Australian Government

Medical Services Advisory Committee

Public Summary Document

Application 1649 – Modification of wording of minimally invasive glaucoma surgery (MIGS) existing item number to encompass the use of a microcatheter

Applicant: **Nova Eye Medical Ltd**

Date of MSAC consideration: 83rd MSAC Meeting, 25-26 November 2021

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 to amend an existing Medicare Benefits Schedule (MBS) item 42504 to include ab-interno canaloplasty (ABiC) using a microcatheter to treat glaucoma was received from Nova Eye Medical by the Department of Health.

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 did not support amending MBS item 42504 to include ABiC using a microcatheter to treat glaucoma. MSAC advised there is insufficient evidence to demonstrate non-inferior safety and effectiveness of ABiC using a microcatheter compared with implantation of micro-bypass stents. MSAC advised that issues with the clinical evidence, including uncertainty in the reintervention rate and the likely potential that ABiC will be used adjunctive to (rather than substitute) insertion of micro-bypass stents, created significant uncertainty in the cost-effectiveness and financial estimates for ABiC using a microcatheter.

Consumer summary
Nova Eye Medical applied to amend Medical Benefits Schedule (MBS) item 42504 to include ab-interno canaloplasty (ABiC) using a microcatheter to treat glaucoma. Currently, MBS item 42504 covers the implantation of micro-bypass stents for glaucoma treatment. Glaucoma refers to a group of eye diseases where vision is lost due to damage to the optic nerve. This is usually caused by an increase in intraocular pressure (IOP), which is the fluid pressure of the eye. Fluid in the eye usually drains through the trabecular meshwork and canal of Schlemm – a circular canal found where the clear outer layer of the eye (cornea) and white of the eye (sclera) meet. If these become blocked, fluid builds up in the

Consumer summary

eye causing an increase in IOP. Loss of sight from glaucoma usually happens gradually and is permanent.

There are several minimally invasive glaucoma surgery (MIGS) options available for glaucoma treatment. One option, which is already in use, is to insert micro-bypass stents, a tiny tube implanted into the trabecular meshwork, which helps to create a new pathway (by pass the meshwork) to allow the outflow of fluid to reduce IOP. A more recent option is an ABiC procedure where a microcatheter (a very thin tube) is inserted into the Schlemm's canal. The insertion and removal of the microcatheter re-opens and widens the canal to help improve fluid drainage and reduce IOP. Unlike micro-bypass stents, the microcatheter does not stay in the eye.

MSAC noted some patients may prefer ABiC using a microcatheter instead of having a micro-bypass stent permanently implanted. However, MSAC did not consider there was enough evidence to demonstrate that ABiC is as safe and effective as insertion of micro-bypass stents. Further, MSAC noted that patients who are treated with ABiC using a microcatheter may subsequently require further retreatment and/or undergo another treatment such as insertion of a micro-bypass stent. MSAC noted there was no evidence to inform who would best be treated with ABiC using a microcatheter versus micro-bypass stents. Further, MSAC was uncertain about how many patients would use the service and the associated costs.

MSAC's advice to the Commonwealth Minister for Health

MSAC did not support amending MBS item 42504 to include ABiC using a microcatheter. MSAC consider that there was insufficient evidence to demonstrate that ABiC using a microcatheter is as safe and effective as micro-bypass stents, and was uncertain whether ABiC using a microcatheter was good value for money.

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

MSAC noted this application from Nova Eye Medical requested that existing MBS item 42504, which encompasses implantation of micro-bypass stents as a standalone treatment for glaucoma, be amended to include ABiC using a microcatheter. Currently, MBS item 42504 excludes the use of a microcatheter. MSAC noted that ABiC using a microcatheter in conjunction with cataract surgery is being claimed under MBS item 42705, which encompasses implantation of micro-bypass stents in conjunction with cataract surgery. Unlike MBS item 42504, the descriptor for MBS item 42705 could be interpreted as including the use of a microcatheter, but this was not the intent of the item.

MSAC noted the target population are patients with primary open angle glaucoma who have failed conservative treatment (or where conservative treatment is contraindicated), with or without concomitant cataracts. Glaucoma occurs in 1.5% of non-Indigenous Australians (>50 years) and 0.6% of Indigenous Australians (>40 years)[1]. It is a major cause of blindness if left untreated.

MSAC noted consultation feedback was generally supportive for this application. MSAC agreed that ABiC using a microcatheter device may be useful for paediatric patients, but

[1] Keel S, et al. (2019) *British Journal of Ophthalmology*, 103:191.

considered this to be a rare subgroup as glaucoma is typically a degenerative disorder that mainly affects patients that are over 45 years of age. MSAC also queried why funding ABiC using a microcatheter device would benefit rural patients, as the procedure can only be performed by trained and specialised ophthalmologists that are usually based in major city centres.

MSAC noted that micro-bypass stents, which are left in-situ, are included on the Protheses List (PL). However, the microcatheter device manufactured by the applicant, iTrack, is not listed on the PL. As a result, the cost of the microcatheter is currently an out-of-pocket (OOP) cost borne by the patient. MSAC noted that an application for listing the iTrack microcatheter on the PL has been submitted for consideration by the Protheses List Advisory Committee (PLAC).

MSAC noted the clinical management algorithm but considered there was insufficient evidence to define the clinical place of ABiC using a microcatheter in the treatment pathway for glaucoma patients who have failed conservative treatment. MSAC considered that ABiC using a microcatheter may provide a standalone treatment option that could be used as either a bridge to or to potentially avoid the need for stent insertion or more invasive trabeculectomy. MSAC also considered that there was insufficient evidence and guidance to inform clinical decisions on whether ABiC using a microcatheter or a micro-bypass stent is used for initial intervention and the choice of procedure at reintervention. Further, glaucoma treatment is moving towards a multi-procedure approach, not just a single, standalone treatment as suggested by the application.

MSAC considered the evidence base for ABiC using a microcatheter, which comprised seven case series studies, was limited and of low quality. There was a lack of studies reporting success/failure rate of treatment and rate of reoperation following standalone ABiC using a microcatheter, or combined cataract plus ABiC procedures. Further, as there were no studies directly comparing ABiC using a microcatheter with the insertion of a micro-bypass stent into the trabecular network, only naïve comparisons were possible. MSAC noted the population was pooled and included patients receiving glaucoma surgery with and without concomitant cataract surgery. The population was not stratified by the severity of glaucoma and often not able to be stratified by the presence/absence of cataract surgery. Therefore, MSAC considered the impact of cataract surgery on the safety and effectiveness of ABiC using a microcatheter to be uncertain (cataract surgery may bias results or obscure differences in the data). MSAC also noted the available evidence base lacked data on health-related quality of life or quality of life, and rarely reported adverse events. MSAC noted there is a clinical trial (TRIDENT[2]) comparing ABiC using another microcatheter device to micro-bypass stents, but this is not due for completion until 2023 at the earliest.

MSAC noted the pre-MSAC response claimed the lack of prospective, comparative data was not a concern because of 10 years of real-world data; in 2020–2021, **redacted** iTrack procedures were performed around the world. However, MSAC agreed with the rejoinder response which highlighted that naïve comparisons and retrospective studies are considered a low-level of evidence susceptible to potential risks of bias and uncertainties.

Regarding the naïve comparison of safety, MSAC noted that, overall, ABiC using a microcatheter appeared to have equivalent short-term safety compared to MIGS using a

[2] NCT04658095 - A prospective, randomized, multicenter study to compare the safety and effectiveness of the OMNI surgical system and the iStent inject in pseudophakic eyes with open angle glaucoma. The TRIDENT European Trial - https://clinicaltrials.gov/ct2/show/NCT04658095

micro-bypass stent. Additionally, the rates of some adverse events reported in the studies – specifically, intraoperative bleeding, incorrect device position and postoperative hyphema – were marginally higher for micro-bypass stents with concomitant cataract surgery. However, MSAC considered the long-term safety of ABiC using a microcatheter was uncertain. MSAC noted that endothelial cell loss (ECL) is an important safety outcome. The pre-MSAC response claimed that ECL after one year is less for the microcatheter device (3.2%) than micro-bypass stents (4.2%). MSAC considered this may be because nothing is left in-situ following ABiC using a microcatheter, but decided there was insufficient follow-up on ECL for ABiC using a microcatheter to determine its long-term safety; the maximum length of follow-up in the intervention studies was only 24 months.

Regarding the naïve comparison of clinical effectiveness, MSAC noted the uncertainty regarding reoperation rates for ABiC using a microcatheter. MSAC also noted the pre-MSAC response provided new evidence on reoperation rates that indicated the reoperation rate was **redacted**% for patients with mild-moderate glaucoma and **redacted**% for patients with severe glaucoma, after 3 years. MSAC considered that the reoperation rate appeared to be low but remained uncertain as the data was from small single arm studies with short follow-up. For both the intervention and the comparator, the decrease in intraocular pressure was greater in those who had concomitant cataract surgery than those who had the standalone procedure. MSAC considered this to be expected, as drainage is improved following cataract removal. Conversely, there was a greater decrease in medication use for those who received the standalone glaucoma procedures. While visual acuity was sustained following the standalone procedures, it was improved in those who also had concomitant cataract surgery. MSAC also considered this to be expected as cataract surgery results in a new lens. Due to the limited low quality evidence and lack of direct comparative evidence, MSAC considered the claim of non-inferior effectiveness to be uncertain.

MSAC noted that a cost minimisation analysis (CMA) was presented, based on the assumptions that:

- the cost of the microcatheter and micro-bypass stent was the same and costed based on the average PL benefit for micro-bypass stents ($1,350/unit)
- the pre-surgical assessment cost was the same
- the MBS fees for ABiC using a microcatheter and implantation of a micro-bypass stent were the same ($310.15 for the standalone procedure and $939.60 for the procedure with concomitant cataract surgery)
- ABiC using a microcatheter has non-inferior effectiveness and safety compared to micro-bypass stent insertion (very uncertain, based on a naïve comparison using very low-quality evidence).

