation was worse in the Hydrus group (-8.43 ± 6.84 dB, CI: -2.8 to -3.3 versus -3.04 ± 0.65 dB, CI: -6 to -10.8; p < 0.001). After 12 months, there was a significant decrease in IOP and medications in the Hydrus group compared with baseline values. In the SLT group, only the decrease in IOP was
significant. There was 3-fold greater reduction in medication use in the Hydrus group compared with SLT (-1.4 ± 0.97 versus -0.5±1.05, p = 0.001); 47% of patients were medication-free at 12 months in the Hydrus group (4% in the SLT group). No complications were recorded in the SLT group. In the Hydrus group, 3 patients experienced a temporary reduction of VA post-operatively, and 2 patients had post-operative IOP spikes that resolved within 1 week. The authors concluded that both SLT and Hydrus implantation reduced IOP without serious AEs; and Hydrus implantation led to a significant and further reduction in medication dependence at 12 months.

Al-Mugheiry and co-workers (2017) evaluated learning effects with respect to outcomes of a MIGS inserted during CS in glaucoma patients. This trial was a single-surgeon, observational cohort study of 25 consecutive Hydrus microstent insertions, with a minimum follow-up of 12 months. A learning curve analysis was performed by assessing hypotensive effect, AEs, and surgical procedure duration, with respect to consecutive case number. Success was defined with respect to various IOP targets (21, 18, 15 mm Hg) and reduction in required anti-glaucoma medications. Complete success was defined as achieving target IOP without anti-glaucoma therapy. No clinically significant AEs or learning effects were identified, although surgical time reduced with consecutive case number. Mean follow-up was 16.8 months. At final follow-up the mean IOP for all eyes was reduced from 18.1 (± 3.6) mm Hg [and a simulated untreated value of 25.9 (± 5.2) mm Hg] to 15.3 (± 2.2) mm Hg (p = 0.007; p < 0.0001) and the mean number of topical anti-glaucoma medications was reduced from 1.96 (± 0.96) to 0.04 (± 0.20) (p < 0.0001). Complete success (IOP of less than 21 mm Hg, no medications) was 96% at final follow-up. Complete success (IOP of less than 18 mm Hg, no medications) was 80% at final follow-up, but only 32% with a target IOP of less than 15 mm Hg (no medications). The authors concluded that no significant learning curve effects were observed for a trained surgeon with respect to MIGS microstent insertion performed at the time of CS. Adjunctive MIGS surgery was successful in lowering IOP to less than 18 mm Hg and reducing/abolishing the requirement for anti-glaucoma medication in eyes with OAG, but less successful at achieving low IOP levels (less than 15 mm Hg).
In a prospective, multi-center, single-masked, RCT, Samuelson and colleagues (2019) compared CS with implantation of a Schlemm canal microstent with CS alone for the reduction of IOP and medication use after 24 months. Subjects with concomitant POAG, visually significant cataract, and washed-out modified DIOP (MDIOP) between 22 and 34 mmHg were enrolled in this trial. They were randomized 2:1 to receive a single Hydrus microstent in the Schlemm canal or no stent after uncomplicated phacoemulsification. Comprehensive eye examinations were conducted 1 day, 1 week, and 1, 3, 6, 12, 18, and 24 months postoperatively. Medication washout and MDIOP measurement were repeated at 12 and 24 months. The primary and secondary effectiveness end-points were the proportion of subjects demonstrating a 20 % or greater reduction in unmedicated MDIOP and change in mean MDIOP from baseline at 24 months, respectively. Hypotensive medication use was tracked throughout the course of follow-up. Safety measures included the frequency of surgical complications and AEs. A total of 369 eyes were randomized after phacoemulsification to Hydrus microstent (HMS) and 187 to no microstent (NMS). At 24 months, unmedicated MDIOP was reduced by greater than or equal to 20 % in 77.3 % of HMS group eyes and in 57.8 % of NMS group eyes (difference = 19.5 %, 95 % CI: 11.2 % to 27.8 %, p < 0.001). The mean reduction in 24-month unmedicated MDIOP was -7.6±4.1 mmHg (mean ± standard deviation) in the HMS group and -5.3±3.9 mmHg in the NMS group (difference = -2.3 mmHg; 95 % CI: -3.0 to -1.6; p < 0.001). The mean number of medications was reduced from 1.7 ± 0.9 at baseline to 0.3 ± 0.8 at 24 months in the HMS group and from 1.7 ± 0.9 to 0.7 ± 0.9 in the NMS group (difference = -0.4 medications; p < 0.001). There were no serious ocular AEs related to the microstent, and no significant differences in safety parameters between the 2 groups. The authors concluded that this 24-month multi-center RCT demonstrated superior reduction in MDIOP and medication use among subjects with mild-to-moderate POAG who received a Schlemm canal microstent combined with phacoemulsification compared with phacoemulsification alone.

