



**Australian Government**

**Department of Health**

## **Application 1496:**

# **Micro-invasive glaucoma surgery (MIGS) device implantation (external to Schlemm's canal) in patients with mild-to-moderate primary open-angle glaucoma**

## **PICO Confirmation**

**(to guide a new application to MSAC)**

**(Version 0.1)**

This PICO Confirmation Template is to be completed to guide a new request for public funding for new or amended medical service(s) (including, but not limited to the Medicare Benefits Schedule (MBS)). It is relevant to proposals for both therapeutic and investigative medical services.

Please complete all questions that are applicable to the proposed service, providing relevant information only.

Should you require any further assistance, departmental staff are available through the Health Technology Assessment (HTA Team) on the contact number and email below to discuss the application form, or any other component of the Medical Services Advisory Committee process.

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## Version Control

### Document History

Version Number	Date Changed	Author	Reason for Change
0.1	10 March 2016	Bianca Ledbrook	Final for Publication
1.0	3 April 2017	Adelaide Health Technology Assessment	PICO confirmation for discussion at PASC
2.0	19 May 2017	Adelaide Health Technology Assessment	Amendments to PICO Confirmation, based on ratified PASC outcomes

### Document Approval

Version Number	Date Changed	Author	Reason for Change
1.0			Document released for publication

## Summary of PICO criteria to define the questions to be addressed in an Assessment Report to the Medical Services Advisory Committee (MSAC)

### Population 1

Component	Description
Patients	Patients with primary open-angle glaucoma (POAG) who have a current cataract co-morbidity and are receiving topical hypotensive drugs to lower intraocular pressure (IOP)
Intervention	Cataract surgery with concurrent suprachoroidal micro-invasive glaucoma surgery (MIGS) stent implantation with/without additional medication
Comparators	Cataract surgery plus medical management with topical hypotensive drugs Cataract surgery with concurrent trabecular bypass MIGS stent implantation with/without additional medication
Outcomes	<p><b>Clinical Effectiveness:</b> Rate of vision impairment/loss, proportion of vision impairment/loss, time to vision impairment/loss, mean IOP reduction from baseline, proportion of patients with IOP reduction <math>\geq 20\%</math>, proportion of patients with IOP <math>\leq 18</math> mmHg, time to increase in IOP, change in the number of ocular hypotensive medications, proportion of patients on medication quality of life (effect on daily living activities, e.g. driving, walking, and reading), health-related quality of life (psychological burden due to fear of blindness, social withdrawal, and depression).</p> <p><b>Safety:</b> Intraoperative complications, post-operative ocular complications, secondary surgical interventions, corrected distance visual acuity, visual field mean deviation</p> <p><b>Cost-effectiveness:</b> Cost, cost per quality adjusted life year or disability adjusted life year, incremental cost-effectiveness ratio</p> <p><b>Australian Government healthcare costs</b></p>
Research question	<ol style="list-style-type: none"> <li>1. What is the safety, effectiveness, and cost-effectiveness of cataract surgery with concurrent suprachoroidal micro-invasive glaucoma surgery (MIGS) stent implantation with/without additional medication compared with cataract surgery plus medical management with topical hypotensive drugs in patients with POAG who have a cataract co-morbidity?</li> <li>2. What is the safety, effectiveness, and cost-effectiveness of cataract surgery with concurrent suprachoroidal micro-invasive glaucoma surgery (MIGS) stent implantation with/without additional medication compared with cataract surgery with concurrent trabecular bypass MIGS stent implantation with/without additional medication in patients with POAG who have a cataract co-morbidity?</li> </ol>

The PICO criteria for populations 2 and 3, as amended by the PICO Advisory Sub-Committee (PASC) (based on applicant comments), are shown in the next two tables. If the applicant considers that populations 2 and 3 should be combined, the submission will need to be explicit regarding whether laser trabeculoplasty becomes a prior-intervention, or a comparator.

### Population 2

Component	Description
Patients	Patients with primary open-angle glaucoma (POAG) who have previously undergone cataract surgery and in whom medical management with topical hypotensive drugs alone is either no longer effective or not tolerated
Intervention	Suprachoroidal micro-invasive glaucoma surgery (MIGS) stent implantation
Comparators	Laser trabeculoplasty Trabecular bypass MIGS stent implantation
Outcomes	<p><b>Clinical Effectiveness:</b> Rate of vision impairment/loss, proportion of vision impairment/loss, time to vision impairment/loss, mean IOP reduction from baseline, proportion of patients with IOP reduction <math>\geq 20\%</math>, proportion of patients with IOP <math>\leq 18</math> mmHg, time to increase in IOP, change in the number of ocular hypotensive medications, proportion of patients on medication quality of life (effect on daily living activities, e.g. driving, walking, and reading), health-related quality of life (psychological burden due to fear of blindness, social withdrawal, and depression)</p> <p><b>Safety:</b> Intraoperative complications, post-operative ocular complications, secondary surgical interventions, corrected distance visual acuity, visual field mean deviation</p> <p><b>Cost-effectiveness:</b> Cost, cost per quality adjusted life year or disability adjusted life year, incremental cost-effectiveness ratio</p> <p><b>Australian Government healthcare costs</b></p>
Research question	<p>3. What is the safety, effectiveness, and cost-effectiveness of suprachoroidal MIGS stent implantation compared with laser trabeculoplasty in patients with POAG who have previously undergone cataract surgery?</p> <p>4. What is the safety, effectiveness, and cost-effectiveness of suprachoroidal MIGS stent implantation compared with trabecular bypass MIGS stent implantation in patients with POAG who have previously undergone cataract surgery?</p>

