Australian Government

Medical Services Advisory Committee

Public Summary Document

Application No. 1496 - Micro-bypass stenting for open-angle glaucoma (external to Schlemm's canal)

Applicant: **Alcon Laboratories (Australia) Pty Ltd**

Date of MSAC consideration: **MSAC 71st Meeting, 23 November 2017**

Context for decision: MSAC makes its advice in accordance with its Terms of Reference, visit the MSAC website

1. Purpose of application

An application requesting a new Medical Benefits Schedule (MBS) item for expanded access by ophthalmologists to MBS listings of suprachoroidal micro-invasive glaucoma surgery (SC-MIGS) stent implantation for open-angle glaucoma (external to Schlemm's canal) was received from Alcon Laboratories (Australia).

2. MSAC's advice to the Minister

After considering the strength of the available evidence in relation to comparative safety, clinical effectiveness and cost effectiveness, MSAC supported the inclusion in the MBS of SC-MIGS stent implantation for patients with open-angle glaucoma (OAG) who are also undergoing cataract surgery. MSAC accepted that SC-MIGS stent implantation was similar to trabecular bypass micro-invasive glaucoma surgery (TB-MIGS) stent implantation in this population and suggested both services be covered by a single generic MBS item at a fee of $911.10.

MSAC did not support listing of SC-MIGS as a standalone procedure due to insufficient evidence of effectiveness and because the population who would be eligible for the service could not be adequately defined.

For cases where there is failure of the original stent placement, MSAC suggested a single MBS item at a fee of $300.75 for stent removal regardless of whether it is undertaken with or without stent replacement.

MSAC recommended that usage of MIGS be revisited in 12 months to assess whether it is being used as intended.

3. Summary of consideration and rationale for MSAC's advice

MSAC noted that a similar application using stents implanted in the trabecular meshwork (TB-MIGS) - Application 1483: Micro-bypass stenting for open angle glaucoma (in the trabecular meshwork) - is also under consideration at the November 2017 MSAC meeting.

MSAC noted that despite never having been assessed for safety, clinical effectiveness and cost effectiveness, implantation of MIGS stents was performed under MBS item 42758 (goniotomy) until this use was explicitly prohibited in May 2017. MSAC noted that since then, implantation of MIGS stents has been allowed to continue under an interim MBS item (42705).

MSAC noted that there were two patient populations being considered — patients with diagnosed OAG undergoing SC-MIGS stent implantation in conjunction with cataract surgery (population 1) and patients with diagnosed OAG undergoing SC-MIGS stent implantation as a standalone procedure (population 2).

MSAC did not support the use of SC-MIGS in population 2 due to a lack of evidence on comparative safety, effectiveness and cost effectiveness. MSAC noted that while information from the DUETTE study and the CYCLE study had been provided to support listing in the standalone population, both were single-armed observational studies classified as being at high risk of bias.

MSAC noted that the evidence to support the listing of SC-MIGS stents in population 1 was restricted to a single randomised trial, the COMPASS study (n = 505), in which patients undergoing cataract surgery were randomised to SC-MIGS stent implantation or usual care (Vold S et al 2016).

MSAC noted that SC-MIGS stent implantation in population 1 had a similar safety profile to cataract surgery alone. The COMPASS study reported similar rates of any post-operative adverse events (36.9% for SC-MIGS and cataract surgery vs 35.9% for cataract surgery alone) and secondary surgical interventions (5.1% vs 5.3%, respectively).

MSAC noted that the COMPASS study indicated that patients undergoing SC-MIGS implantation had a greater reduction in mean IOP compared with cataract surgery alone at 12 months (7.6 mmHg vs 6.2 mmHg, respectively) and at 24 months (7.0 mmHg vs 5.3 mmHg, respectively). The patients who underwent SC-MIGS were also using an average of 0.4 fewer medicines to reduce IOP at 24 months.

MSAC noted that because the COMPASS study only had 24 months follow-up, the long-term effectiveness of the procedure, including its impact upon disease progression and avoidance of laser trabeculoplasty or trabeculectomy, remained uncertain.

MSAC accepted that outcomes using SC-MIGS or TB-MIGS in population 1 were likely to be similar. MSAC noted that when SC-MIGS was indirectly compared with TB-MIGS using cataract surgery alone as the common comparator, there were no significant differences in adverse events, mean change in IOP, reduction in medicine use from baseline and proportion of patients no longer requiring medicines.

MSAC noted that the economic model comparing SC-MIGS stent implantation plus cataract surgery with cataract surgery alone suggested that SC-MIGS stent implantation was dominant in the base case. However, MSAC queried the robustness of this finding given that reducing the time horizon from 15 years in the base case to 5 years increased the ICER to more than $12,000.

MSAC conceded that some increase in the ICER would be expected with a reduced time horizon given the costs of the surgery are all up front, but the magnitude of the increase raised doubts regarding the strength of the model assumptions.

MSAC noted that there was considerable uncertainty with regards to the financial estimates of the introduction of SC-MIGS. MSAC noted the use of SC-MIGS had the potential to be cost saving to the MBS if it reduces or delays surgery (laser trabeculoplasty or trabeculectomy). MSAC noted that it may also reduce PBS expenditure on medicines to treat raised IOP. MSAC noted that the CyPass Microstent is already listed on the Prostheses List.