On August 10, 2018, the FDA approved the Hydrus Microstent for use in conjunction with cataract surgery for the reduction of IOP in adult patients with mild-to-moderate POAG.
The Hydrus Microstent should not be used in patients with the following types of glaucoma:

- Angle closure glaucoma
- Malignant glaucoma
- Neovascular glaucoma
- Traumatic glaucoma
- Uveitic glaucoma.

Furthermore, the Hydrus Microstent should not be used in patients with birth defects of the anterior chamber angle of the eye.

CPT Codes / HCPCS Codes / ICD-10 Codes

Information in the [brackets] below has been added for clarification purposes. Codes requiring a 7th character are represented by “+”:

<table>
<thead>
<tr>
<th>Code</th>
<th>Code Description</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Laser Trabeculoplasty or Food and Drug Administration (FDA) - approved aqueous</td>
</tr>
<tr>
<td></td>
<td>drainage/shunt implants:</td>
</tr>
<tr>
<td></td>
<td><strong>CPT codes covered if selection criteria are met:</strong></td>
</tr>
<tr>
<td>0191T</td>
<td>Insertion of anterior segment aqueous drainage device, without extraocular</td>
</tr>
<tr>
<td></td>
<td>reservoir, internal approach, into the trabecular meshwork; initial insertion</td>
</tr>
<tr>
<td>0376T</td>
<td>Insertion of anterior segment aqueous drainage device, without extraocular</td>
</tr>
<tr>
<td></td>
<td>reservoir, internal approach, into the trabecular meshwork; each additional</td>
</tr>
<tr>
<td></td>
<td>device insertion (List separately in addition to code for primary procedure)</td>
</tr>
<tr>
<td>0449T</td>
<td>Insertion of aqueous drainage device, without extraocular reservoir, internal</td>
</tr>
<tr>
<td></td>
<td>approach, into the subconjunctival space; initial device</td>
</tr>
<tr>
<td>Code</td>
<td>Code Description</td>
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<td>--------</td>
<td>----------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>0450T</td>
<td>Insertion of aqueous drainage device, without extraocular reservoir, internal approach, into the subconjunctival space; each additional device (List separately in addition to code for primary procedure)</td>
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<tr>
<td>65855</td>
<td>Trabeculoplasty by laser surgery</td>
</tr>
<tr>
<td>66180</td>
<td>Aqueous shunt to extraocular equatorial plate reservoir, external approach; with graft</td>
</tr>
<tr>
<td>66183</td>
<td>Insertion of anterior segment aqueous drainage device, without extraocular reservoir, external approach</td>
</tr>
<tr>
<td>66185</td>
<td>Revision of aqueous shunt to extraocular equatorial plate reservoir; with graft</td>
</tr>
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</table>

CPT codes not covered for indications listed in the CPB:

<table>
<thead>
<tr>
<th>Code</th>
<th>Code Description</th>
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<tbody>
<tr>
<td>0253T</td>
<td>Insertion of anterior segment aqueous drainage device, without extraocular reservoir, internal approach, into the suprachoroidal space</td>
</tr>
<tr>
<td>0444T</td>
<td>Initial placement of a drug-eluting ocular insert under one or more eyelids, including fitting, training, and insertion, unilateral or bilateral</td>
</tr>
<tr>
<td>0445T</td>
<td>Subsequent placement of a drug-eluting ocular insert under one or more eyelids, including re-training, and removal of existing insert, unilateral or bilateral</td>
</tr>
<tr>
<td>0474T</td>
<td>Insertion of anterior segment aqueous drainage device, with creation of intraocular reservoir, internal approach, into the supraciliary space</td>
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</tbody>
</table>

Other CPT codes related to the CPB:

<table>
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<th>Code</th>
<th>Code Description</th>
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<tbody>
<tr>
<td>66150</td>
<td>Fistulization of sclera for glaucoma; trephination with iridectomy</td>
</tr>
<tr>
<td>66155</td>
<td>thermodenaturation with iridectomy</td>
</tr>
<tr>
<td>Code</td>
<td>Code Description</td>
</tr>
<tr>
<td>--------</td>
<td>---------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>66160</td>
<td>Sclerectomy with punch or scissors, with iridectomy</td>
</tr>
<tr>
<td>66710</td>
<td>Ciliary body destruction; cyclophotocoagulation, transscleral</td>
</tr>
<tr>
<td>66720</td>
<td>Cryotherapy</td>
</tr>
<tr>
<td>66761</td>
<td>Iridotomy/iridectomy by laser surgery (e.g., for glaucoma) (one or more sessions)</td>
</tr>
</tbody>
</table>