### Population 3

Component	Description
Patients	Patients with primary open-angle glaucoma (POAG) who have no history of cataracts and in whom laser trabeculoplasty has either failed or is unlikely to be successful
Intervention	Suprachoroidal micro-invasive glaucoma surgery (MIGS) stent implantation
Comparators	Trabeculectomy Other incisional surgical procedures Trabecular bypass MIGS stent implantation
Outcomes	<p><b>Clinical Effectiveness:</b> Rate of vision impairment/loss, proportion of vision impairment/loss, time to vision impairment/loss, mean IOP reduction from baseline, proportion of patients with IOP reduction <math>\geq 20\%</math>, proportion of patients with IOP <math>\leq 18</math> mmHg, time to increase in IOP, change in the number of ocular hypotensive medications, proportion of patients on medication quality of life (effect on daily living activities, e.g. driving, walking, and reading), health-related quality of life (psychological burden due to fear of blindness, social withdrawal, and depression)</p> <p><b>Safety:</b> Intraoperative complications, post-operative ocular complications, secondary surgical interventions, corrected distance visual acuity, visual field mean deviation</p> <p><b>Cost-effectiveness:</b> Cost, cost per quality adjusted life year or disability adjusted life year, incremental cost-effectiveness ratio</p> <p><b>Australian Government healthcare costs</b></p>
Research question	<p>5. What is the safety, effectiveness, and cost-effectiveness of suprachoroidal MIGS stent implantation compared trabeculectomy or other incisional surgical procedures in patients with POAG who have no history of cataracts?</p> <p>6. What is the safety, effectiveness, and cost-effectiveness of suprachoroidal MIGS stent implantation compared trabecular bypass MIGS stent implantation in patients with POAG who have no history of cataracts?</p>

## PICO rationale for therapeutic and investigative medical services only

### Population

Glaucoma is a chronic, degenerative optic neuropathy characterised by progressive vision loss due to the loss of retinal ganglion cells and optic nerve damage (Kwon et al. 2009; Quigley 2011). It is the number one cause of irreversible vision loss and the second leading cause of blindness worldwide (Conlon, Saheb & Ahmed 2017). Peters et al. (2013) reported that the risk of blindness in at least 1 eye and bilateral blindness from glaucoma were 26.5% and 5.5%, respectively, after 10 years, and 38.1% and 13.5% at 20 years.

An increase in intraocular pressure (IOP) is thought to be a major cause of glaucoma. IOP increases either when too much aqueous humour fluid is produced or when aqueous humour outflow is decreased. There are two outflow pathways, for a diagram of the structure of the eye showing these pathways, see footnote below<sup>1</sup>. In the trabecular pathway, the trabecular meshwork is responsible for draining the aqueous humour from the anterior chamber. It is a spongy tissue located around the base of the cornea, between Schlemm's canal and the anterior chamber. The trabecular meshwork drains the aqueous humour into Schlemm's canal, which is a circular lymphatic-like vessel that delivers the collected the aqueous humour into the episcleral blood vessels. The uveo-scleral pathway starts with the aqueous humour filtering between the muscle bundles of the ciliary body; with this being the rate-limiting step. The aqueous humour flows into the suprachoroidal space, through the sclera and into the lymphatics to be drained away from the eye.

Glaucoma is referred to as open-angle or closed-angle depending on whether the drainage channels for aqueous humour in the front of the eye appear open or closed (Boland et al. 2013). In primary open angle glaucoma (POAG), the decreased outflow is attributed to increased resistance due to age-related thickening or sclerosis of the trabecular meshwork and absence of giant cells in Schlemm's canal. POAG is the most common form and is triggered by both environmental and genetic risk factors; up to 50% of patients have a positive family history of POAG (Allingham, Liu & Rhee 2009; Janssen et al. 2013).

A diagnosis of POAG is made only after the other types of glaucoma have been excluded and is based on a characteristic progressive enlargement of the optic cup (disc cupping) (Foster et al. 2002; Leske 1983). The vertical cup:disc ratio is a simple, relatively robust index of glaucomatous loss of the neuroretinal rim. Vision field defects may not yet be detected in mild disease, but as the disease progresses visual field abnormalities become more apparent. High IOP >21 mmHg, is a major risk factor for both developing POAG and for progression to irreversible vision loss, however, 15–40% of patients with POAG have normal IOP (Maier et al. 2005).