MSAC recommended that insertion of a SC-MIGS stent or TB-MIGS stent in conjunction with cataract surgery be covered by a single generic MBS item. MSAC agreed that a fee of $911.10 was reasonable — this was arrived at by bundling the fee for the interim MBS item 42705 ($760.65) with 50% of the fee for in-hospital MBS eye injections (to account for the multiple services rule; MBS items 42738–40 $300.75). MSAC noted a single MBS item for MIGS implantation and cataract surgery would prevent the use of the item for standalone MIGS implantation and limit MBS reimbursement of the procedure to once per eye per lifetime.

MSAC noted MIGS stents were not expected to be used as first-line treatment of glaucoma but that it would be difficult to tighten the wording of the item descriptor to preclude this use. MSAC noted that there is no agreed IOP threshold for undertaking treatment and many patients fail to fully adhere to topical anti-glaucoma medicines making it difficult to define what constitutes non-response to, or intolerance of, these medicines. MSAC noted that clinicians are likely to make treatment decisions based upon individual patient characteristics and the presence or absence of visual deterioration. MSAC noted that restricting use of MIGS to people undergoing cataract surgery would limit first-line use to some extent.

MSAC suggested a single MBS item for stent removal with an associated fee of $300.75 regardless of whether it is undertaken with or without stent replacement. MSAC noted that this fee is equivalent to the fee for in-hospital MBS eye injections (MBS items 42738–40).

MSAC acknowledged that while there may still be out-of-pocket costs for consumers using the service, this was largely outside the Committee's control.

MSAC recommended that usage of MIGS be revisited in 12 months, under the Predicted vs Actual monitoring process, to assess whether it is being used as intended.

4. Background

MSAC has not previously considered this application.

MBS item 42758 was not intended to cover implantation of MIGS stents, and the procedure had not been assessed for safety, clinical effectiveness and cost effectiveness. An amendment explicitly excluding implantation of MIGS drainage devices under MBS item 42758 (goniotomy) took effect on 1 May 2017.

A new interim MBS item 42705 was listed for the insertion of MIGS devices when performed in conjunction with cataract surgery, sunsetting on 31 December 2018.

5. Prerequisites to implementation of any funding advice

The device is ARTG listed and on the Prostheses List for the proposed purpose.

6. Proposal for public funding

In the pre-ESC response, the applicant proposed an updated MBS item descriptor which removes the distinction between the cataract and stand-alone procedures and positions any SC MIGS procedure as second-line to topical anti-hypotensive treatment (changes are marked in Table 1).

Table 1 Applicant proposed changes to the MBS item descriptor to remove the distinction between the cataract and standalone settings

Category 3 – THERAPEUTIC PROCEDURES
MBS item number XXXXX GLAUCOMA, implantation of, a micro-invasive glaucoma surgery stent system into the suprachoroidal space, in patients diagnosed with open-angle glaucoma. ~~Can be delivered as a stand-alone procedure or in combination with cataract surgery~~ ~~When delivered in conjunction with cataract surgery or other intraocular surgery,~~ The patient must be currently treated with ocular hypotensive medication, have previously been treated with ocular hypotensive medication, or be contraindicated to ocular hypotensive medication ~~When delivered as a stand-alone procedure, other therapies must have failed, be likely to fail, or be contraindicated.~~ Multiple Services Rule **Fee:** $699.45 **Benefit**: 75% = 524.60
MBS item number XXXXX GLAUCOMA, removal or replacement of, a micro-invasive glaucoma surgery stent system from the supraciliary space. Multiple Services Rule **Fee:** $699.45 **Benefit**: 75% = 524.60

Population

Patients with confirmed POAG expected to access suprachoroidal MIGS stent implantation through the MBS can be broadly divided into two groups:

Population 1: Patients who will undergo MIGS stent implantation in conjunction with cataract surgery. 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 where still needed by the patient.

Population 2: Patients who will undergo MIGS stent implantation as a stand-alone procedure. 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.

7. Summary of Public Consultation Feedback/Consumer Issues

The department received no responses from public consultation.

8. Proposed intervention's place in clinical management

Glaucoma is a chronic degenerative optic neuropathy in which the neuro-retinal rim of the optic nerve becomes progressively thinner, caused by an acquired loss of retinal ganglion cell axons and atrophy of the optic nerve. In open-angle glaucoma aqueous outflow is diminished,

leading to an elevation of IOP. Patients with glaucoma typically lose peripheral vision, and may suffer complete vision loss if not treated.

Micro-stent implantation involves placement of a minimally invasive glaucoma surgery (MIGS) device. The device improves aqueous outflow through the uveoscleral outflow pathway, thereby lowering IOP and dependence on pressure-lowering topical medication. The procedure is generally performed as a day surgery procedure in an ophthalmology surgical setting, in conjunction with cataract surgery or as a stand-alone treatment.