MSAC noted a key driver of the model was the rate of reoperation. MSAC noted the rates of reoperation in the CMA for ABiC using a microcatheter (6.9%) and micro-bypass stents (4.1%) seen from two published retrospective studies. As a result, the base case analysis estimated the incremental cost of ABiC using a microcatheter versus micro-bypass stents to be $43 for the standalone procedure, and $61 for the procedure with concomitant cataract surgery. The model allowed for the microcatheter to have the same rate of reoperation as micro-bypass stents, but MSAC considered that the microcatheter reoperation rate may be higher in the long term due to the potential use for repeat dilation. MSAC also noted that the studies reported a wide range of rate of reoperation, with severe glaucoma having a higher rate of reoperation than mild or moderate glaucoma. Further, MSAC questioned whether a

CMA was appropriate given the uncertainty regarding the clinical place of ABiC using a microcatheter, including the likely potential that ABiC using a microcatheter may be used as a bridge to or adjunctive to (rather than substitute) implantation of a micro-bypass stent.

MSAC noted another key driver of the model was the cost of the microcatheter. MSAC noted there was no justification presented as to why the cost of the microcatheter would be the same as that for micro-bypass stents. MSAC noted the applicant had proposed to reduce the cost for the iTrack microcatheter to $**redacted**/unit which was equivalent to the PL benefit for the Hydrus and XEN micro-bypass stent and therefore would not achieve cost-neutrality. MSAC questioned why this could not be reduced further; if the cost of the microcatheter was to decrease by 20% (to $1,080), the comparison would become favourable.

MSAC considered that incorporating ABiC using a microcatheter device in MBS item 42504 should not alter the impact on the MBS, as it would require the same surgeons that are needed for MIGS with micro-bypass stents; use of this item is currently restricted to approximately 50 specialised ophthalmologists already trained in MIGS. However, this is only applicable if the rate of reintervention is not high, and MSAC considered this rate to be uncertain. MSAC also considered it likely that ABiC using a microcatheter device would require subsequent definitive surgery (i.e. trabeculectomy) if the disease were to progress.

MSAC noted the estimated net cost to the MBS is $705.83–$1,104 over 5 years for the standalone procedure, and $19,937–$31,219 over 5 years for the procedure with concomitant cataract surgery. MSAC noted the number of patients estimated to undergo ABiC using a microcatheter was based on the current utilisation of MBS item 42705 (micro-bypass stent insertion in conjunction with cataract surgery), as well as a 10% substitution for existing MIGS (this rate was defended by three glaucoma surgeons in the pre-MSAC response). However, MSAC considered the utilisation rate to be uncertain, as ABiC using a microcatheter is a technically challenging procedure that would only be performed by specialised surgeons. MSAC considered that uncertainty in the clinical place, reoperation rates and choice of reintervention procedure created significant uncertainty in the utilisation and estimated financial impact to the MBS.

Overall, MSAC considered there was insufficient evidence to demonstrate that ABiC using a microcatheter device offered clear benefit in safety, effectiveness, together with an increased need for reoperation compared to permanent implantable stents. MSAC also noted there are several MIGS options currently available to patients. MSAC advised that issues with the clinical evidence, including uncertainty in the reintervention rate and the likely potential that ABiC using a microcatheter will be used adjunctive to (rather than substitute) insertion of micro-bypass stents, created significant uncertainty in the cost-effectiveness and financial estimates for the procedure. Additionally, as the cost of the microcatheter is likely to be borne as an OOP costs by patients, MSAC considered there may only be a small group of patients who would choose this procedure and concerns about potential OOP for patients was not outweighed by the lack of evidence of comparative safety and effectiveness. MSAC considered that any resubmission would require prospective comparative trial data (including outcomes such as medication effect, reintervention rates and procedures), revised clinical algorithm and supporting evidence to appropriately define the clinical place of ABiC using a microcatheter, along with updated economic model and financial estimates that reflect the clinical place of ABiC using a microcatheter.

4. Background

This is the first submission (Department Contracted Assessment Report [DCAR]) to MSAC seeking MBS funding for ABiC using a microcatheter device to treat glaucoma.

MSAC has previously considered and supported MBS listing of minimally invasive glaucoma surgical procedures, specifically micro-bypass glaucoma surgery (MBGS) with implantation of a drainage device (i.e. micro-bypass stent).

In November 2017, MSAC supported MBS listing for the insertion of trabecular MBGS devices and suprachoroidal MBGS[3] devices (MSAC Applications 1483 and 1496, respectively) for patients with open angle glaucoma undergoing concomitant cataract surgery. This resulted in MBS item 42705, initially allocated an interim item number and amended to a permanent listing on 1 November 2018.

In August 2019, MSAC recommended a service for the insertion of trabecular MBGS devices in a standalone procedure (MSAC Application 1541). MBS item 42504 was listed on 1 May 2020.

MSAC application 1649 was subsequently submitted to amend MBS item 42504 (standalone MBGS procedure) to include ABiC using a microcatheter but did not request amendment of MBS item 42705 (MBGS in conjunction with cataract surgery). During development of the PICO Confirmation for MSAC application 1649, the applicant advised that ABiC using a microcatheter is currently being performed in conjunction with cataract surgery under MBS item 42705. As the use of ABiC with a microcatheter in conjunction with cataract surgery has not previously been considered by MSAC (i.e. was not assessed as part of MSAC application 1483), as per the ratified PICO, it was agreed that MSAC application 1649 would assess the use of ABiC using a microcatheter as a standalone procedure and in conjunction with cataract surgery.

5. Prerequisites to implementation of any funding advice

Items on the Australian Register of Therapeutic Goods (ARTG) that are relevant to this application are shown in Table 1. Other microcatheter devices such as the OMNI Surgical system and VISCO630 system by SightSciences were not identified on the ARTG.

Table 1 Microcatheter devices included on the ARTG

ARTG no.	Product	Manufacturer	Product category / GMDN	Intended purpose
244570	iTrack	Ellex iScience (iTrack) (parent company Nova Eye Medical)	Medical device (Class IIa)	Fluid infusion and aspiration during surgery, catheterisation and viscodilation of Schlemm's canal, placement of a tensioning suture within the canal to reduce the IOP of patients with glaucoma

Source: ARTG website, accessed 29 July 2021
Abbreviations: ARTG = Australian Register of Therapeutic Goods, GMDN = Global Medical Device Nomenclature, IOP = intraocular pressure

[3] There are currently no suprachoroidal MBGS devices in use in Australia, following the global withdrawal of the CyPass Micro-stent when it was found to have long term adverse effects on endothelial cell density.

6. Proposal for public funding

The applicant proposed amending the existing MBS item 42504, which is currently for implantation of micro-bypass stents as a standalone procedure for the treatment of glaucoma, to include ABiC using a microcatheter device as shown in Table 2.

The item descriptor for MBS item 42705, for implantation of micro-bypass stents performed in conjunction with cataract surgery is shown in Table 3. Although the applicant did not request amendment of MBS item 420705 to include ABiC using a microcatheter device, as noted the safety and effectiveness ABiC using a microcatheter in this population has not previously been considered by MSAC and has been included as part of this assessment.

Table 2 Proposed amendment to MBS item 42504 descriptor

Category 3
MBS item 42504 Glaucoma, minimally invasive surgery of the trabecular meshwork involving (i) implantation of a micro-bypass surgery stent system; or (ii) insertion of a microcatheter, with administration of a viscoelastic solution ~~implantation of a micro-bypass surgery stent system or insertion of a microcatheter into the trabecular meshwork~~, if: (a)conservative therapies have failed, are likely to fail, or are contraindicated; and (b) the service is performed by a specialist with training that is recognised by the Conjoint Committee for the Recognition of Training in Micro-Bypass Glaucoma Surgery **Multiple Operation Rule** (Anaes.) Fee: $312.95 Benefit: 75% = $234.75 85% = $266.05 **Extended Medicare Safety Net Cap**: $46.95

Source: Table 15, p37 of the DCAR with applicant proposed amendments in red text and Department proposed amendments in blue text and strikethrough indicates amendment suggested by the Department.
Note: Fee values ($) updated as of July 1st 2021.

Table 3 MBS item 42705 descriptor

Category 3
MBS item 42705 LENS EXTRACTION AND INSERTION OF INTRAOCULAR LENS, excluding surgery performed for the correction of refractive error except for anisometropia greater than 3 dioptres following the removal of cataract in the first eye, performed in association with insertion of a trans-trabecular drainage device or devices, in a patient diagnosed with open angle glaucoma who is not adequately responsive to topical antiglaucoma medications or who is intolerant of antiglaucoma medication. **Multiple Operation Rule** (Anaes.) Fee: $948.05 Benefit: 75% = $711.05 85% = $863.35 **Extended Medicare Safety Net Cap**: $142.25

Source: Table 16, pg 37 of the DCAR.
Notes: Fee values ($) updated as of July 1st 2021.

Other funding
The applicant has submitted an application to PLAC seeking to list the iTrack microcatheter device on the PL for funding by private health insurers. The PLAC is responsible for considering applications for the PL.

7. Summary of public consultation feedback/consumer issues

Consultation feedback was received from three organisations: Australian Society of Ophthalmologists Ltd. (ASO), Private Healthcare Australia (PHA), and Royal Australian and New Zealand College of Ophthalmologists (RANZCO). No feedback was received from consumer organisations or individual consumers or carers for this application. Responses were generally supportive of the application. Feedback suggested that the expected utilisation of intervention in the application would likely to be an underestimation. It was also suggested that ABiC using a microcatheter device may benefit paediatric patients and patients in rural or remote locations. One response questioned the strength of evidence for the clinical effectiveness of ABiC using a microcatheter; and also considered that patients who failed the intervention should remain eligible for MIGS stent implantation.