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<sup>1</sup> In SlideShare, *Pharmacotherapy of glaucoma, Aqueous humour dynamics*. Slide 7 shows the structure of the eye with the two aqueous humour outflow pathways and is available from URL: <<https://www.slideshare.net/manjuprasad16/pharm-of-glaucoma>> accessed 23 March 2017

Patients with confirmed POAG expected to access suprachoroidal micro-invasive glaucoma surgery (MIGS) stent implantation through the Medicare Benefits Schedule (MBS) can be broadly divided into two groups:

- Patients who will undergo implantation in conjunction with cataract surgery (population 1). MIGS stent implantation would be considered earlier in the management pathway for these patients (depending on the need for cataract surgery), and would be an adjunct to topical hypotensive medication;
- Patients who will receive the intervention as a stand-alone procedure. These patients can be further divided in two sub-groups:
  - patients who have previously undergone cataract surgery (referred to as pseudophakic) and who are currently unable to maintain target IOP with maximally tolerated topical hypotensive medication (population 2); and
  - patients who do not exhibit any signs of cataract development (referred to as phakic) in whom conventional medication management and less invasive interventional techniques (i.e. laser trabeculoplasty) have not been successful (population 3).

As patients from populations 2 and 3 comprise less than 5% of all patients having a MIGS implantation procedure, the applicant proposed that populations 2 and 3 be combined and defined as:

- Patients who will receive the intervention as a stand-alone procedure (population 2). In clinical practice, MIGS will be positioned where conservative therapies have failed, are likely to have failed, or are contraindicated. In this population, MIGS stent implantation would supplant or delay other incisional surgeries, such as trabeculectomy (population 2).

PASC considered this was a reasonable approach (i.e. an assessment in which populations 2 and 3 have been combined), given the paucity of evidence for these patients. The submission will need to define 'conservative therapies', and be explicit on whether this includes laser trabeculoplasty or not. If it does, then the implication of combining the populations will be that MIGS stent implantation for population 2 will be later in the pathway (after laser trabeculoplasty, rather than an alternate to laser trabeculoplasty). If 'conservative therapies' exclude laser trabeculoplasty, population 3 will be expanded to allow earlier treatment (i.e. laser trabeculoplasty becomes a comparator, rather than required prior-treatment).

#### Prevalence of POAG and cataracts among adults in Australia

Glaucoma affects approximately 66.8 million people worldwide, and up to 50% of people in the industrialised world are unaware of their condition and are therefore not receiving appropriate treatment (Conlon, Saheb & Ahmed 2017). In 2004, it was estimated that between 2.7% and 3.7% of Australians aged 55 years or more had glaucoma<sup>2</sup>. There was no significant difference in prevalence rates between men and women.

Although glaucoma and cataracts are not related conditions, co-morbidity will occur in many patients. This is likely due to the large number of older people with cataracts. Approximately 31% of

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<sup>2</sup> Based on Australian Bureau of Statistics and National Health survey data, Table A4 in *Vision problems among older Australians*. Available from <<http://www.aihw.gov.au/publication-detail/?id=6442467733>> (accessed 7 March 2017)

Australians aged 55 or more suffer from cataracts<sup>3</sup>. Age-specific rates for cataracts are well over 70% for both men and women aged 80 or more.

### Rationale

There is one randomised controlled trial (RCT) investigating the effectiveness of combined suprachoroidal MIGS and cataract surgery listed in the summary of evidence (Vold et al. 2016). The patients enrolled in this trial all had a diagnosis of POAG, with mild to moderate disease and an elevated IOP (un-medicated IOP >21 and ≤33 mmHg). Therefore, the population in the evidence base matches population 1.

In addition, the summary of evidence listed two completed non-comparative clinical trials that are registered on ClinicalTrials.gov but have not yet published their results provide information of the safety and effectiveness of suprachoroidal MIGS in patients as a stand-alone procedure (NCT01166659) and in any patient in whom suprachoroidal stent implantation was attempted (NCT01097174).

This suggests there may be little evidence to support the use of suprachoroidal MIGS in either population 2 or population 3.

### **Intervention**

Suprachoroidal MIGS stent implantation procedures involve a minimally invasive micro-incision approach (usually into the cornea), to minimise tissue scarring, and allow for the possibility of other glaucoma procedures (such as trabeculectomy or aqueous/tube stent implantation) to be performed in the future if needed (Gonnermann et al. 2017).

The CyPass micro-stent is a polyimide tube with a fenestrated lumen. It is 6.35mm long, with an inner diameter of 0.30 mm and outer diameter of 0.43 mm. The CyPass Micro-Stent is designed for placement in the angle of the eye, with the proximal end extending into the anterior chamber to allow outflow of aqueous fluid in the supraciliary and suprachoroidal space, where the distal end resides, via the uveoscleral pathway.

The proposed service involves the delivery of the CyPass micro-stent – pre-loaded on an inserter specific to the device – into the suprachoroidal space of the eye. The implantation of the stent ab interno (from inside the eye), via a corneal incision, is guided by gonioscopy. For a diagram that shows the positioning of the CyPass stent in the suprachoroidal space, see footnote below<sup>4</sup>.