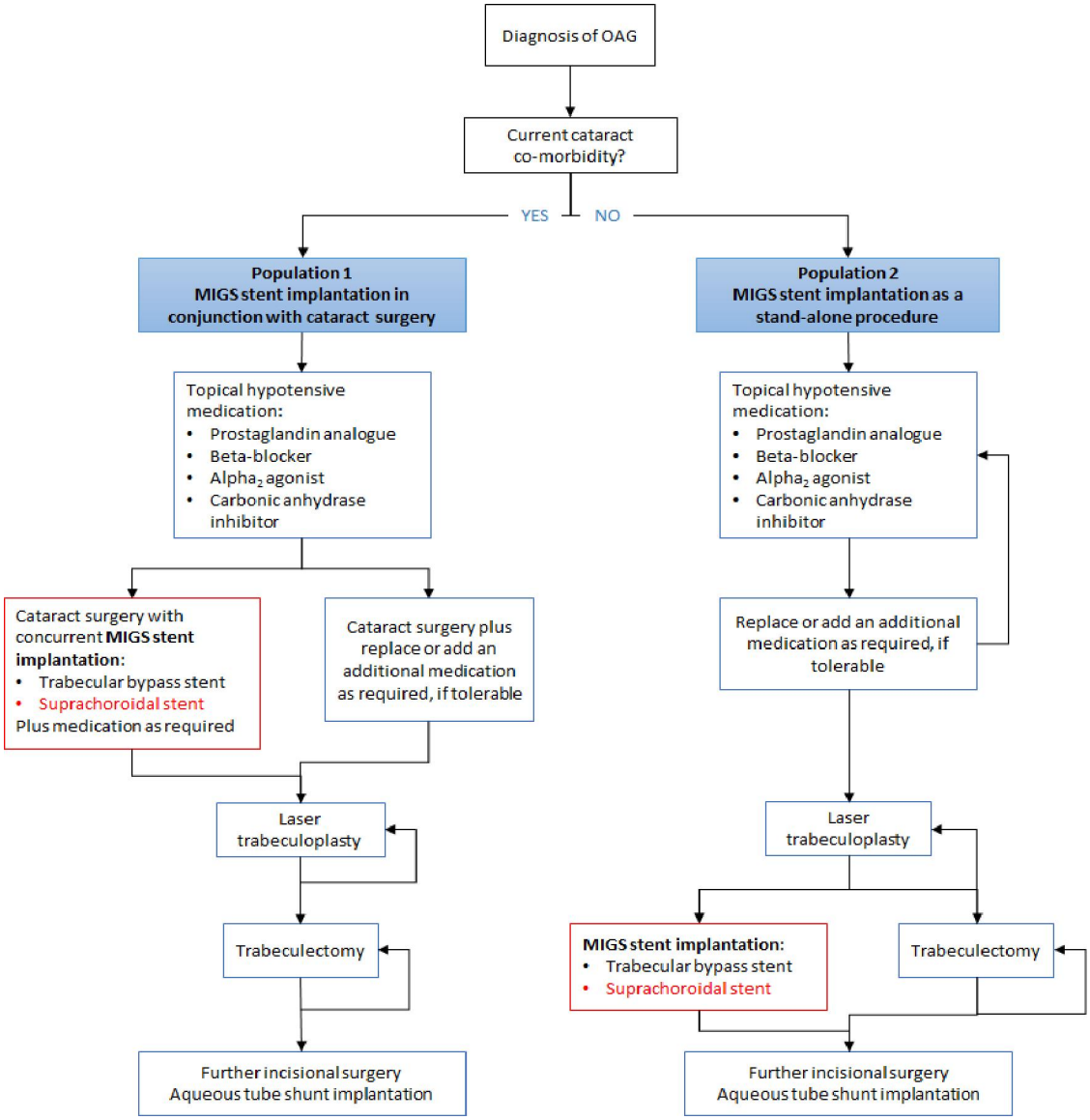
MIGS stent implantation in combination with cataract surgery

For patients with current cataract co-morbidity, suprachoroidal MIGS stent implantation would be performed in conjunction with cataract surgery early in the treatment algorithm. Patients will be required to be treated with at least one topical hypotensive medication. Following suprachoroidal MIGS stent implantation, patients will move through the treatment algorithm as usual, with downstream treatment options including laser trabeculoplasty and filtering surgery (i.e. trabeculectomy).

MIGS stent implantation as a stand-alone procedure

For patients undergoing suprachoroidal MIGS stent implantation as a stand-alone procedure, the intervention will likely supplant or delay other incisional surgeries, such as trabeculectomy. In a small proportion of patients who would be considered poor candidates for incisional surgery, suprachoroidal MIGS stent implantation may be an alternative to laser trabeculoplasty.

Figure 1 Clinical management algorithm for suprachoroidal MIGS stent implantation in each requested patient population, as it fits into the current treatment algorithm



9. Comparator

MIGS stent implantation in combination with cataract surgery

The primary comparator to MIGS stent implantation for patients with OAG with cataract co-morbidity was cataract surgery with continued medical management of IOP with ocular hypotensive medication.

A secondary comparator for this patient population is an alternative form of MIGS using trabecular bypass MIGS implantation stents. Trabecular bypass MIGS implantation stenting is being considered by MSAC at the same meeting as the current application for suprachoroidal MIGS stent implantation (MSAC Application 1483).