8. Proposed intervention's place in clinical management

Description of Proposed Intervention
The proposed medical service is ABiC using a microcatheter for glaucoma treatment which can be performed as a standalone procedure or in conjunction with cataract surgery. The microcatheter is inserted ab-internally (via the cornea) into Schlemm's canal in the trabecular meshwork via the anterior chamber. The microcatheter serves to dilate the canal, perforate any adhesions, and resolve any herniations. On retraction of the device, a viscoelastic solution (active component hyaluronic acid) is administered to the canal. This solution chemically dilates the canal, trabecular meshwork and collector channel ostia.

Description of Medical Condition
The population of interest for ABiC using a microcatheter device is patients with glaucoma with or without concurrent cataract surgery. Glaucoma is a disease process involving progressive atrophy of the optic nerve, loss of retinal cells and, ultimately, blindness. Older age, family history and prior ocular trauma are risk factors for the development of glaucoma. Globally, the prevalence of glaucoma is 3.54% in individuals aged 40–80 years[4]. The prevalence of glaucoma in Australia is estimated to be 1.5% in non-Indigenous Australians (≥50 years) and 0.6% in Indigenous Australians (≥40 years)[5]. Because of the aging population, the prevalence of glaucoma in Australia is expected to increase significantly, and by 2025 is it estimated that 379,000 individuals would have primary open-angle glaucoma (OAG)[6].

The clinical management algorithm and the proposed place of ABiC using a microcatheter to treat glaucoma as a standalone procedure or in conjunction with cataract surgery is presented in Figure 1 and Figure 2.

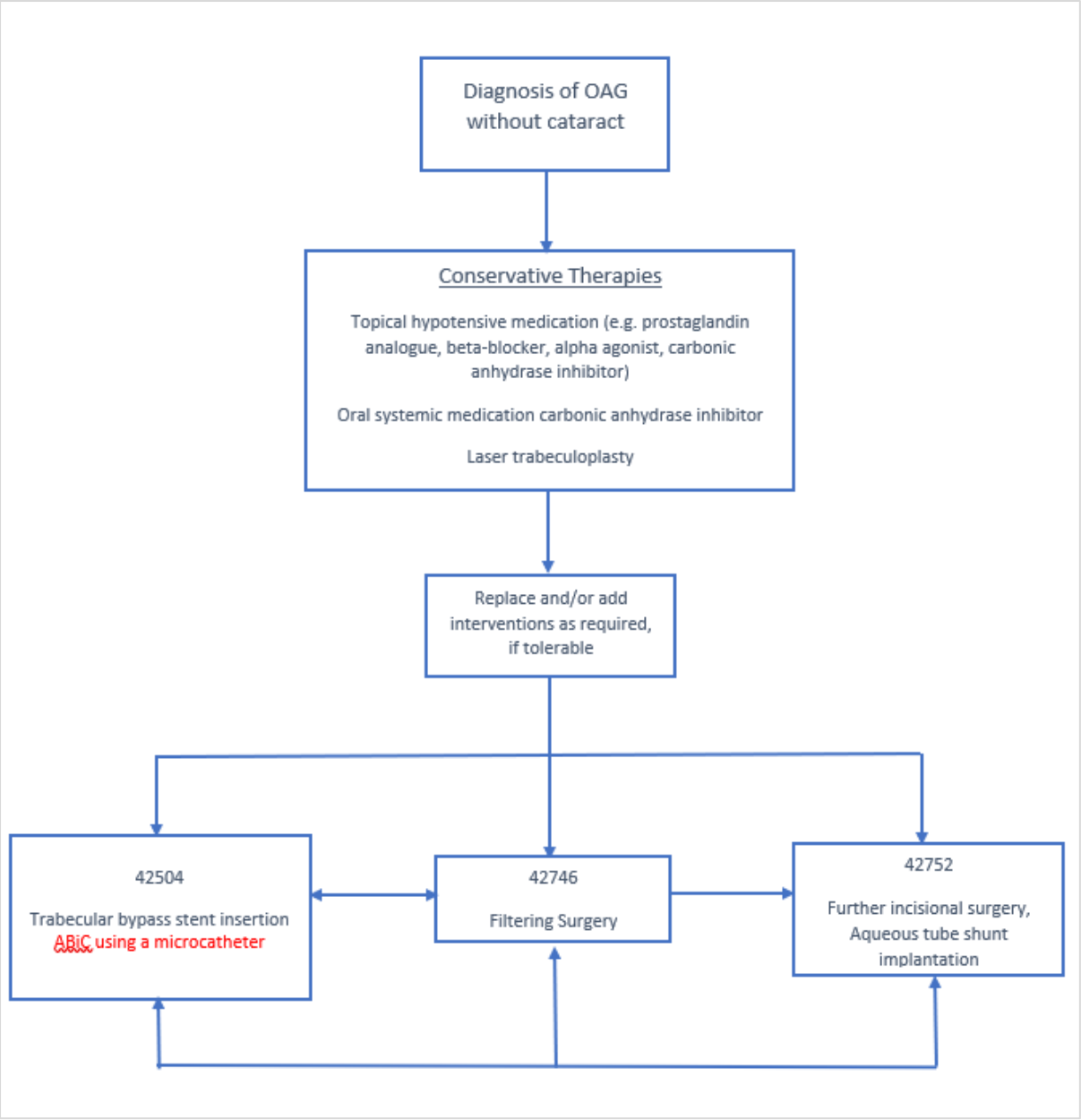
The applicant proposed that the MBS listing of ABiC using a microcatheter would provide an alternative intervention to the currently MBS listed micro-bypass stent insertion for the treatment of patients with glaucoma. Surgical intervention, including ABiC with a

[4] Tham Y-C, et al. (2014) *Ophthalmology*, 121:2081-2090.
[5] Keel S, et al. (2019) *British Journal of Ophthalmology,* 103:191.
[6] Dirani M, et al. (2011) *Clinical & Experimental Ophthalmology*, 39:623-632.

microcatheter, would be available as a standalone procedure or for patients simultaneously undergoing cataract surgery. This service is offered when other medical therapies have failed or where there are compliance issues with medications.

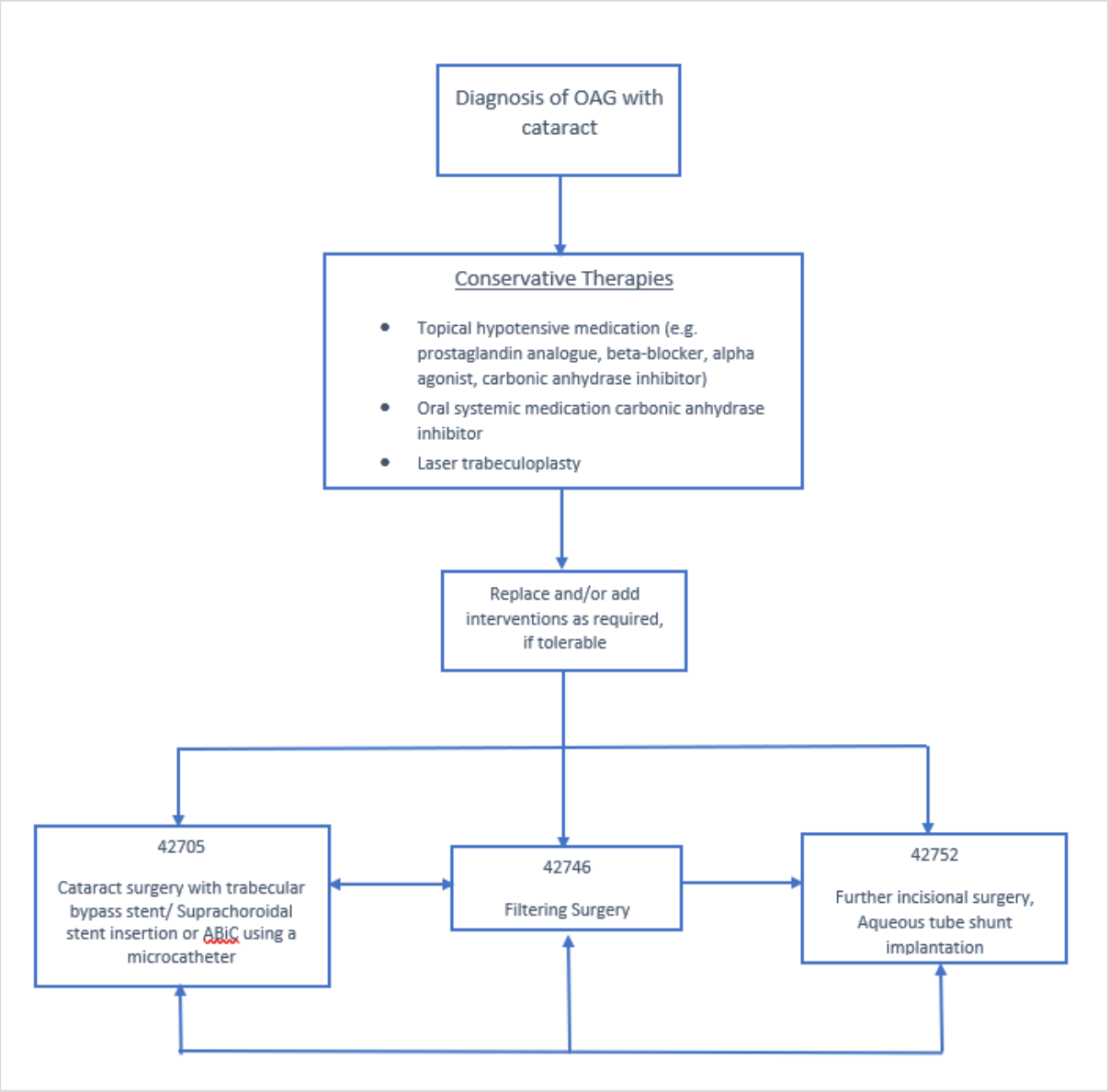
The procedures involving ABiC using microcatheter devices and insertion of micro-bypass stents both aim to reduce IOP by increasing aqueous humour outflow from the anterior chamber through the Schlemm's canal. Key differences are that the proposed intervention involves the temporary insertion of a microcatheter to inject a viscoelastic substance to dilate the Schlemm's canal, whereas the comparator involves the permanent implantation of a micro-bypass stent in the eye.