The applicant indicated the procedure requires approximately 30-60 minutes of operating and preparation time when performed as a stand-alone procedure. A response to the targeted consultation survey indicated it would take approximately 15 minutes of a surgeon's time and significantly less than 15 minutes if combined with cataract surgery. The applicant advised that fifteen minutes is considered the minimum amount of professional time required when the stent implantation procedure is performed in conjunction with cataract surgery. PASC considered that, if

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<sup>3</sup> AIHW website. Available from <<http://www.aihw.gov.au/media-release-detail/?id=6442464587>> (accessed 7 March 2017)

<sup>4</sup> In SlideShare, *Minimally invasive glaucoma surgery*. Slide 25 shows the positioning of the suprachoroidal stent within the eye and is available from URL: <<https://www.slideshare.net/aditisingh77985/minimally-invasive-glaucoma-surgery>> accessed 30 March 2017



the length of time did not vary for cataract removal (with or without MIGS), further justification of the MBS fee will be needed during the assessment phase.

PASC noted goniotomy is traditionally performed in a paediatric patient population for congenital glaucoma, and this application expands that population to an older patient group.

### Rationale

Suprachoroidal MIGS stent implantation would be performed only once per eye (maximum of two procedures per person). However, the patient may need repositioning or removal of the stent at a later date, which would be performed under a separate MBS item number. The MIGS procedure is expected to take approximately the same amount of time whether or not it is combined with cataract surgery.

MIGS stent implantation in patients with POAG is intended to reduce the medication burden for patients, while maintaining IOP at a target level. This may be achieved by either directly reducing the number of hypotensive medications required per day (on average one less medication is required), or avoiding the need for an increase in medication over time.

Cataract surgery is common among patients with POAG, especially those aged 55 years or older. Thus, MIGS stent implantation will take place at the same time as cataract surgery in approximately 20% of patients with cataracts (population 1), because addressing these two conditions in a single operation minimises the risk of surgery-related complications (i.e. infection). In pseudophakic patients who have had previous cataract surgery and in whom medical management with topical hypotensive drugs alone is either no longer effective or not tolerated (population 2), MIGS stent implantation would occur as a stand-alone procedure instead of laser trabeculoplasty. In these patients, there is no likelihood of damaging the lens. Therefore, MIGS can occur earlier in the progression of glaucoma than in phakic patients (with no history of cataracts) who still have their natural lens (population 3). In patients with a natural lens, there is less space in the eye and risk of damaging the lens; therefore, MIGS stent implantation is delayed until laser trabeculoplasty has failed (or is unlikely to be successful) and is performed instead of a trabeculectomy.

Suprachoroidal MIGS stent implantation can also be performed as a stand-alone procedure in patients with a failed trabecular bypass stent. The potential for MIGS to be performed prophylactically in patients requiring cataract surgery should be addressed in the assessment.

### **Comparators**

There are two different types of comparators to suprachoroidal MIGS stent implantation: the comparators that would be considered in the absence of MIGS stent implantation, and an alternative form of MIGS stent implantation, using trabecular bypass MIGS stents.

PASC noted that cyclodialysis surgery is similar to suprachoroidal MIGS stent implantation and may be an additional comparator to suprachoroidal MIGS.

### Trabecular bypass MIGS stent implantation

The trabecular bypass MIGS stent is implanted via a micro-incision (usually into the cornea) and guided by gonioscopy, within the trabecular meshwork and Schlemm's canal, such that the aqueous humour drains into the canal. The exact positioning is specific to each trabecular bypass MIGS stent.

Three stent devices are relevant to trabecular bypass MIGS in the treatment of patients with mild-to-moderate POAG, with or without cataracts: the iStent, the iStent inject system, and the Hydrus Microstent.

Population 1: Patients with POAG and a current cataract co-morbidity

In patients who require cataract surgery, MIGS stent implantation would be considered early in the management algorithm, as an adjunctive treatment to topical hypotensive medication. The cataract and MIGS stent implantation would be performed together as one procedure. These patients would not yet be considered for laser trabeculoplasty in the current clinical algorithm. Thus, the only appropriate comparator for POAG patients with a cataract co-morbidity is cataract surgery with medical management of IOP with ocular hypotensive drugs.

Topical hypotensive medication represents the first-line therapy for patients with POAG. Patients start with a single topical medication, and increase the dosing frequency and number of therapies, as required, in order to maintain a target IOP. There are four main classes of pharmacotherapy available through the Pharmaceutical Benefits Scheme (PBS) that are used to treat glaucoma in Australia:

- Prostaglandin analogues are the first choice for most newly diagnosed patients and are the most commonly prescribed hypotensive medications for glaucoma:
  - Currently available on the PBS: bimatoprost, latanoprost, tafluprost and travoprost;
- Beta-blockers are the second most commonly prescribed class of topical glaucoma medications and are also used as first-line therapy for some patients:
  - Currently available on the PBS: betaxolol and timolol;
- Alpha agonists and carbonic anhydrase inhibitors are commonly used as adjunctive therapy when IOP is inadequately controlled with one medication;
  - Currently available on the PBS: brimonidine, apraclonidine, brinzolamide, dorzolamide;
- Fixed combination agents of the above classes are also available:
  - Currently available on the PBS:
    - Prostaglandin analogues bimatoprost, latanoprost and travoprost in combination with beta-blocker timolol;
    - Alpha agonists and carbonic anhydrase inhibitors brimonidine, brinzolamide and dorzolamide in combination with beta-blocker timolol;
    - Alpha agonist (brimonidine) in combination with a carbonic anhydrase (brinzolamide).