MIGS stent implantation as a stand-alone procedure

Patients experiencing inadequate IOP control with maximal-tolerated hypotensive medication or due to poor compliance, or other treatment-related adverse effects would be considered for MIGS stent implantation as a standalone procedure.

The comparator for patients experiencing inadequate IOP control with maximal-tolerated hypotensive medication or due to poor compliance, or other treatment-related adverse effects, would be trabeculectomy.

As with Population 1, trabecular bypass MIGS implantation stents as a standalone procedure is a secondary comparator relevant for this patient population.

10. Comparative safety

MIGS stent implantation in combination with cataract surgery

The risks of intra- and post-operative adverse events when using the device, either delivered alone or in conjunction with cataract surgery, are low. Adverse events are infrequent and rarely serious.

Consequences of stent implantation that may result in under-performance of the SC MIGS device(s) or need for a corrective surgical procedure (such as laser photocoagulation or stent repositioning), include stent malposition, migration or obstruction. Four studies (all populations) reported stent malposition in four of 848 patients (<1%) and obstruction in 43 of 848 patients (5%). Stent migration was reported in one RCT and occurred in two of 374 patients (0.5%). Post-marketing surveillance data on the SC stent was not available.

A summary of the direct comparison of CyPass with cataract surgery vs. cataract surgery only is presented in Table 3. Overall, patients who underwent CyPass in combination with cataract surgery had significantly more postoperative ocular adverse events of interest compared to patients who had cataract surgery only (OR=2.59, 95% CI: 1.20, 5.61], p=0.0154). The results suggest that cataract surgery in combination with suprachoroidal MIGS stent implantation is inferior to cataract surgery only in terms of comparative safety.

MIGS stent implantation as a stand-alone procedure

Based on the two single arm studies (CYCLE and DUETTE), there were no serious or unanticipated ocular AEs considered related to the CyPass Micro-Stent.

11. Comparative effectiveness

MIGS stent implantation in combination with cataract surgery

The key features of the evidence base for suprachoroidal stent implantation in combination with cataract surgery is presented in Table 2.

Table 2 Key features of the included trials for CyPass in combination with cataract surgery

Trial/Study	Design/ duration	Quality of evidence (GRADE)	Patient population	Key outcome(s)
COMPASS NCT01085357	Prospective, randomised comparative, interventional multicentre, clinical study 24 months	⊕⊕⊕⊙ MODERATE	Subjects aged ≥45 years with diagnosed or confirmed POAG within 90 days of screening, with a screening medicated IOP 25 mmHg or unmedicated IOP between 21 and 33 mmHg	Primary • Proportion of eyes with unmedicated diurnal IOP reduction ≥20% at 24 months versus unmedicated baseline IOP. Secondary • Mean unmedicated IOP reduction at 24 months • Proportion of eyes with unmedicated IOP between 6 and 18 mmHg inclusive at 24 months • Number of ocular hypotensive medications required to maintain target IOP at 24 months versus baseline
CYCLE NCT01097174	Interventional case series; open label registry (cataract surgery cohort)	⊕⊕⊙⊙ LOW QUALITY	Subjects with glaucoma who underwent implantation with the CyPass Micro-Stent in combination with cataract surgery	• Mean change in IOP from baseline to 1 month postoperatively and beyond • Mean change in required glaucoma medications used from baseline to 1 month postoperatively and beyond • Incidence of intraoperative and postoperative safety events

Abbreviations: IOP, intraocular pressure; POAG, primary open-angle glaucoma

Patients in the CyPass in combination with cataract surgery treatment group performed significantly better than patients in the cataract surgery only treatment group with respect to mean reduction in IOP from baseline, mean reduction in ocular medication use from baseline and in the proportion of patients achieving ≥20% reduction in IOP (see Table 3). Therefore, the results suggest that cataract surgery in combination with suprachoroidal MIGS stent implantation is superior to cataract surgery only in terms of comparative effectiveness.

Table 3 Summary of results: direct comparison of CyPass with cataract surgery vs. cataract surgery only

Outcome	Timepoint	Direct treatment effect OR (95% CI); p value	MD [95% CI]; p-value
Safety outcomes			
		OR > 1 favours intervention	**MD> 1 favours intervention**
Best corrected visual acuity	Baseline	1.04 [0.66, 1.63]; 0.8609	
	12 months	1.44 [0.36, 5.86]; 0.6072	
	24 months	1.11 [0.21, 5.80]; 0.9005	
Visual field mean deviation	3 months		-0.30 [-0.76, 0.16]; 0.2004
	6 months		-0.40 [-0.87, 0.07]; 0.1228
	12 months		0.00 [-0.52, 0.52]; 1.0000
	24 months		-0.20 [-0.87, 0.47]; 0.5077
		OR < 1 favours intervention	
Postoperative ocular adverse events of interest		2.59 [1.20, 5.61]; 0.0154	
Secondary surgical interventions	24 months	0.9481 [0.3892, 2.3096]; 0.9066	
Efficacy outcomes			
		OR > 1 favours intervention	**MD> 1 favours intervention**
IOP reduction ≥ 20% from baseline	12 months	1.82 [1.17, 2.84]; 0.0075	
	24 months	1.90 [1.26, 2.88]; 0.0023	
IOP≥ 6 mmHg and ≤ 18 mmHg	12 months	1.82 [1.21, 2.73]; 0.0038	
	24 months	2.05 [1.37, 3.07]; 0.0005	
Mean reduction in IOP from baseline	12 months		1.40 [0.59, 2.21];0.0012
	24 months		1.70 [0.88, 2.52]; 0.0002
Mean reduction in the number of ocular hypotensive medications	12 months		0.60 [0.40, 0.80]; 0.0000
	24 months		0.40 [0.20, 0.60]; 0.0001