Figure 1 Proposed clinical management algorithm for patients without concurrent cataract pathology



Source: Figure 4, p46 of the DCAR
Abbreviations: ABiC = ab-interno canaloplasty, OAG = open angle glaucoma
Note: Filtering surgery is alternatively known as trabeculectomy

Figure 2 Current clinical management algorithm for patients with concurrent cataract pathology



Source: Figure 3, p45 of the DCAR
Abbreviations: ABiC = ab-interno canaloplasty, OAG = open angle glaucoma
Note: Filtering surgery is alternatively known as trabeculectomy

9. Comparator

Where ABiC using a microcatheter is performed as a standalone procedure, the nominated comparator is the insertion of a micro-bypass stent into the trabecular meshwork (MBS item 42504). Where ABiC using a microcatheter is performed in conjunction with cataract surgery, the nominated comparator is the insertion of a micro-bypass stent into the trabecular meshwork at the same time when the cataract surgery is performed (MBS item 42705).

Surgeons performing the micro-bypass stent insertion procedure must be registered with the Conjoint Committee for the Recognition of Training in Micro-bypass Glaucoma Surgery. In Australia, approximately 50 ophthalmologists are trained in stent insertion.

10. Comparative safety

No direct comparative evidence between ABiC using a microcatheter and micro-bypass stents was identified through the systematic literature review. In total, seven (7) case series studies (545 eyes from 407 participants) were identified for the intervention, ABiC using a microcatheter to treat glaucoma (Table 4). In the 7 cases series studies, patients underwent ABiC with the iTrack device (n = 134 eyes of 114 patients, k = 3), the VISCO360 device (n = 286 eyes of 201 participants, k = 2), the VISCO360 or OMNI surgical system (n = 89 eyes of 64 participants, k = 1), or ABiC with the device not reported (n = 36 eyes of 28 participants, k = 1). Two studies also compared standalone and cataract-combined procedures. Across all the included studies, the maximum length of follow up was up to 24-months. Mean participant age ranged from 70–76 years (k = 5) (participant ages ranging from 43–91 years, k = 7). Reported outcomes include IOP (k = 7), change in medication (k = 7), visual acuity (k = 3), surgical success (k = 2) and surgical failure or need for secondary glaucoma surgery (k = 4).

Due to the limitations in the evidence base for the intervention, only a naïve comparison between the intervention and the comparator was possible. Seven (7) studies (633 eyes from 521 participants) on micro-bypass stents (the comparator device, including iStent, iStent inject, Hydrus and XEN gel stent) with or without cataract surgery were included (Table 4). All comparator studies provided single arm data, of which two were extracted from randomised clinical trials (RCT). Comparisons from the RCTs were not relevant to this assessment as they were designed to compare combined micro-bypass stent implantation to cataract surgery alone or to compare the safety and effectiveness of varying numbers of implanted stents. Therefore, the relevant arm of the RCTs was extracted and considered as case series data. Follow-up times ranged from 12–48 months. Sample sizes varied from 21 to 226 participants. The mean age of participants ranged from 65–78 years (k = 6). Four studies performed micro-bypass stent implantation concurrent to cataract surgery, and 4 studies performed micro-bypass stent implantation as a standalone procedure. One study provided data on both standalone and combined procedures. This was the only study with comparative data between standalone and combined procedures of a micro-bypass stent device (XEN gel stent). All studies reported on IOP, change in medication burden, and safety. Three studies assessed visual acuity. Surgical failure or need for secondary surgeries was reported by most studies (k = 6); however, surgical success was only reported by 2 studies. Two of the included comparator studies were also studies (RCTs) included in MSAC application 1483; one of these was also included in MSAC application 1496. Both applications were submission-based assessments performed in 2017.

Key features of the included studies are summarised in Table 4.

Table 4 Key features of the included evidence on ABiC using a microcatheter (intervention) and micro-bypass stents (comparator)

	Study	Device	SA/C	N (p/e)	Study duration	Risk of bias (max. 20)	Patient population	Key outcome(s)
Intervention	Davids et al., 2019	NR	SA vs C	28/36	12m	15	OAG	IOP, Med, VA, Failure/SS
	Hughes and Traynor, 2020	VISCO360/ OMNI Surgical system	SA vs C	64/89	18m	17	OAG	IOP, Med, Failure/SS
	Gallardo, 2021	iTrack	SA vs C	53/60	24m	14	OAG	IOP, Med, VA
	Gillmann et al., 2021	iTrack	C	41/54	12m	14	OAG/PXG/PG	IOP, Med, Success, Failure/SS
	Körber, 2018	iTrack	T	20/20	12m	11	OAG	IOP, Med
	Ondrejka and Körber, 2019	VISCO360	T	71/106	12m	16	OAG	IOP, Med, VA
	Tracer et al., 2020	VISCO360	C	130/180	12m	16	OAG/PXG/PG/other	IOP, Med, Failure/SS
Comparator[7]	Katz et al., 2015[8]	iStent	SA	38/38	18m	19	OAG	IOP, Med, VA, Failure/SS
	Ferguson et al., 2017	iStent	C	66/115	24m	15	PXG	IOP, Med, Failure/SS
	Lindstrom et al., 2020	iStent inject	SA	57/57	48m	16	OAG	IOP, Med, VA, Failure/SS
	Gandolfi et al., 2016[8]	Hydrus	SA	21/21	24m	11	OAG/PXG/PG	IOP, Med, VA, Success, Failure/SS
	Pfeiffer et al., 2015[9,8]	Hydrus	C	50/50	24m	19	OAG/ PXG	IOP, Med, Failure/SS
	Karimi et al., 2019	XEN gel stent	SA vs C	226/259	18m	15	OAG/PXG/PG/other	IOP, Med, Success, Failure/SS
	Fernández-García et al., 2020	XEN gel stent	T	63/93	36m	15	OAG	IOP, Med

Source: Table 20, p54 of the DCAR

Abbreviations: C = glaucoma procedure combined with cataract surgery, e = eyes, IOP = intraocular pressure, m = months, med = medication burden, T = total cohort including both SA and C population, N = sample size, NR = not reported, OAG = open angle glaucoma, p = participants, PG = pigmentary glaucoma, PXG = pseudoexfoliative glaucoma, SA = standalone procedure, SS = secondary surgery, VA = visual acuity

The pre-ESC response suggested that the study by Davids et al. (2019) and publications for XEN Gel Stent should be excluded, and a study by Lewis et al. (2011)[10] should have been

[7] The evidence base for the comparator was pragmatically refined to a representative selection of studies for naïve comparison with the 7 case series studies on the intervention, as documented in section B and Appendix C of the DCAR.

[8] Study was also included in MSAC application 1483 SBA (*Trabecular bypass micro-invasive glaucoma surgery (TB MIGS) device implantation in patients with mild-to-moderate primary open-angle glaucoma*, 2017)

[9] Study was also included in MSAC application 1496 (*Micro-invasive glaucoma surgery (MIGS) device implantation (external to Schlemm's canal) in patients with mild-to-moderate primary open-angle glaucoma*, 2017)

[10] Lewis RA, et al. (2011) *J. Cataract Refract*. Surg. 37, 682–690

included. The rejoinder clarified that the inclusion of Davids et al. (2019) and publications for XEN Gel Stent were appropriate as these meet the pre-defined PICO criteria. Further the PICO is specific to the ABiC procedure and excluded ab-externo canaloplasty with a tensioning suture, as guided by the applicant during the PICO development. On this basis the study by Lewis et al. is not appropriate for inclusion (i.e. the study was performed using ab-externo canaloplasty with a tensioning suture).

The pre-MSAC response provided new data from two unpublished studies and one recently published study:

- Gallardo (unpublished) – 36 month data from a retrospective case series study of patients with glaucoma treated with iTrack ab-interno canaloplasty as a standalone procedure (n=**redacted** eyes) or in combination with cataract surgery (n=**redacted** eyes). The 24 month published data (Gallardo 2021) was included in the DCAR.
- Koerber and Ondrejka (unpublished) - retrospective case series study of **redacted** patients (n=**redacted** eyes) with glaucoma were treated with ABiC performed as a standalone procedure (n=**redacted** eyes) or combined with cataract surgery (n=**redacted** eyes).
- Khaimi (2021)[11] - retrospective case series study of patients with controlled mild or moderate glaucoma who underwent iTrack ab-interno canaloplasty as a standalone procedure (n=34 eyes) or in combination with cataract surgery (n=11 eyes).

Adverse events and complications

Adverse events were rarely reported among the included studies. Thirty-one various adverse events were reported and extracted from 14 studies. As most adverse events were only reported by a singular study each, a comparative analysis was not possible. Four adverse events were reported by more than one study. Thus, these 4 adverse events (intraoperative bleeding, device failure or malposition, hyphema and postoperative IOP spikes) were the focus of the assessment (Table 5).