Population 2: Patients with POAG who have previously undergone cataract surgery

Under the proposed clinical pathway, patients who have had previous cataract surgery and are experiencing inadequate IOP control with maximal-tolerated hypotensive medication or due to poor compliance, or other treatment-related adverse events would be considered for MIGS stent implantation instead of laser trabeculoplasty. This is because these patients are not at risk of damage to the lens from MIGS. As the alternative treatment for these patients would be laser trabeculoplasty, this would be the correct comparator to MIGS stent implantation for these patients. Laser trabeculoplasty is reimbursed under MBS item numbers 42782 (up to 4 treatments in 2-year period) and 42783 (5<sup>th</sup> or subsequent treatment in 2-year period).

There are two main types of laser trabeculoplasty. Argon laser trabeculoplasty uses a laser to initiate cellular and biochemical changes to the junction of the anterior pigmented and posterior non-pigmented trabecular meshwork, with the power titrated to achieve blanching (Sihota 2011). These changes result in increased aqueous humour flow and lower IOP. However, selective laser trabeculoplasty is now more commonly performed in many countries including Australia as the thermally mediated radiation damage caused by the argon laser is confined to the pigmented trabecular meshwork cells, which absorb more of the applied laser energy than the surrounding cells (Realini 2008). The two laser trabeculoplasty methods are compared in Table 1. According to the National Health and Medical Research Council (NHMRC) *Guidelines for the Screening, Prognosis, Diagnosis, Management and Prevention of Glaucoma 2010* (NHMRC 2010), the literature reports that argon laser trabeculoplasty and selective laser trabeculoplasty are equally effective in reducing IOP.

**Table 1 Comparison of argon laser trabeculoplasty and selective laser trabeculoplasty surgeries**

	<b>Argon laser trabeculoplasty</b>	<b>Selective laser trabeculoplasty</b>
Spot size	50 µm	400 µm
No. of spots	50 spots equally spaced over 180° of the TM	50 spots covering a total of 360° of the TM
Energy used	500 mW	<1% of ALT
Fluence	40,000 mJ/mm <sup>2</sup>	>0.00015% of ALT
Exposure time	0.1 second	3 nanoseconds
Effect	Thermal damage	No thermal damage

Source: Sihota (2011)

The NHMRC guidelines recommend laser trabeculoplasty for older patients with glaucoma who are at risk of visual loss within their lifetime, particularly when the following factors apply:

- there is difficulty with administering eye drops;
- patients are unresponsive to medication alone; or,
- patients are poor candidates for incisional surgery.

*The patients in population 2 fall within these parameters.*

*Population 3: Patients with POAG who have no history of cataracts*

Currently, patients with no history of cataracts in whom the target IOP is not being achieved and laser trabeculoplasty has failed or is not likely to succeed would be considered for incisional surgical approaches, such as trabeculectomy. As MIGS stent implantation is being proposed as an alternative procedure at this stage, trabeculectomy as well as other incisional surgical approaches would be the appropriate comparators to MIGS stent implantation in this population. Incisional filtration surgery, including trabeculectomy, is reimbursed under MBS item numbers 42746 (first surgery) and 42749 (subsequent surgeries).

The purpose of surgical treatment for POAG is to prevent glaucoma-induced visual disability. Incisional surgery is often considered a third choice approach after medication and laser therapy due to the risk of damaging the natural lens. Incisional surgical procedures include:

*Trabeculectomy:*

Incisional filtering microsurgery that involves surgically creating a drainage channel between the anterior chamber and subconjunctival space. The subconjunctival space consists of loose connective

tissue and the surgical dissection and subsequent aqueous flow are believed to stimulate fibrosis in this tissue which reduces the outflow of aqueous over time.

If populations 2 and 3 are combined, the applicant has indicated trabeculectomy would be the appropriate comparator for the merged population. The submission-based assessment should be explicit regarding whether laser trabeculoplasty is a prior-treatment, or a possible comparator.

*Filtrating surgeries, such as deep sclerectomy, viscocanalostomy and canaloplasty:*

These surgeries are not widely used in Australia. They have common elements involving the dissection of a superficial and deep scleral flap to create an intra-scleral lake, removal of the juxtacanalicular tissue, and a Descemet's window. They can be performed after a trabeculectomy has failed.

Viscocanalostomy involves removal of the inner wall endothelium of Schlemm's canal as well as the juxtacanalicular tissue, the normal site of outflow resistance and the superficial flap is closed with 10-0 monofilament nylon sutures that are applied loosely.

During canaloplasty, the entire circumference of Schlemm's canal is dilated and extended with a viscoelastic compound, followed by placement of 10/0 polypropylene sutures in the canal under tension.