A summary of the indirect comparison of suprachoroidal vs. trabecular MIGS stent implantation (both used in combination with cataract surgery) is presented in Table 4. None of the safety or efficacy outcomes assessed produced significantly different results between the two different stent types. The results suggest that suprachoroidal MIGS stent implantation is non-inferior to trabecular MIGS stent implantation in terms of comparative safety and effectiveness.

Table 4 Summary of results: indirect comparison of CyPass with cataract surgery vs. TB MIG stent implantation with cataract surgery via cataract surgery only common comparator

Outcome	Timepoint	Indirect treatment effect (SC MIGS vs. TB MIGS) OR (95% CI); p value	Indirect treatment effect (SC MIGS vs. TB MIGS) WMD (95% CI); p value
Safety outcomes			
		OR < 1 favours SC MIGS	
Adverse events	24 months	1.591 (0.861, 2.94); 0.1384	
Secondary surgical interventions	24 months	1.234 (0.441, 3.449); 0.6888	
Efficacy outcomes			
		OR > 1 favours SC MIGS	**WMD < 0 favours SC MIGS**
IOP reduction ≥ 20% from baseline	12 months	0.892 [0.467, 1.704]; 0.7296	
	24 months	0.936 [0.371, 2.2361]; 0.8885	
Mean reduction in IOP from baseline	12 months		-0.5 (-2.329, 1.329); 0.5921
	24 months		-0.55 (-1.839, 0.739); 0.4031
Mean reduction in the number of ocular hypotensive medications	12 months		-0.16 (-0.429, 0.109); 0.2438
	24 months		-0.14 (-0.445, 0.165); 0.3680

MIGS stent implantation as a stand-alone procedure

The key features of the evidence base for suprachoroidal stent implantation as a standalone procedure is presented in Table 5.

Table 5 Key features of the included trials for CyPass as a standalone procedure

Trial/Study	Design/ duration	Quality of evidence (GRADE)	Patient population	Key outcome(s)
CYCLE NCT01097174	Interventional case series; open label registry (standalone cohort)	⊕⊕⊙⊙ LOW QUALITY	Subjects with glaucoma who underwent implantation with the CyPass Micro-Stent	• Mean change in IOP from baseline to 1 month postoperatively and beyond • Mean change in required glaucoma medications used from baseline to 1 month postoperatively and beyond • Incidence of intraoperative and postoperative safety events
DUETTE NCT01166659	Multicentre, prospective, single-arm interventional clinical trial	⊕⊕⊙⊙ LOW QUALITY	Patients with POAG refractory to medical therapy and under consideration for additional glaucoma intervention.	• Proportion of eyes with IOP reduction of ≥ 20% at 12 months postoperatively who were on fewer or the same number of ocular hypotensive medications as compared with baseline. • Proportion of eyes with IOP ≥ 6 mmHg and ≤ 21 mmHg • IOP change from baseline • Mean number of IOP lowering medications • Ocular adverse events

Abbreviations: IOP, intraocular pressure; POAG, primary open-angle glaucoma

No direct RCTs of suprachoroidal MIGS stent implantation as a standalone procedure were identified. Two single arm studies (CYCLE and DUETTE) found that suprachoroidal MIGS stent implantation as a standalone procedure reduces mean reduction in IOP from baseline and mean reduction in ocular medication use from baseline.

Non-inferiority between suprachoroidal and trabecular MIGS stents as standalone procedures may be inferred by the direct comparison of suprachoroidal and trabecular MIGS when used in combination with cataract surgery.

Based on a naïve comparison, trabeculectomy is likely to be superior to both topical medication and suprachoroidal MIGS stent implantation in terms of comparative effectiveness.

Given the evidence base for the use of suprachoroidal MIGS stent implantation, no formal conclusions regarding the comparative safety or effectiveness of these interventions can be drawn.

Clinical Claim

MIGS stent implantation in conjunction with cataract surgery

The application clinical claim for suprachoroidal MIGS stent implantation in conjunction with cataract surgery versus cataract surgery alone is superior comparative effectiveness and inferior comparative safety.

The application clinical claim for suprachoroidal MIGS stent implantation in conjunction with cataract surgery versus trabecular bypass stent implantation in conjunction with cataract surgery alone is non-inferior comparative effectiveness and non-inferior comparative safety.

MIGS stent implantation as a stand-alone procedure

The application clinical claim for suprachoroidal MIGS stent implantation as a stand-alone procedure versus trabeculectomy is inferior comparative effectiveness and superior comparative safety.

The clinical claim for suprachoroidal MIGS stent implantation as a stand-alone procedure versus trabecular bypass stent implantation as a stand-alone procedure is non-inferior comparative effectiveness and non-inferior comparative safety.