**HCPCS codes covered if selection criteria are met:**

<table>
<thead>
<tr>
<th>Code</th>
<th>Code Description</th>
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<tbody>
<tr>
<td>J7315</td>
<td>Mitomycin, ophthalmic, 0.2 mg</td>
</tr>
<tr>
<td>J9190</td>
<td>Injection, fluorouracil, 500 mg</td>
</tr>
<tr>
<td>L8612</td>
<td>Aqueous shunt [covered if FDA approved] [DeepLight Gold Micro-Shunt and Eyepass Glaucoma Implant are not covered]</td>
</tr>
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</table>

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

<table>
<thead>
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<th>Code</th>
<th>Code Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>C9257</td>
<td>Injection, bevacizumab, 0.25mg [Avastin] [intraocular dose]</td>
</tr>
<tr>
<td>J0178</td>
<td>Injection, aflibercept, 1 mg</td>
</tr>
<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>
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<tr>
<td>J1040</td>
<td>Injection, methylprednisolone acetate, 80 mg</td>
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<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>Code</td>
<td>Code Description</td>
</tr>
<tr>
<td>---------</td>
<td>------------------------------------------------------------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>J1720</td>
<td>Injection, hydrocortisone sodium succinate, up to 100 mg (i.e., Solu-Cortef)</td>
</tr>
<tr>
<td>J2503</td>
<td>Injection, pegaptanib sodium, 0.3 mg</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>J2778</td>
<td>Injection, ranibizumab, 0.1 mg</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>J7509</td>
<td>Methylprednisolone, oral, per 4 mg</td>
</tr>
<tr>
<td>J7510</td>
<td>Prednisolone, oral, per 5 mg</td>
</tr>
<tr>
<td>J7512</td>
<td>Prednisone, immediate release or delayed release, oral, 1 mg</td>
</tr>
<tr>
<td>J8540</td>
<td>Dexamethasone, oral, 0.25 mg</td>
</tr>
<tr>
<td>J9035</td>
<td>Injection, bevacizumab, 10 mg [Avastin] [chemotherapy dose]</td>
</tr>
<tr>
<td>J9280</td>
<td>Injection, mitomycin, 5 mg</td>
</tr>
<tr>
<td>Q5107</td>
<td>Injection, bevacizumab-awwb, biosimilar, (mvasi), 10 mg</td>
</tr>
</tbody>
</table>

**Other HCPCS codes related to the CPB:**

<table>
<thead>
<tr>
<th>Code</th>
<th>Code Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>J0171</td>
<td>Injection, adrenaline, epinephrine, 0.1 mg</td>
</tr>
<tr>
<td>Code</td>
<td>Code Description</td>
</tr>
<tr>
<td>--------</td>
<td>----------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>J1120</td>
<td>Injection, acetazolamide sodium, up to 500 mg</td>
</tr>
</tbody>
</table>

ICD-10 codes covered if selection criteria are met:

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>H40.1110</td>
<td>Primary open-angle glaucoma</td>
</tr>
<tr>
<td>H40.1194</td>
<td></td>
</tr>
</tbody>
</table>

iStent Trabecular Micro-Bypass Stent System:

CPT codes covered if selection criteria are met:

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>0191T</td>
<td>Insertion of anterior segment aqueous drainage device, without extraocular reservoir, internal approach, into the trabecular meshwork; initial insertion</td>
</tr>
<tr>
<td>0376T</td>
<td>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)</td>
</tr>
</tbody>
</table>

CPT codes not covered for indications listed in the CPB:

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>0253T</td>
<td>Insertion of anterior segment aqueous drainage device, without extraocular reservoir, internal approach, into the suprachoroidal space [iStent G3 Supra]</td>
</tr>
<tr>
<td>0474T</td>
<td>Insertion of anterior segment aqueous drainage device, with creation of intraocular reservoir, internal approach, into the suprachiliary space [Cypass]</td>
</tr>
</tbody>
</table>

Other CPT codes related to the CPB:

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>66820 - 66821</td>
<td>Discussion of secondary membranous cataract (opacified posterior lens capsule and/or anterior hyaloid); stab incision technique (Ziegler or Wheeler knife) or laser surgery (eg, YAG laser) (1 or more stages)</td>
</tr>
<tr>
<td>Code</td>
<td>Code Description</td>
</tr>
<tr>
<td>---------</td>
<td>------------------</td>
</tr>
<tr>
<td>66830</td>
<td>Removal of secondary membranous cataract (opacified posterior lens capsule and/or anterior hyaloid) with corneo-scleral section, with or without iridectomy (iridocapsulotomy, iridocapsulectomy)</td>
</tr>
<tr>
<td>66840</td>
<td>Removal of lens material; aspiration technique, 1 or more stages</td>
</tr>
<tr>
<td>66850</td>
<td>Removal of lens material; phacofragmentation technique (mechanical or ultrasonic) (eg, phacoemulsification), with aspiration</td>
</tr>
<tr>
<td>66852</td>
<td>Removal of lens material; pars plana approach, with or without vitrectomy</td>
</tr>
</tbody>
</table>

**HCPCS codes covered if selection criteria are met:**

- C1783  | Ocular implant, aqueous drainage assist device
- L8612  | Aqueous shunt

**ICD-10 codes covered if selection criteria are met:**

- H25.011 - H26.9  | Cataract [must be billed with H40.011+]
- H40.1111  | Primary open-angle glaucoma, right eye, mild stage
- H40.1112  | Primary open-angle glaucoma, right eye, moderate stage
- H40.1121  | Primary open-angle glaucoma, left eye, mild stage
- H40.1122  | Primary open-angle glaucoma, left eye, moderate stage
- H40.1131  | Primary open-angle glaucoma, bilateral, mild stage
- H40.1132  | Primary open-angle glaucoma, bilateral, moderate stage
- Q12.0 - Q12.9  | Congenital cataract and lens malformations

**ICD-10 codes not covered for indications listed in the CPB:**
<table>
<thead>
<tr>
<th>Code</th>
<th>Code Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>C69.60</td>
<td>Malignant neoplasm of orbit [retrobulbar tumor]</td>
</tr>
<tr>
<td>C69.62</td>
<td></td>
</tr>
<tr>
<td>E05.00</td>
<td>Thyrotoxicosis with diffuse goiter [thyroid eye disease]</td>
</tr>
<tr>
<td>E05.01</td>
<td></td>
</tr>
<tr>
<td>H40.20</td>
<td>Primary angle-closure glaucoma</td>
</tr>
<tr>
<td>H40.2494</td>
<td></td>
</tr>
<tr>
<td>H40.50</td>
<td>Glaucoma secondary to other eye disorders</td>
</tr>
<tr>
<td>H40.53</td>
<td></td>
</tr>
<tr>
<td>H40.89</td>
<td>Other specified glaucoma [neovascular glaucoma]</td>
</tr>
<tr>
<td>Q85.8</td>
<td>Other phakomatoses, not elsewhere classified [Sturge-Weber Syndrome]</td>
</tr>
</tbody>
</table>

**Hydrus Microstent:**

**CPT codes covered if selection criteria are met:**

<table>
<thead>
<tr>
<th>Code</th>
<th>Code Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>0191T</td>
<td>Insertion of anterior segment aqueous drainage device, without extraocular reservoir, internal approach, into the trabecular meshwork; initial insertion</td>
</tr>
<tr>
<td>0376T</td>
<td>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)</td>
</tr>
</tbody>
</table>

**HCPCS codes covered if selection criteria are met:**

<table>
<thead>
<tr>
<th>Code</th>
<th>Code Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>C1783</td>
<td>Ocular implant, aqueous drainage assist device</td>
</tr>
<tr>
<td>L8612</td>
<td>Aqueous shunt</td>
</tr>
</tbody>
</table>