With sclerectomy, the Schlemm's canal was de-roofed and the corneal stroma was excised down to Descemet's membrane so that the aqueous humour percolates through the thin remaining trabeculo-Descemet membrane. Deep sclerectomy can also be performed with a cylindrical collagen drainage device placed radially in the centre of the deep sclerectomy dissection.

*Aqueous/tube shunt implantation:*

Aqueous shunts or tube shunts are devices that create an alternate path for the aqueous humour to leave the anterior chamber of the eye and lower IOP. In general, a tube is implanted into the anterior chamber of the eye that drains through a plate attached to the sclera and is covered by the eyelid. The fluid that collects is then absorbed into the bloodstream and transported out of the eye cavity. This procedure is usually considered a last-line procedure in patients with advanced disease. Therefore, aqueous/tube shunt implantation is not an appropriate comparator for MIGS stent implantation in this population. Insertion of aqueous/tube shunts is reimbursed under MBS item numbers 42752 (insertion) and 42755 (removal).

*Rationale*

There are two types of MIGS stent implantation procedures currently being reviewed for MBS funding: suprachoroidal MIGS stent implantation (this application) and trabecular bypass MIGS stent implantation (MBS application 1483). PASC advised that trabecular bypass MIGS should be an additional comparator to suprachoroidal MIGS for all three populations.

There is one RCT listed in the summary of evidence investigating the effectiveness of combined suprachoroidal MIGS stent implantation and cataract surgery compared with cataract surgery alone. Thus, there is some evidence to inform effectiveness of suprachoroidal MIGS in population 1.

There may be a lack of comparative evidence to inform effectiveness of suprachoroidal MIGS compared with either laser trabeculoplasty in population 2 or trabeculectomy in population 3. Thus, the effectiveness of MIGS stent implantation may need to be assessed using indirect evidence.

## Outcomes

### Patient relevant outcomes

**Clinical Effectiveness:** Rate of vision impairment/loss, proportion of vision impairment/loss, time to vision impairment/loss, mean IOP reduction from baseline, proportion of patients with IOP reduction  $\geq 20\%$ , proportion of patients with IOP  $\leq 18$  mmHg, time to increase in IOP, change in the number of ocular hypotensive medications, proportion of patients on medication quality of life (effect on daily living activities, e.g. driving, walking, and reading), health-related quality of life (psychological burden due to fear of blindness, social withdrawal, and depression).

**Safety:** Intraoperative complications, post-operative ocular complications, secondary surgical interventions, corrected distance visual acuity, visual field mean deviation.

### Healthcare system

**Cost-effectiveness** Cost, cost per quality adjusted life year or disability adjusted life year, incremental cost-effectiveness ratio.

**Financial implications** Number of patients suitable for treatment, number of patients who have successful procedure, number of patients who require additional treatment (medical or surgical).

## The clinical management algorithm with and without suprachoroidal MIGS for the identified populations

The clinical management algorithm for patients with suspected POAG, showing treatment options with and without MIGS stent implantation for patients with mild disease through progression to advanced disease are shown in Figure 1. The algorithm was adapted from the NHMRC Guidelines *For the screening, prognosis, diagnosis, management and prevention of glaucoma* (NHMRC 2010).

The objective of glaucoma management is to provide a significant and sustained decrease in IOP to minimise the risk of progression (i.e. visual field loss), which impacts on the patient's QoL.

For the majority of POAG patients, topical hypotensive medication represents the first-line of therapy as they represent the least invasive treatment option. Patients will initiate with a single topical medication, and the dosing frequency and number of therapies will increase, as required, in order to maintain a target IOP. In patients with cataracts requiring surgery, concurrent MIGS stent implantation (either suprachoroidal or trabecular bypass) offers additional options for lowering IOP.