12. Economic evaluation

Based on the evidence presented in the application, a cost-utility analysis was conducted for MIGS versus standard of care (SOC) in conjunction with cataract surgery for the treatment of glaucoma.

The economic model measures the incremental cost per quality-adjusted life years (QALY) gained of adding MIGS to the treatment algorithm. A summary of the economic evaluation is presented in Table 6.

Table 6 Summary of the economic evaluation

Perspective	Health care system
Comparator	Standard of Care (i.e. treatment algorithm without MIGS)
Type of economic evaluation	Cost-utility analysis
Sources of evidence	The pivotal clinical trial evidence upon which the economic model is based is the COMPASS trial
Time horizon	15 years
Outcomes	QALYs
Methods used to generate results	Individual patient microsimulation
Health states	Mild, Moderate, Advanced, Severe, End stage (defined by visual field Humphrey scores)
Cycle length	3 months
Discount rate	5% per annum
Software package used	TreeAge

Over the model duration, MIGS therapy is associated with increased healthcare cost savings of $128 per patient. In decreasing order of magnitude, the cost of MIGS is offset by lower surgery ($919), laser therapy ($517) and medication costs ($441).

The updated costs and outcomes for both populations (provided in the applicant pre-MSAC response), allowing for the cost of stent removal or re-positioning with an additional $105 to the total cost of treatment for patients MIGS+SOC treatment arm, are shown in Table 7.

Table 7 Updated incremental cost-effectiveness of MIGS

	Population 1			Population 2		
Parameter	**MIGS+SOC**	**SOC**	**Incremental**	**MIGS+SOC**	**SOC**	**Incremental**
Total costs	$8,693	$8,821	-$128	$7,619	$6,229	$1,390
Total costs (including removal)	*$8,798 (+$105)*	$8,821	*-$23 (+$105)*	*$7,724 (+$105)*	$6,229	*$1,495 (+$105)*
Total QALYs	6.719	6.579	0.139	6.719	6.579	0.139
Incremental cost-effectiveness			MIGS dominant			$9,985
Incremental cost-effectiveness (including removal)			MIGS dominant			*$10,755*

Sensitivity analyses indicated that the ICER had greater sensitivity to medication persistence, non-MIGS surgery costs and modelled time horizon.

13. Financial/budgetary impacts

A market share approach was used to estimate the financial implication of listing CyPass on the MBS.

The financial implications to the MBS resulting from the proposed listing of CyPass are summarised in Table 8. Through reductions in the number of SLT procedures the listing of CyPass is estimated to result in a yearly net savings of between $1.1 million and $1.6 million from 2018 to 2022.

Table 8 Total costs to the MBS associated with CyPass

Service/Budget	**2018**	**2019**	**2020**	**2021**	**2022**
Services delivered	**redacted**	**redacted**	**redacted**	**redacted**	**redacted**
Cost of the service to the MBS ($266.08 per service)	**$redacted**	**$redacted**	**$redacted**	**$redacted**	**$redacted**
Laser trabeculoplasty (savings of $540 per MIGS service)	**$redacted**	**$redacted**	**$redacted**	**$redacted**	**$redacted**
Total MBS	-$1,107,717	-$1,279,432	-$1,411,371	-$1,520,219	-$1,605,976

Table 9 outlines the broader budget impact of the MBS listing of CyPass. CyPass listing is estimated to save the Pharmaceutical Benefits Scheme (PBS) between $330,000 and $2.6 million a year over the next five years. A net cost to private health funds of between $2.1 million and $3.8 million is expected due to the additional costs incurred for MIGS devices despite cost savings through the reduction of trabeculectomy procedures.

Table 9 Broader budget impact of CyPass listing on public and private healthcare

Service/Budget	2018	2019	2020	2021	2022
PBS perspective					
Hypotensive medication	-$324,976	-$818,764	-$1,340,267	-$1,925,507	-$2,596,581
Private health funds perspective					
SC MIGS stent device	$6,174,933	$7,407,400	$8,639,867	$9,872,333	$11,104,800
Standalone hospitalisations	$65,264	$271,428	$633,179	$1,085,252	$1,627,646
Trabeculectomy	-$4,054,949	-$4,864,283	-$5,673,618	-$6,482,953	-$7,292,288
Total Private Health	$2,185,249	$2,814,545	$3,599,427	$4,474,632	$5,440,158

14. Key issues from ESC for MSAC

ESC noted that the application is for suprachoroidal micro-invasive glaucoma surgery (SC-MIGS) stent implantation for patients with open-angle glaucoma (OAG). The proposed service involves the insertion of the Cy-pass Microstent with one end in the anterior chamber of the eye and the other in the suprachoroidal space. This augments the drainage of aqueous humour via the uveoscleral pathway, reducing pressure within the eye (intraocular pressure [IOP]) and slowing the progression of glaucoma. The stent is implanted from inside the eye via a corneal incision using an inserter specific to the device.

ESC noted that a similar application — Application 1483: Trabecular bypass micro-invasive glaucoma surgery (TB-MIGS) stent implantation for open angle glaucoma — is also currently under consideration. ESC noted that many of the concerns raised were relevant to both applications.