**ICD-10 codes covered if selection criteria are met:**

<table>
<thead>
<tr>
<th>Code</th>
<th>Code Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>H25.011</td>
<td>Cataract [must be billed with H40.011+]</td>
</tr>
<tr>
<td>H26.9</td>
<td></td>
</tr>
<tr>
<td>H40.1111</td>
<td>Primary open-angle glaucoma, right eye, mild stage</td>
</tr>
<tr>
<td>H40.1112</td>
<td>Primary open-angle glaucoma, right eye, moderate stage</td>
</tr>
<tr>
<td>Code</td>
<td>Code Description</td>
</tr>
<tr>
<td>--------------</td>
<td>----------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>H40.1121</td>
<td>Primary open-angle glaucoma, left eye, mild stage</td>
</tr>
<tr>
<td>H40.1122</td>
<td>Primary open-angle glaucoma, left eye, moderate stage</td>
</tr>
<tr>
<td>H40.1131</td>
<td>Primary open-angle glaucoma, bilateral, mild stage</td>
</tr>
<tr>
<td>H40.1132</td>
<td>Primary open-angle glaucoma, bilateral, moderate stage</td>
</tr>
<tr>
<td>H40.151</td>
<td>Residual stage of open-angle glaucoma, right eye</td>
</tr>
<tr>
<td>H40.152</td>
<td>Residual stage of open-angle glaucoma, left eye</td>
</tr>
<tr>
<td>H40.153</td>
<td>Residual stage of open-angle glaucoma, bilateral</td>
</tr>
<tr>
<td>Q 12.0 – Q 12.9</td>
<td>Congenital cataract and lens malformations</td>
</tr>
<tr>
<td>H40.20x0 – H40.249</td>
<td>Primary angle-closure glaucoma</td>
</tr>
<tr>
<td>H40.50x0 – H40.534</td>
<td>Glaucoma secondary to other eye disorders [secondary angle-closure glaucoma]</td>
</tr>
<tr>
<td>H40.831 – H40.839</td>
<td>Aqueous misdirection</td>
</tr>
<tr>
<td>H40.30x0 – H40.33x4</td>
<td>Glaucoma secondary to eye trauma</td>
</tr>
<tr>
<td>H40.40x0 – H40.43x4</td>
<td>Glaucoma secondary to eye inflammation [uveitic glaucoma]</td>
</tr>
</tbody>
</table>

**ICD-10 codes not covered for indications listed in the CPB:**

<table>
<thead>
<tr>
<th>Code</th>
<th>Code Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Q 13.00 – Q 13.89</td>
<td>Congenital malformations of anterior segment of eye [birth defects of the anterior chamber angle of the eye]</td>
</tr>
</tbody>
</table>

**XEN Glaucoma Treatment System:**

**CPT codes covered if selection criteria are met:**
<table>
<thead>
<tr>
<th>Code</th>
<th>Code Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>0449T</td>
<td>Insertion of aqueous drainage device, without extraocular reservoir, internal approach, into the subconjunctival space; initial device</td>
</tr>
</tbody>
</table>

ICD-10 codes covered if selection criteria are met:

<table>
<thead>
<tr>
<th>Code</th>
<th>Code Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>H40.1110</td>
<td>Glaucoma</td>
</tr>
<tr>
<td>H40.1194</td>
<td></td>
</tr>
<tr>
<td>H40.1311</td>
<td>Pigmentary glaucoma</td>
</tr>
<tr>
<td>H40.1394</td>
<td></td>
</tr>
</tbody>
</table>

Beta radiation for glaucoma:

CPT codes not covered for indications listed in the CPB:

<table>
<thead>
<tr>
<th>Code</th>
<th>Code Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>77401</td>
<td>Radiation treatment delivery</td>
</tr>
<tr>
<td>77412</td>
<td></td>
</tr>
</tbody>
</table>

HCPCS codes not covered for indications listed in the CPB:

<table>
<thead>
<tr>
<th>Code</th>
<th>Code Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>G6001</td>
<td>Radiation treatment delivery</td>
</tr>
<tr>
<td>G6014</td>
<td></td>
</tr>
</tbody>
</table>

ICD-10 codes not covered for indications listed in the CPB:

<table>
<thead>
<tr>
<th>Code</th>
<th>Code Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>H40.001</td>
<td>Glaucoma</td>
</tr>
<tr>
<td>H40.9</td>
<td>Glaucoma</td>
</tr>
<tr>
<td>Q15.0</td>
<td>Congenital glaucoma</td>
</tr>
</tbody>
</table>

Drug-eluting implant into the lacrimal canaliculus:

CPT codes not covered for indications listed in the CPB:

<table>
<thead>
<tr>
<th>Code</th>
<th>Code Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>0356T</td>
<td>Insertion of drug-eluting implant (including punctual dilation and implant removal when performed) into lacrimal canaliculus, each</td>
</tr>
</tbody>
</table>

ICD-10 codes not covered for indications listed in the CPB:

<table>
<thead>
<tr>
<th>Code</th>
<th>Code Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>H40.001</td>
<td>Glaucoma</td>
</tr>
</tbody>
</table>

The above policy is based on the following references:


37. Optonol Inc. The Ex-PRESS™ miniature glaucoma implant in combined surgery with cataract extraction: Prospective study. Publications & Presentations [website]. Kansas City,


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


98. Jacobs DS. Open-angle glaucoma: Treatment. UpToDate [online serial]. Waltham, MA: UpToDate; reviewed March 2016.


Amendment to
Aetna Clinical Policy Bulletin Number: 0484 Glaucoma Surgery

There are no amendments for Medicaid.