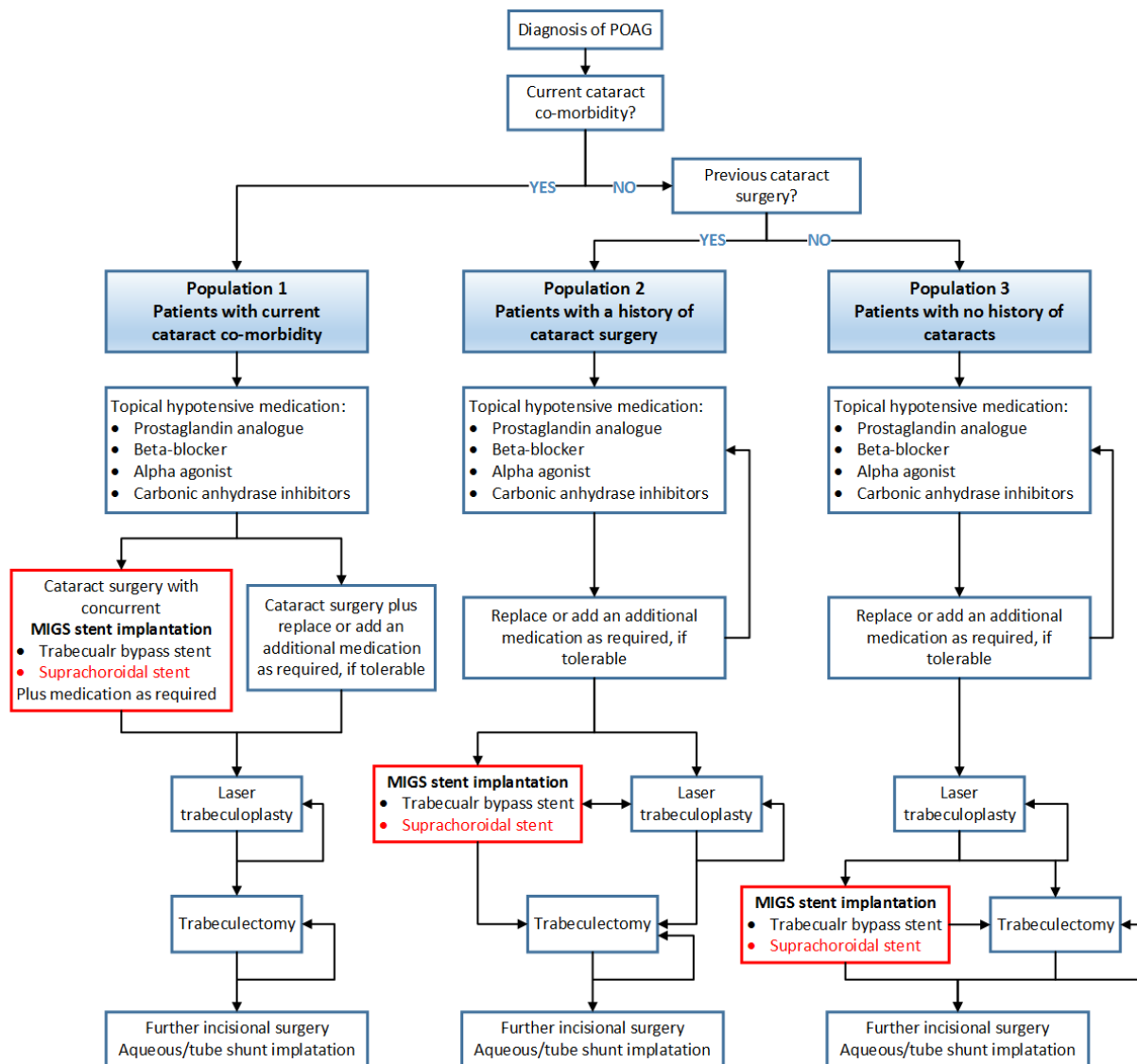
As the condition progresses, hypotensive medication may become less efficacious, or patients may become non-compliant. For such patients, surgical treatment options are considered.

Laser trabeculoplasty is usually considered as the first procedure in patients where IOP cannot be adequately managed with medication alone. MIGS stent implantation is also considered to be an alternative treatment for patients who have had previous cataract surgery at this stage. As the natural lens takes up more space in the eye, there is a risk that MIGS may damage the natural lens. However, there is no such risk in patients who have had cataract surgery.

Following laser trabeculoplasty, more invasive surgical treatment options, known broadly as 'filtering' surgeries, may be considered. The most common first invasive procedure is trabeculectomy. In phakic patients who have no history of cataracts and still have their natural lens, MIGS stent implantation is considered to be an alternative option at this stage. In these patients trabeculectomy could still be performed after the MIGS stent implant has failed.

Sclerectomy, viscocanalostomy and canaloplasty are not widely used in Australia but may offer further options to patients in whom all previous treatments have failed. The last line of treatment is aqueous/tube shunt implantation. These surgeries are generally reserved for patients with advanced disease.

In combining populations 2 and 3 in the assessment, the appropriate clinical management algorithm (for the combined population) will be that shown for population 2 in Figure 1 (if 'conservative therapies' exclude laser trabeculoplasty), or population 3 if it includes laser trabeculoplasty.



**Figure 1 The clinical management algorithm for patients with POAG, showing treatment options with and without suprachoroidal MIGS stent implantation for patients with mild to moderate disease through progression to advanced disease**

Source: NHMRC Guidelines: *For the screening, prognosis, diagnosis, management and prevention of glaucoma* (NHMRC 2010)

The addition of suprachoroidal MIGS stent implantation as a treatment option is shown in red for all three populations  
IOP = intraocular pressure; MIGS = micro-invasive glaucoma surgery; POAG = primary open-angle glaucoma

## Proposed economic evaluation

The applicant has predicted that suprachoroidal MIGS (in conjunction with cataract surgery, plus topical hypotensive medication) will be superior in terms of comparative clinical effectiveness, and inferior in terms of safety (compared with patients treated for cataract surgery, plus topical hypotensive medication) in population 1. The applicant also predicts a claim of at least non-inferiority for effectiveness and safety of suprachoroidal MIGS, plus standard of care (compared with laser trabeculoplasty, plus standard of care) for population 2. For population 3, the claim is inferiority for effectiveness, and superiority for safety of suprachoroidal MIGS (over trabeculectomy). On the basis of these claims, PASC advised the appropriate type of economic evaluation would be either a cost-effectiveness or cost-utility analysis.