[11] Khaimi, M.A. (2021) *Therapeutic Advances in Ophthalmology.* 13:1-10

Table 5 Most commonly reported outcomes across included studies

Intraoperative adverse events	Intervention	Comparator
Intraoperative bleeding	[T] 1.7% (Gallardo, 2021) [T] 100.0% (Davids et al., 2019) [C] 100.0% (Gillmann et al., 2021)	NI
Failure/multiple attempts at stent implantation or microcatheter insertion	[C] 0.9% (Ondrejka and Körber, 2019) *Device malfunction	[C] 4.0% (Pfeiffer et al., 2015) [T] 1.1% (Fernández-García et al., 2020)
Postoperative adverse events	**Intervention**	**Comparator**
Hyphema	[T] 12.3% (<3 mm) (Ondrejka and Körber, 2019) [T] 0.0% (Hughes and Traynor, 2020) [T] 2.8% (Davids et al., 2019) [C] 1.7% (<30 day FU) (Tracer et al., 2020)	[SA] 19.0% (Gandolfi et al., 2016)
Postoperative IOP spikes	[T] 0.9% (≥10 mmHg) (Ondrejka and Körber, 2019) [C] 7.0% (<30 day) / 1.1% (>30 day FU, 10 ≥mmHg) (Tracer et al., 2020) [C] 22.2% (<1 month, >30 mmHg) (Gillmann et al., 2021)	[T] 12.7% (>30 mmHg) (Karimi et al., 2019) [C] 6.0% (≥15 mmHg) (Ferguson et al., 2017) [SA] 4.8% (Gandolfi et al., 2016)

Source: Table 4, pg 23 of the DCAR
Abbreviations: C = glaucoma procedure combined with cataract surgery, FU = follow-up, IOP = intraocular pressure, NI = no information, SA = standalone procedure, T = total cohort (mixed population of SA and C)

Among the 14 studies, more adverse events were reported in the comparator studies (n = 18) than then intervention studies (n = 8), noting a single micro-bypass stent study contributed 11 different adverse events (Karimi et al., 2019[12]). Among reported intraoperative and postoperative events, multiple studies reported intraoperative bleeding, failure (or multiple attempts) to perform implantation or insertion of the device, hyphema and postoperative IOP spikes (Table 5).

Among studies:

- Intraoperative bleeding was only reported by intervention studies (k = 3).
- Both intervention (k = 1) and comparator (k = 2) studies reported failure or multiple attempts for the application of the device.
- Intervention studies (k = 4) reported hyphema more often than comparator studies (k = 1).
- Both intervention (k = 3) and comparator (k = 3) studies reported postoperative IOP spikes.

Naïve comparisons between the intervention and the comparator could be made where studies stratify results by procedure (i.e. standalone intervention against standalone comparator and combined intervention against combined comparator, Table 6). Intervention studies generally reported adverse events pooled from both standalone and combined cataract surgery study arms (k = 5). The remaining studies only included patients who underwent combined glaucoma and cataract surgery. Thus, the event rate for participants who underwent standalone procedures could not be compared between the intervention and comparator devices. More intraoperative adverse events were reported in the combined intervention

[12] Karimi A, et al. (2019) *Eye (Lond)*, 33:469-477

studies (4 adverse events, k = 2) than in the combined comparator studies (1 adverse event, k = 2). Postoperative adverse events in intervention studies had a similar rate of reported adverse events (5 adverse events, range 8.7–27.9%, k = 2) relative to comparator studies (4 adverse events, range 6.0–22.9%, k = 2).

Due to the paucity of data in the current evidence base, it is unclear whether the adverse events reported in the included studies were attributable to the micro-bypass stent or the cataract surgery. It is assumed that cataract surgery itself has associated adverse events. Due to the limited data on standalone intervention procedures, it is unclear how the addition of cataract surgery affects the adverse event rates.

Table 6 presents comparative intraoperative and postoperative adverse event data, which has been stratified into standalone and combined subpopulations. Fewer postoperative adverse events were reported in the standalone micro-bypass stent studies (1 adverse event, range 0.0–1.8%, k = 2) compared to the combined micro-bypass stent studies (4 adverse events, range 6.0–22.9%, k = 2). Markedly large ranges of reported intraoperative events in combined intervention studies did not allow for meaningful conclusions to be drawn from the data (Table 6). In patients undergoing glaucoma surgery and concurrent cataract surgery, the data suggest similar numbers of postoperative adverse events in patients undergoing the intervention as the comparator devices.

Table 6 Number of different reported adverse events and incidence of events stratified as standalone or combined cataract surgery

Study	Intraoperative event number (patients reported %)	Postoperative event number (patients reported %)
	Pooled AEs (range any AE)	Pooled AEs (range any AE)
Intervention Combined		
Gillmann et al., 2021	4* (0.0–100.0%)	5 (8.7–27.9%)
Tracer et al., 2020		
Comparator combined		
Ferguson et al., 2017	1 (0.0–4.0%)	4 (6.0–22.9%)
Pfeiffer et al., 2015		
Comparator standalone		
Katz et al., 2015	0 (0.0%)	1 (0.0–1.8%)
Lindstrom et al., 2020		

Source: Table 5, pg 24 of the DCAR
Abbreviations: AEs = adverse events, NI = no information
Notes: Event number refers to the number of different adverse events reported by the study. Several interventional studies are not presented here as they pooled standalone and combined cataract surgery patients and consequently were not useful for comparative analysis. The pooled AEs figures omit double reporting of AEs.
*100% bleeding; 4.7% for any other AE

Extended assessment of harms

The extended assessment of harms identified ECL as a safety outcome to watch for over coming years. This outcome was highlighted due to the 2018 global recall of the CyPass Microstent device due to unacceptable ECL (>30%) over a 5-year study (COMPASS-XT)[13]. A non-systematic search was performed to identify intervention and comparator studies where high ECL levels were reported (Table 7). No studies on OMNI surgical system or VISCO360 microcatheter devices regarding ECL were identified. Only conference abstracts

[13] The COMPASS trial (data up to 24 months) was a major component of MSAC application 1496 SBA (2017).

were identified for iTrack evidence. However, compared to the 5-year follow-up of patients in the COMPASS-XT study, the identified intervention (iTrack) and comparator (iStent, iStent inject, Hydrus, XEN gel stent) literature on ECL had considerably shorter follow-up times (6–36 months), thus studies with longer follow-up times are necessary.

The extended assessment of harms also identified 2 active/ongoing clinical trials of interest. One is a comparative multicentre RCT between ABiC using the OMNI surgical system and the iStent in adult patients with pseudophakic OAG eyes involved in the European TRIDENT trial (ClinicalTrials.gov: NCT04658095[14], sponsored by SightSciences). The primary outcome to be investigated is mean unmedicated DIOP at 12 months follow-up. When published (estimated study completion July 2023), this German trial may provide the only comparative evidence. The inclusion criteria are unclear regarding the recruitment of patients with cataracts or undergoing concurrent cataract surgery. However, the title posits all patients will be pseudophakic and therefore, the surgeries are expected to be performed as standalone procedures.

Table 7 Studies reporting on endothelial cell loss after iTrack or micro-bypass stent procedures (with or without cataract surgery).

Device	Follow-up	Endothelial cell loss (ECL)
ABiC iTrack Lubeck 2020 (conference abstract) †	6 months n = unknown	ASCRS 2020: iTrack alone: 2% iTrack combined: 5% Cataract alone: 5% ESCRS 2020: 5% at 12 months (ongoing to 36 months)
ABiC iTrack *	12 months n = unknown	ASCRS 2021: iTrack combined: 4.8% (Nova-Eye Medical, N.D.)
iStent (Dorairaj and Balasubramani, 2020)	n = 21 subjects, 42 eyes (21 received combined iStent)	Treatment combined: 9.0% KDB combined: 3.4% Significantly different between groups
iStent inject (Samuelson et al., 2019) (RCT) Treatment group: iStent inject and combined cataract surgery Control group: cataract surgery (no stent)	24 months n = 505 eyes (387 treatment)	Treatment group: 13.1% ± 12.4% (CI 95% 14.4–11.8) Control group: 12.3% ± 12.7% (CI 95% 14.8–9.8%) Patients with >30% loss Treatment group: 10.4% Control group: 9.5%
Hydrus Microstent (Ahmed et al., 2021) June 2021	3 years n = 556 (369 treatment)	Treatment combined: 15% (CI 95% 13–16%) Cataract alone:11% (CI 95% 9–13%) No significant difference between groups
XEN gel stent (Gillmann et al., 2020)	2 years N = 23 (17 combined)	XEN combined: 14.3% Cataract alone:14.5% No significant difference

Source: Table 29, p74 of the DCAR

Abbreviations: ABiC = ab-interno canaloplasty, ASCRS = American Society of Cataract and Refractive Surgery, ESCRS = European Society of Cataract and Refractive Surgery, KDB = kahook dual blade, n = number of patients, RCT = randomised controlled trial

Note: No literature on ECL after OMNI or VISCO360 was identified in the non-systematic literature search.

† = Additional data was planned to be presented at the ASCRS 2021 (July 23–27). These results were not available at the time of finalisation of the DCAR.

* = (Data to be presented 13-17 August ASCRS Las Vegas

[14] A Prospective, Randomized, Multicenter Study to Compare The Safety And Effectiveness Of The OMNI Surgical System And The iStent Inject In Pseudophakic Eyes With Open Angle Glaucoma. The TRIDENT European Trial - NCT04658095 - https://clinicaltrials.gov/ct2/show/NCT04658095

11. Comparative effectiveness

IOP reduction
For intervention studies, large ranges of IOP reduction were reported in standalone (32.7–49.7% at 12 or 24 months, k = 3) and combined (21.8–39.8% at 12 or 24 months, k = 5) procedures. Among the comparator studies, the reporting of IOP reduction results was inconsistent with or without the concurrent cataract surgery. The standalone micro-bypass stents resulted in an IOP reduction of 27.0–42.2% at 12 or 24 months (k = 4). In combined procedures, the comparator devices resulted in an IOP reduction of 20.6–39.5% at 12 and 24 months (k = 4). The ranges, albeit large, were similar between devices (ABiC using a microcatheter and micro-bypass stents) and between devices used as standalone or combined procedures (Table 8).