ESC noted that implantation of MIGS stents had previously been performed under MBS item 42758 (goniotomy) despite never having been assessed for safety, clinical effectiveness and cost effectiveness. ESC noted that MBS item 42758 had never been intended to cover implantation of MIGS stents and in May 2017 use of this item to do so was explicitly prohibited.

ESC noted that since then, implantation of MIGS stents has been allowed to continue under an interim MBS item (42705) which will lapse on 31 December 2018. ESC noted that the Cy-Pass Microstent is already listed on the Prostheses List but it was likely that it would be removed if this application is unsuccessful.

ESC noted that it was originally proposed that the service be restricted to primary open-angle glaucoma (POAG) but that the patient population has been expanded to OAG. ESC noted arguments that restricting the service to people with POAG would disadvantage patients with rarer types of open-angle glaucoma (e.g. pseudoexfoliation glaucoma, pigmentary glaucoma) who are treated in the same manner.

ESC noted that other changes to the item descriptor introduced since the PICO Confirmation had the potential to result in leakage.

ESC noted that there were two patient populations considered in this application. The populations are:

- patients with diagnosed OAG undergoing SC-MIGS stent implantation in conjunction with cataract surgery (population 1); and
- patients with diagnosed OAG undergoing SC-MIGS stent implantation as a standalone procedure (population 2); such patients may have previously undergone cataract extraction and intraocular lens (IOL) implantation (pseudophakic) or may have never undergone cataract surgery (phakic).

ESC noted that SC-MIGS stent implantation was reasonably safe with a low risk of usually minor adverse events reported in both populations. ESC noted that patients who had an intra-operative adverse event during and attributed to cataract surgery were excluded from the COMPASS study (see below; Vold S et al 2016).

ESC noted that the evidence base for population 1 relied upon a single randomised controlled study, the COMPASS study (n = 505), in which patients undergoing cataract surgery were randomised to SC-MIGS stent implantation or usual care. ESC noted that this study had been assessed as being at moderate risk of bias.

ESC noted that with regards to effectiveness in population 1, the submission argued SC-MIGS stent implantation was superior to cataract surgery alone but the critique argued for non-inferiority. ESC noted that this largely came down to interpretations of what constituted an appropriate minimal clinically important difference (MCID) in the COMPASS study. ESC noted that:

- the submission argued that significantly more patients who underwent SC-MIGS stent implantation achieved a ≥ 20% reduction in IOP compared with cataract surgery alone at 12 months (79% vs 67%, respectively) and at 24 months (73% vs 58%, respectively). The critique argued the MCID for this outcome was a 20% difference in the proportion of patients between the two arms who achieved a ≥ 20% reduction in IOP. The critique argued that because the difference in proportion of patients between the two arms did not reach 20%, the evidence could only be interpreted as indicating non-inferiority. The applicant argued that the 20% difference in the proportion of patients was used for sample size calculation purposes only and was not an MCID.

- the submission argued that SC-MIGS stent implantation significantly reduced IOP from baseline more than cataract surgery — the mean difference at 12 months between the two groups was 1.4 mmHg. The critique argued that as a 1.5 mmHg decrease in IOP was an appropriate MCID since this value is accepted by the PBAC for new glaucoma medicines, this evidence could only be interpreted as indicating non-inferiority. The applicant argued that every 1 mmHg reduction in IOP is associated with a 10% reduction in glaucoma progression.

ESC noted the evidence base for population 2 relied upon two studies — the DUETTE study which was a prospective, open-label, single-arm study (n = 65), and the CYCLE study which was a single-arm registry study which included patients with cataracts (n = 136) and without cataracts (n = 167 eyes). Both studies were classified as being at high risk of bias and had attrition rates of 15–50%.

ESC noted that there was insufficient evidence to assess the effectiveness of standalone SC-MIGS stent implantation (population 2). ESC noted that no attempt to compare standalone SC-MIGS stent implantation to laser trabeculoplasty (SLT) or trabeculectomy was made due to the lack of evidence in this population.

ESC noted that SC-MIGS stent implantation appeared to be non-inferior when compared to the alternative procedure, TB-MIGS stent implantation, in population 1. ESC noted there

were no significant differences in safety or efficacy outcomes in population 1 (using cataract surgery alone to indirectly compare SC-MIGS and TB-MIGS) regardless of whether one or two TB-MIGS stents were used. ESC noted that while the submission argued that the evidence of non-inferiority from population 1 could be extrapolated to standalone SC-MIGS stent implantation (population 2); there was no direct or indirect evidence to support this argument.

ESC noted the proposed fee for implantation of SC-MIGS stents in conjunction with cataract surgery, the proposed fee for implantation as a standalone procedure and the current fee for goniotomy were all the same. ESC requested further justification for the proposed fees and also noted that the time and resources needed to implant in conjunction with cataract surgery would be different to a standalone procedure.

ESC noted that when MBS item 42758 was being used 97.5% of MIGS stents appear to be implanted in conjunction with cataract surgery and as such the benefit paid would be lower than the proposed MBS fee under the multiple services rule. However, ESC noted the application estimated 20% of MIGS implantations would be standalone procedures by 2022. ESC noted that this 20% figure had not been justified.