PASC considered that a comparison between suprachoroidal MIGS and trabecular bypass MIGS stent implantation procedures be included in the submission-based assessment. If the evidence suggests the different MIGS stent implantation procedures are equivalent, a cost-minimisation approach would be appropriate.

The *Technical Guidelines for preparing assessment reports for the Medical Services Advisory Committee*<sup>5</sup> outline how to structure the decision analytic model underpinning the proposed economic evaluation, which is informed by the final structure of the PICO agreed to by PASC.

## Proposed item descriptor

The CyPass suprachoroidal stent has been registered by the TGA since 2009 and suprachoroidal MIGS has been funded under MBS item number 42758 (goniotomy). However, an MBS review determined that item 42758 was never intended to cover implantation of MIGS stents, and an amendment explicitly excluding this procedure was included in this item number from 1 May 2017. This MSAC application is seeking a new MBS item for delivery of MIGS suprachoroidal stent in the nominated patient populations (Table 2).

The cost of the suprachoroidal stent prosthesis is not included in the MBS fee. Prostheses are funded through the Prostheses List.

The implantation procedure would be performed once per eye (maximum two procedures per patient), as the stents are designed to last a lifetime. However, they may need repositioning or removal at a later date.

Differences in duration and complexity of the procedure when performed as a 'stand-alone procedure' (compared to being performed 'in conjunction with cataract surgery') needs clarification, and costs need to be justified. These procedures may require separate MBS item numbers, if costs vary.

The applicant advised that the total service fee must account for other aspects of the procedure (broader than the surgeon's time), such as preparation time, clinic overheads, observation and post-operative recovery time. There is an economy of scale in performing MIGS implantation in conjunction with cataract surgery, which is recognised by application of the Multiple Services Rule.

The proposed MBS fee for repositioning and removal of the stent is the same as for its insertion, and PASC considered that this needs justification.

Potential for leakage should also be addressed. PASC noted the concern that, given only 20% of patients with cataracts have increased IOP, MIGS may be performed prophylactically in patients requiring cataract surgery. Therefore, the risk that more procedures may be performed than actually required, needs to be considered.

The CyPass suprachoroidal stent is listed on the Prostheses List (Billing code: AL042). The CyPass suprachoroidal stent is TGA approved for implantation into the eye to relieve elevated IOP due to glaucoma, with no specific conditions recorded.

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<sup>5</sup> Available from URL: <<http://www.msac.gov.au/internet/msac/publishing.nsf/Content/assessment-groups>>, accessed 16 March 2017.



Prostheses List benefits for glaucoma drainage devices range from \$800 to \$1,600 each. PASC recommended that the difference between usage of these devices (and their impact on the treatment populations) be investigated further.

**Table 2 MBS item descriptors for suprachoroidal MIGS stent implantation**

Category 3 – THERAPEUTIC PROCEDURES	
MBS item number	<p>GLAUCOMA, implantation of a micro-invasive glaucoma surgery stent system placed into the supraciliary space, in patients diagnosed with primary open-angle glaucoma currently treated with ocular hypotensive medication. Can be delivered as a stand-alone procedure or in conjunction with cataract surgery.</p> <p>When delivered as a stand-alone procedure, pseudophakic patients must have inadequate IOP control with maximally-tolerated ocular hypotensive medication, and phakic patients must have failed or be likely to fail laser trabeculoplasty, or be contraindicated for this procedure</p> <p>Multiple Services Rule</p> <p>Fee: \$699.45 [approximate fee based on MBS item 42758 – to be determined]</p>
MBS item number	<p>GLAUCOMA, repositioning or removal of, a micro-invasive glaucoma surgery stent system from the placed into the supraciliary space</p> <p>Multiple Services Rule</p> <p>Fee: \$699.45 [approximate fee based on MBS item 42758 – to be determined]</p>

The MBS item descriptor for filtering surgeries restricts the intervention to glaucoma patients “where conservative therapies have failed, are likely to fail, or are contraindicated”. If populations 2 and 3 are combined, the patient population likely to access stand-alone MIGS stent implantation through the MBS are those otherwise eligible for incisional filtering surgeries. Thus, the wording of the proposed MBS item descriptor could be amended to read: “When delivered as a stand-alone procedure, conservative therapies must have failed, be likely to fail, or be contraindicated”

The applicant has indicated that a comprehensive cost analysis of the proposed service will be undertaken during development of the submission-based assessment, and the MBS fee would be similar to the current fee for MBS item 42758 (goniotomy). Advice from the Royal Australian and New Zealand College of Ophthalmologists (RANZCO) suggests the fee for this service (\$699.45, as for goniotomy) is a reasonable representation of the true cost of delivering the proposed service.

A response to the consultation survey indicated the proposed fee are possibly higher than the procedure warrants, whereas the Australian and New Zealand Glaucoma Society (ANZGS) stated the proposed fee is already lower than in other developed countries for insertion of the trabecular device.

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