Table 8 IOP reduction at 12 or 24 months follow-up for procedures with intervention and comparator devices as standalone or combined cataract surgery

	Standalone	Combined cataract
Intervention	32.7–49.7%	21.8–39.8%
Comparator	27.0–42.2%	20.6–39.5%

Source: Table 6, pg 26 of the DCAR
Note: Two intervention studies were not included in this table as they reported outcomes as a mixed population of patients who underwent standalone and combined cataract procedures.

The data generally indicate that average IOP reduction could be sustained between 12- and 24-months follow-up for both the intervention and comparator (k = 1 intervention, k = 4 comparator). Two comparator studies with longer follow-up periods indicate that IOP reduction may be sustained up to 36 and 48 months postoperatively (Fernández-García et al., 2020[15], Lindstrom et al., 2020[16]). In some studies where IOP reduction was sustained, the medication use increased over follow-up times. Based on the currently available data, it was unclear whether the sustained IOP reductions were solely due to the procedure or the combined effect with medication. One comparator and two intervention studies provided comparative IOP data between standalone and combined procedures. Studies drawing comparisons between arms reported that IOP reduction was similar between arms. Through naïve comparison of all 14 included studies, IOP reduction appeared to be slightly greater in the intervention studies compared to the comparator study.

Reduction of medication burden
A high level of inconsistency was observed in the reported reduction in medication across the studies on the use of a microcatheter in combination with cataract surgery (reduction in average medication 11.1–79.3%). Similarly, among the studies on the use of micro-bypass stents in combination with cataract surgery, the average medication reduction ranged from 51.1–83.4% at 12 months and 49.6–81.1% at 24 months. Although the reported reduction in medication use appears similar between intervention and comparator devices, the data either rely on a single study (standalone) (Gallardo, 2021[17]) or have distinctly large ranges (Table 9).

One intervention and one comparator study reported comparative data on reduced medication burden between the glaucoma procedures combined with cataract surgery and standalone. The intervention study (iTrack) saw a greater reduction in average medication use in the

[15] Fernández-García A, et al. (2020) *Int Ophthalmol*, 40:709-715
[16] Lindstrom R, et al. (2020) *Clinical ophthalmology (Auckland, N.Z.)*, 14, 71-80
[17] Gallardo M (2021) *Clin Ophthalmol,* 15**,** 1591-1599

combined surgery group compared with the standalone group (70.4% and 53.3%, respectively). The comparator study (XEN gel) saw a similar reduction in average medication use with or without the combined cataract surgery (62.7% and 68.8%, respectively). These data indicate the impact of cataract surgery on medication burden may differ between intervention and comparator devices, however this remains uncertain due to the limited available evidence.

Table 9 Medication burden reduction at 12 months follow-up for procedures with intervention and comparator devices as standalone or combined cataract surgery

	Standalone	Combined cataract
Intervention	53.3% (k = 1)	11.1–79.3% (k = 5)
Comparator	68.8% (k = 1)	51.1–83.4% (k = 4)

Source: Table 7, pg 27 of the DCAR
Note: Two intervention studies were not included in this table as they reported outcomes as a mixed population of patients who underwent standalone and combined cataract procedures.

Visual acuity
Visual acuity improved from baseline in groups of patients with cataracts. The standalone procedure was able to sustain but not improve visual acuity compared with baseline. This finding was similar for both the intervention (k = 3) and comparator devices (k = 5), indicating that the devices are similarly effective. This is likely explained by the cataract surgery rather than the MIGS.

Surgical success or failure
Surgical failure was defined differently among included studies. It is generally related to the failure to meet predefined success criteria or the requirement for additional surgeries. Failure and the need for secondary glaucoma surgeries were more commonly reported than was procedure success rates. In one intervention study, the qualified success of the standalone procedure was considerably lower than was the success of the combined procedures with cataract surgery (65% versus 93%). The study also noted that all failures had occurred in ABiC participants (8.3%). Varying definitions of surgical success and failure have prevented meaningful comparisons between the intervention and the comparator.

GRADE quality assessment
The summary of findings for the intervention only (critical and important outcomes, both benefits and harms) is shown in Table 10. GRADE assessment was undertaken for the intervention arm only due to the limitations of the naïve comparison with the comparator. The assessment was severely limited by the very low quality of the evidence and the paucity of data among the evidence base for the intervention.

Table 10 Clinical benefits and harms of ABiC using a microcatheter, and as measured by the critical patient-relevant outcomes in the key studies

Outcomes (units) Follow-up	Participants, eyes (studies)	Quality of evidence (GRADE)	Risk of bias	Range of effect
IOP reduction (%), 12–24 months	407 participants, 545 eyes (k = 7)	⊕⊙⊙⊙	Serious	Reduction in average IOP: 21.8–49.7%
Medication burden (%), 12–24 months	407 participants, 545 eyes (k = 7)	⊕⊙⊙⊙	Serious	Reduction in average medication use: 11.1–93.3%
Visual acuity (Snellen line loss)	124 participants, 166 eyes (k = 2)	⊕⊙⊙⊙	Serious	Loss of Snellen lines: No loss versus reported loss of between 1 and ≥2 Snellen lines
Surgical success/failure (%)*	263 participants, 359 eyes (k = 4)	⊕⊙⊙⊙	Serious	Surgical success: 24%–93% Surgical failure: <1%–38%
Safety (%)	407 participants, 545 eyes (k = 7)	⊕⊙⊙⊙	Serious	Intraoperative bleeding: 1.7–100% (k = 3) Hyphema: 0–12.3% (k = 4) Postoperative IOP spikes: 0.9–22.2% (k = 3) Total number of reported intraoperative Aes: 6 (k = 7) Total number of reported postoperative Aes: 8 (k = 7) Reported number of intraoperative or postoperative events: (k = 1)

Source: Table 8, pg 28 of the DCAR
Abbreviations: Aes = adverse events, IOP = intraocular pressure, GRADE Working Group grades of evidence (Guyatt et al., 2013)
Note: * = Studies implemented different definitions of surgical success and failure, contributing to highly variable data. This GRADE table represents the intervention arm only. Studies of standalone, combination and mixed populations have been pooled together for this analysis. A more detailed GRADE table is available in Table 81.
⊕⊕⊕⊕ **High quality:** We are very confident that the true effect lies close to that of the estimate of effect.
⊕⊕⊕⊙ **Moderate quality:** We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
⊕⊕⊙⊙ **Low quality:** Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect.
⊕⊙⊙⊙ **Very low quality:** We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect.

Clinical claim

On the basis of the benefits and harms reported in the evidence base (summarised above), it is suggested that, relative to micro-bypass stents, ABiC using a microcatheter has uncertain safety and uncertain effectiveness due to the paucity and very low-quality of evidence.

12. Economic evaluation

A CMA was performed for the comparison of ABiC using a microcatheter and insertion of a micro-bypass stent into the trabecular meshwork as either a standalone procedure or in conjunction with cataract surgery. The main assumption in using CMA is the non-inferiority or equivalence in clinical effectiveness and safety of ABiC using a microcatheter compared to the insertion of a micro-bypass stent into the trabecular meshwork. Key information regarding the model and parameter inputs are outlined in Table 11.

Table 11 Summary of the economic evaluation

Perspective	Australian health care systems
Comparator	Insertion of a micro-bypass stent into the trabecular meshwork as a standalone procedure (MBS item 42504) or in conjunction with cataract surgery (MBS item 42705).
Type of economic evaluation	Cost minimisation analysis (CMA)
Sources of evidence	Clinical evidence presented in Section B
Time horizon	Not applicable
Outcomes	Cost differences
Methods used to generate results	Cost analysis
Discount rate	Not applied
Software packages used	Excel

Source: Table 9, p29 of the DCAR

The key assumptions made during the economic analysis are:

- Equivalent or non-inferior clinical effectiveness and safety of ABiC using microcatheter compared with the insertion of the micro-bypass stent into the trabecular meshwork. This relies on the following assumptions:
    - The cost of the microcatheter is similar to the cost of the micro-bypass stent. Microcatheter cost was based on the average cost of micro-bypass stents (Hydrus, iStent, XEN45) on the PL.
    - The presurgical assessment procedure for glaucoma patients with or without cataract pathology is generally the same for the intervention and the comparator. The costs were not included in CMA.
    - The frequency of adverse events, and surgical and postsurgical complications associated with ABiC using microcatheter or micro-bypass stent implantation are low in frequency and generally resolve within the time period of the index hospitalisation.

The costs associated with surgery (device and procedural costs), postoperative specialist consultation and reoperation were included in the CMA comparing ABiC using microcatheter with the insertion of the micro-bypass stent into the trabecular meshwork. The incremental cost between ABiC using a microcatheter and insertion of the micro-bypass stent into the trabecular meshwork is presented in Table 12 and Table 13.

Table 12 Result of cost-minimisation analysis comparing ABiC with microcatheter and insertion of micro-bypass stents as a standalone procedure in patients with glaucoma

Model base-case	ABiC with microcatheter (iTrack)	Micro-bypass stents (iStent, iStent inject, Hydrus, XEN45)
Device cost	$1,353.00	$1,353.00 (average cost)
Intraocular viscoelastic fluid cost	$69.00	$69.00
Procedure and related cost	$477.75	$477.75
Hospitalisation cost	$1,260.00	$1,260.00
Pre- and post-surgical cost	$271.95	$271.95
Complication cost	$108.53	$65.14
Subtotal	$3,540.23	$3,496.84
Incremental (microcatheter vs micro-bypass stent)	$43.40	

Source: Table 10, p30 of the DCAR
Abbreviations: ABiC = ab-interno canaloplasty.