ESC noted that the fees requested for implantation of a MIGS stent and replacement or removal of a MIGS stent are the same. ESC queried whether the time and resources required to replace or remove a MIGS stent justified paying the same amount for both procedures. In addition, ESC requested information on the proportion of MIGS stents that would require removal or replacement and requested that the associated costs be included in the economic and financial models.

ESC noted that the economic model comparing SC-MIGS stent implantation plus cataract surgery compared with cataract surgery alone suggested that SC-MIGS stent implantation was dominant in the base case. ESC noted that this was based upon weak clinical evidence and queried whether this was a robust finding.

ESC noted that if the time horizon were reduced from 15 years in the base case to 5 years SC-MIGS stent implantation would no longer be dominant (ICER ~$12,000). ESC requested a probabilistic sensitivity analysis of the modelling to be undertaken.

ESC noted that information on adherence to hypotensive medicines and treatment failure or revision should be included in the model.

ESC noted the economic modelling of standalone SC-MIGS stent implantation was restricted to a sensitivity analysis which compared it to standard of care by removing the costs of the MBS fee for cataract surgery (standalone theatre costs were included). ESC questioned whether this was a reasonable approach.

ESC noted that there was no economic modelling comparing SC-MIGS stent implantation with TB-MIGS stent implantation in either population. ESC noted that there was no economic modelling comparing SC-MIGS stent implantation with SLT or trabeculectomy in the standalone population.

ESC noted that both application 1483 and application 1496 extrapolated data from MBS item 42758 (goniotomy) to estimate uptake of MIGS stent implantation.

ESC also noted that as it was not possible to separate the numbers of MBS item 42758 services carried out using TB-MIGS stents from those using SC-MIGS stents, application 1483 assumed that 100% of these services used TB-MIGS stents while application 1496 assumed 100% of these services used SC-MIGS stents. ESC noted that this makes it appear

that, should both TB-MIGS stent implantation and SC-MIGS stent implantation be listed, the uptake would be double that expected in reality.

ESC suggested that the Prostheses List Advisory Committee (PLAC) may be able to provide figures on the relative numbers of each type of MIGS stent used in Australian practice which could be used to better model the expected uptake of either or both of these services on the MBS.

ESC noted that a lack of information about how many procedures would be undertaken per year and what proportion of services would be undertaken in private or public hospitals added uncertainty to the financial costs.

ESC expressed concerns that there may be out-of-pocket expenses for consumers. ESC suggested that information from the Department on the fees being charged for MBS items 42758 (goniotomy) prior to the exclusion of MIGS stent implantation, interim MBS item 42705 and MBS item 42702 (cataract surgery) could provide some guidance on potential out-of-pocket expenses.

ESC also noted that if SC-MIGS stent implantation were recommended as a standalone procedure (population 2) there was a risk that some patients could undergo cataract surgery and then undergo a separate procedure to implant a SC-MIGS stent at some later stage in order to maximise the benefits paid. ESC noted that the items should be structured and priced to encourage the most appropriate use of the items for the patient.

ESC consumer representatives noted concerns that MIGS stent implantation had been inappropriately subsidised on the MBS without an assessment of its safety, effectiveness and cost-effectiveness. ESC noted that should it be shown to be safe and effective, consumers are likely to welcome a procedure which may slow down progression of OAG.

ESC suggested that the item descriptor:

- restrict use to patients with mild to moderate disease;
- specify use of the item to once per lifetime per eye;
- specify the co-administered interventions used to deliver the service (i.e. cataract surgery and gonioscopy);
- define what constitutes an adequate trial of hypotensive medicines;
- more tightly define what is considered to be failure of, or contraindications to, hypotensive medicines and other treatments to prevent first-line use of SC-MIGS stent implantation, particularly in the standalone population;
- specify whether the service attracts an anaesthetic or an assistant benefit; and
- note any training and/or accreditation requirements.

ESC agreed that using the generic term ‘glaucoma drainage device’ in the item descriptor to describe MIGS stents was probably not appropriate.

ESC Key ISSUES	ESC ADVICE
Evidence	• Evidence for Population1 based on a single RCT (COMPASS) with moderate risk of bias. • Insufficient direct evidence for Population 2. Only 1 registry and 1 single arm study (level IV only) • *Indirect* evidence of equivalence with TB MIGS
Descriptor	• The issue with the descriptor is the wording "other surgery". • Should the application include all micro-invasive glaucoma surgery devices that are on the prosthesis list? Should it be included – as a generic listing?
Safety	Submission Based Assessment and the Critique conflict in relation to safety

15. Other significant factors

Nil

16. Applicant's comments on MSAC's Public Summary Document

Alcon welcomes the recommendation from MSAC for inclusion on the MBS of SC-MIGS in conjunction with cataract. We look forward to working with the Department of Health to implement this advice as soon as possible.

Alcon are disappointed with the decision for the standalone population. Alcon are concerned it will seem counterintuitive to patients with glaucoma that they are only allowed to access this therapeutically important intervention on the basis of a separate condition. Alcon will continue to push for MBS reimbursement for this group of patients with high clinical need.

17. Further information on MSAC

MSAC Terms of Reference and other information are available on the MSAC Website:
visit the MSAC website