Table 13 Result of cost-minimisation analysis comparing ABiC with microcatheter and insertion of micro-bypass stents in conjunction with cataract surgery in patients with glaucoma

Model base-case	ABiC with microcatheter (iTrack)	Micro-bypass stents (iStent, iStent inject, Hydrus, XEN45)
Device cost	$1422.00	$1,422.00
Intraocular viscoelastic fluid cost	$69.00	$69.00
Procedure and related cost	$1,112.85	$1,112.85
Hospitalisation cost	$1,260.00	$1,260.00
Pre- and post-surgical cost	$271.95	$271.95
Complication cost	$152.36	$91.44
Subtotal	$ 4,219.16	$4,158.24
Incremental (microcatheter vs micro-bypass stent)	$60.92	

Source: Table 11, p30 of the DCAR
Abbreviations: ABiC = ab-interno canaloplasty.

Sensitivity analyses were performed to investigate how various uncertainties on the prostheses costs and the reoperation rate impact the outcome of the economic evaluation of ABiC with microcatheter compared to micro-bypass stents. The results are reported in Table 14 and Table 15.

Table 14 Sensitivity analysis of the cost-minimisation model; inputs and results for standalone procedure

Inputs		Results		
Cost category	Description of changes	Incremental cost	Change from base-case	Interpretation
Base case		**$43.40**	**n/a**	
Prosthesis cost				
	Microcatheter device cost (iTrack) +20% of the average cost of the micro-bypass stent ($1,623.60)	$314.00	$270.60	Non-favourable
	Microcatheter device cost (iTrack) -20% of the average cost of the micro-bypass stent ($1,082.40)	-$227.20	$-270.60	Favourable
Cost of reoperations	Reoperation rate post-ABiC with microcatheter equivalent to that for micro-bypass stent insertion (4.1%)	$0	-$43.40	Favourable

Source: Table 41, pg 101 of the DCAR
Abbreviation: ABiC = ab-interno canaloplasty ; n/a = not applicable
Notes: The favourable/non-favourable interpretation relates to microcatheter relative to the comparator.

Table 15 Sensitivity analysis of the cost-minimisation model; inputs and results for procedure with concurrent cataract surgery

Inputs		Results		
Cost category	Description of changes	Incremental cost	Change from base-case	Interpretation
Base case		**$60.92**	**n/a**	
Prosthesis cost				
	Microcatheter device cost (iTrack) +20% of the average cost of the micro-bypass stent ($1,623.60)	$331.52	$270.60	Non-favourable
	Microcatheter device cost (iTrack) -20% of the average cost of the micro-bypass stent ($1,082.40)	-$209.68	-$270.60	Favourable
Cost of reoperations	Reoperation rate post-ABiC with microcatheter equivalent to that for micro-bypass stent insertion (4.8%)	$0	-$60.92	Favourable

Source: Table 42, pg 102 of the DCAR
Abbreviation: ABiC = ab-interno canaloplasty; n/a = not applicable
Notes: The favourable/non-favourable interpretation relates to microcatheter relative to the comparator.

The pre-ESC response posited that the 6.9% reoperation rate were patients with late-stage glaucoma i.e., severe, and were not representative of the mild-moderate glaucoma population

of patients in whom the intervention is considered most appropriate. The rejoinder clarified that ratified PICO defined the patient population as general glaucoma patients without specifying any disease severity and therefore, patients with more severe conditions are a part of eligible patient population. New data from 3 studies (2 unpublished) provided in the pre-MSAC response indicated the reoperation rate was **redacted**% for patients with mild-moderate glaucoma and **redacted**% for patients with severe glaucoma, after 3 years.

The pre-ESC response also proposed a reduced cost (prosthesis rebate and sell price) of $**redacted**/unit (equivalent to Hydrus and XEN) claiming this would reduce the net cost of the intervention and address the 2.9% disparity in reoperation rate between the intervention and comparator.

13. Financial/budgetary impacts

An epidemiological approach was used to estimate the financial implication of including the use of microcatheters for patients with glaucoma with MBS item 42504 (standalone procedure) and MBS item 42705 (in conjunction with cataract surgery).

The number of eligible glaucoma patients having MIGS in conjunction with cataract surgery was estimated using the MBS items report regarding the 4-year uptake (from 2017/2018 to 2020/2021) of MBS 42705. Data from MBS item 42504 (MIGS as a standalone procedure) was not used as this item was only recently added to the MBS (May 2020). Expert advice suggested that of all patients having the MIGS procedure, 90% would be done in conjunction with cataract surgery. It was assumed that the patient numbers derived from the MBS 42705 utilisation data would capture 90% of all patients having the MIGS procedure. The number of patients receiving MIGS as a standalone procedure was then estimated as the additional 10%. The number of patients receiving ABiC with microcatheter, for both the standalone procedure and in conjunction with cataract surgery, was estimated based on the assumption that ABiC using a microcatheter would substitute 10% the micro-bypass stent services (Expert Ophthalmologist, 2021).

The financial implications to the MBS resulting from the proposed inclusion of microcatheters to the MBS are summarised in Table 16. The net cost to the MBS of ABiC using microcatheter is estimated at $19,937.34 in year 1. From years 2 to 5, the net cost of ABiC using microcatheter rises from $22,763.48 to $31,219.22 as the projected patients eligible to uptake microcatheter increases.

Table 16 Total costs to the MBS associated with ABiC using microcatheter

	2022	2023	2024	2025	2026
Standalone glaucoma surgery					
Cost of ABiC with microcatheter	$52,026.23	$59,371.22	$66,716.21	$74,056.43	$81,425.30
Cost of micro-bypass stent insertion into TM	$51,320.40	$58,565.74	$65,811.08	$73,051.72	$80,320.61
Net Cost to MBS	**$705.83**	**$805.48**	**$905.13**	**$1,004.71**	**$1,104.698**
Glaucoma surgery in conjunction with cataract surgery					
Cost of ABiC with microcatheter	$967,451.70	$1,104,035.20	$1,240,618.71	$1,377,113.41	$1,514,140.94
Cost of micro-bypass stent insertion into TM	$948,210.19	$1,082,077.21	$1,215,944.22	$1,349,724.20	$1,484,026.41
Net Cost to MBS	**$19,241.51**	**$21,958.00**	**$24,674.49**	**$27,389.21**	**$30,114.53**
Overall					
Net Cost to MBS	**$19,937.342**	**$22,763.48**	**$25,579.62**	**$28,393.92**	**$31,219.22**

Source: Table 12, pg32 of the DCAR
Abbreviations: ABiC = ab-interno canaloplasty; MBS = Medicare Benefits Schedule; TM = trabecular meshwork

The microcatheter reoperation rate is a major area of uncertainty. The assumption in the base-case scenario includes a reoperation rate of 6.9%, calculated from 2 retrospective studies (Gallardo et al., 2018b[18]; Gillman et al., 2021[19]). Therefore, the impact of the reoperation rate on the financial estimates was explored through sensitivity analyses presented in Table 17.

The sensitivity analyses indicate that the estimated year-1 cost to the MBS range between $0–$30,065.56. By year 5, the potential net cost impact on the MBS of listing ABiC using microcatheter may lie between $0–$47,055.05 (the corresponding base-case estimate was $31,219.22). The lower bound reflects the cost when the reoperation rate of ABiC using microcatheter is equal to the reoperation rate of the micro-bypass stent (4.1%), while the upper bound reflects the potential cost impact where the microcatheter reoperation rate is increased by 20% (8.3%).

[18] Gallardo M, et al. (2018b) *Clin Ophthalmol,* 12**,** 2149-2155
[19] Gillman K, et al. (2021) *International Ophthalmology***,** 1-7

Table 17 Results of sensitivity analyses performed on budget impact assessment

	2022	2023	2024	2025	2026
Base-case					
Reoperation rate	6.9%	6.9%	6.9%	6.9%	6.9%
Number of patients	75	86	96	107	118
Net cost, MBS	**$19,947.34**	**$22,763.48**	**$25,579.62**	**$28,393.92**	**$31,219.22**
Reoperation rate of microcatheter equal to micro-bypass stent					
Reoperation rate	4.1%	4.1%	4.1%	4.1%	4.1%
Number of patients	45	51	58	64	71
Net cost, MBS	**$0.00**	**$0.00**	**$0.00**	**$0.00**	**$0.00**
Reoperation rate (-20%)					
Reoperation rate	5.5%	5.5%	5.5%	5.5%	5.5%
Number of patients	60	68	77	85	93
Net cost, MBS	**$9,829.12**	**$11,216.79**	**$12,604.45**	**$13,991.21**	**$15,100.74**
Reoperation rate (+20%)					
Reoperation rate	8.3%	8.3%	8.3%	8.3%	8.3%
Number of patients	90	103	116	129	142
Net cost, MBS	**$30,065.56**	**$34,310.17**	**$38,554.79**	**$42,796.64**	**$47,055.05**

Source: Table 54, pg 113 of the DCAR
Abbreviations: MBS = Medicare Benefits Schedule

14. Key issues from ESC to MSAC

ESC key issue	ESC advice to MSAC
Lack of safety and effectiveness data	Available clinical data are of poor quality and low volume, and only naïve comparison of the intervention and comparator could be undertaken. However, there is no suggestion of any safety signal of concern from more than ten years 'real world' experience.
Revised MBS descriptor	It is proposed that MBS item 42504 is amended to explicitly permit use of ABiC. However, MSAC may wish to recommend creating a new MBS item for monitoring the intervention due to uncertainty in the estimated utilisation. The item would restrict the use of the technology to trained clinicians (as defined by the profession), and for adults where other treatments have failed. Noting the Departmental plan to review and revise the suite of glaucoma surgery descriptors to clarify their clinical intent and improve consistency and accuracy of their terminology. This review is expected to consider increasing tendency towards minimally invasive options and be device/approach agnostic.
Uncertain economic and financial estimates	The very low level clinical evidence with a serious risk of bias creates uncertainty in economic estimates and financials. A higher level of clinical evidence is essential for meaningful evaluation.
Out-of-pocket costs	Out-of-pocket costs could be significant. It should be clarified whether or not these costs would be covered under hospital procedure costs.
Uncertainties regarding utilisation	The estimated utilisation of ABiC using a microcatheter is highly uncertain as:

	• assumed substitution is based on opinion of one clinical expert • device may be attractive to wider demographic • may become the first of a two-step process prior to implanting a micro-bypass stent • clinical evidence on rates of reoperation are highly uncertain. MSAC may wish to consider limiting the number of times ABiC using a microcatheter could be used prior to micro-bypass stent insertion.

ESC discussion

ESC noted the application seeks to modify the wording of Medicare Benefits Schedule (MBS) item 42504, which currently encompasses implantation of micro-bypass stents as a standalone treatment for glaucoma, to include ab-interno canaloplasty (ABiC) using a microcatheter device. The service would be used in the clinical setting for the treatment of glaucoma with or without concurrent cataract surgery.

ESC noted that ABiC using a microcatheter in conjunction with cataract surgery is being claimed under MBS item 42705, which currently encompasses implantation of micro-bypass stents in conjunction with cataract surgery. ESC noted Department advice that although the current wording of MBS item 42705 could be reasonably interpreted as including ABiC using a microcatheter, this was not the intent of this MBS item and has not been previously considered by MSAC.

ESC considered that ABiC using a microcatheter should be incorporated into the existing MBS item 42504 as per the amendments proposed by the Department. However, ESC noted that incorporating the procedure into MBS item 42504 will make it difficult to measure the utilisation numbers for this procedure. ESC also considered that MBS item 42504 should be restricted to:

- those who have failed conservative therapy, or where conservative therapy is contraindicated
- clinicians with specific training that has been agreed with by the profession
- adults (as there was no evidence available for use in children).

ESC also considered that the item descriptor may need to limit the number of reoperations using a microcatheter due to uncertainty in the rates of reoperation. ESC considered that the applicant should provide data on reoperation rates from the device manufacturer.

ESC noted that the proposed fee for ABiC using a microcatheter, as a standalone procedure or in conjunction with micro-bypass stent insertion, would be the same as micro-bypass stent insertion under MBS items 42504 ($312.95) and 42705 ($948.05). ESC noted that micro-bypass stents are included on the Protheses List (PL) but that the microcatheter device manufactured by the applicant, iTrack, is not listed on the PL. Therefore, the cost of the microcatheter used during ABiC is currently an out-of-pocket (OOP) cost borne by a patient. ESC noted that an application for listing the iTrack microcatheter on the PL has been submitted for consideration by the Protheses List Advisory Committee (PLAC).

ESC noted consumers would be concerned that the safety, effectiveness, and cost-effectiveness of ABiC using a microcatheter appears uncertain, especially the uncertainty regarding rare adverse events. Further, while ABiC using a microcatheter could provide

patients with an alternative procedure to treat glaucoma thereby increasing patient choice, the potential OOP costs may present a barrier to many consumers.

ESC noted that the evidence base for ABiC using a microcatheter, which consisted of seven case series studies, was limited and of very low quality. Further, as there were no studies directly comparing ABiC using a microcatheter (intervention) with insertion of a micro-bypass stent into the trabecular network (comparator), only naïve comparisons were possible. Due to limitations in the evidence base, the population was pooled and not stratified by the severity of glaucoma and often not able to be stratified by presence/absence of cataract surgery. As such the impact of cataract surgery on the safety and effectiveness of ABiC using a microcatheter is uncertain (cataract surgery may bias results or obscure differences in the data). The available evidence base also lacked data on health-related quality of life or quality of life and rarely reported adverse events.

Regarding the naïve comparison of safety, ESC noted that the assessment focused on four adverse events: intraoperative bleeding, device failure, hyphema and a postoperative spike in intraocular pressure (IOP). Bleeding and hyphema appeared to be more common for ABiC using a microcatheter than the micro-bypass stents. The rate of surgery failure/postoperative IOP spike was similar for the microcatheter device and micro-bypass stents. However, because the adverse event data for the intervention could not be stratified by presence/absence of cataract surgery, the effect of cataract surgery on the number of adverse events for ABiC using a microcatheter was unclear. ESC acknowledged the pre-ESC response that there is no suggestion of any safety signal of concern from 'real world' experience. However, due to the nature of the comparisons and paucity of very low quality evidence, ESC considered that the available safety data may not be sufficient to support the applicant's claim that ABiC using a microcatheter has non-inferior safety compared to micro-bypass stents.

Regarding the extended assessment of harms, ESC noted that endothelial cell loss (ECL) was identified as an important safety outcome following the withdrawal of a micro-bypass stent from the market because of unacceptable ECL. ESC noted that there is insufficient data of insufficient follow-up on ECL for ABiC using a microcatheter. The pre-ESC response claimed that ABiC using a microcatheter would result in a reduction in ECL, but did not provide adequate evidence to support this. ESC noted that there is a clinical trial (TRIDENT[20]) comparing ABiC using another microcatheter device to micro-bypass stents. The clinical trial is due to be completed in 2023, but ESC noted that there was not enough information available about the trial to be assured that it would answer the questions and concerns raised around this application.

Regarding the naïve comparison of effectiveness, ESC noted that IOP reduction at 12- or 24-months post-surgery was generally consistent and sustained for both for ABiC using a microcatheter and implantation of micro-bypass stents. This was the same when the intervention was performed as standalone procedure or when performed in conjunction with cataract surgery. Reports on reduction in medication use was found to be inconsistent across studies, and sometimes increased during follow-up which may have confounded the reported sustained IOP reduction. Visual acuity had improved in patients who received the microcatheter device concurrent with cataract surgery, but there was no improvement in those who only received the standalone procedure. ESC noted that the number of failed surgeries

[20] NCT04658095 - A Prospective, Randomized, Multicenter Study to Compare The Safety And Effectiveness Of The OMNI Surgical System And The iStent Inject In Pseudophakic Eyes With Open Angle Glaucoma. The TRIDENT European Trial - https://clinicaltrials.gov/ct2/show/NCT04658095

were marginally higher for ABiC using a microcatheter compared to micro-bypass stents, but the small numbers available made it difficult to draw any conclusions. ESC agreed with the commentary that that a higher level of evidence is essential for meaningful evaluation of the comparative effectiveness and considered the claim of non-inferiority to be very uncertain.

ESC noted that a cost-minimisation analysis (CMA) comparing ABiC using a microcatheter with micro-bypass stent insertion was presented based on key assumptions that:

- the cost of the microcatheter and micro-bypass stent was the same and costed based on the average PL benefit for micro-bypass stents
- the pre-surgical assessment cost was the same
- ABiC using a microcatheter has non-inferior effectiveness and safety compared to micro-bypass stent insertion (very uncertain, based on a naïve comparison using very low-quality evidence).

ESC noted that the only cost difference in the analysis were the complication costs which were based on rates of reoperation observed for ABiC using a microcatheter (6.9%) and micro-bypass stents (4.1%) in two retrospective studies. As a result, the base case analysis estimated the incremental cost of ABiC using a microcatheter versus micro-bypass stents was $43 for the standalone procedure and $61 for the procedure in conjunction with cataract surgery.

ESC noted that the pre-ESC response claimed that the reoperation rates may be overestimates as the studies included patients with late-stage glaucoma; however, ESC agreed with the commentary that the defined patient population does not exclude severe conditions, so it is appropriate to include these patients. ESC also noted that the studies reported a wide range of reoperation rates (from less than 1% to 38%) and varying definitions of failure. ESC noted that, if the upper range of the reoperation rate was applied to the CMA, the cost difference would increase to $532 for the standalone procedure and $747 for the procedure in conjunction with cataract surgery.

ESC noted the pre-ESC response proposed a reduced cost for the iTrack microcatheter of $**redacted**/unit, equivalent to the PL benefit for the Hydrus and XEN micro-bypass stent. ESC noted that a reduced cost for the microcatheter was important because this may potentially be an OOP cost borne by patients. ESC queried whether the microcatheter costs would be covered under hospital procedure costs. ESC also considered that to achieve cost-neutrality, the maximum cost of the microcatheter would need to be lower than the cost of micro-bypass stents (i.e. not equivalent to the Hydrus and XEN micro-bypass stents). Overall, due to limitations with the clinical evidence base creating uncertainty in the non-inferiority claim, along with uncertainty in the reoperations rates, ESC considered the economic evaluation to be highly uncertain.

ESC noted an epidemiological approach was used to estimate the number of patients who may undergo ABiC using a microcatheter, based on the current utilisation of MBS item 42705 (micro-bypass stent insertion in conjunction with cataract surgery) and a number of assumptions informed by the opinion of one clinical expert. ESC also noted that the justification that 10% of the eligible population receiving the microcatheter device was based on the microcatheter device not being included on the PL for 5 years. ESC considered that if the microcatheter device was listed on the PL, the proportion of patients undergoing ABiC using a microcatheter could be much higher. ESC also questioned whether the increase in the use of microcatheters is entirely related to an ageing population, as the device may be attractive to a wider demographic if included on the PL as the microcatheter is not permanent.

ESC also considered that ABiC using a microcatheter has the opportunity to become the first of a two-step management process leading to insertion a micro-bypass stent, and there could be multiple surgeries before a stent is inserted, creating further uncertainty in the utilisation estimates. ESC also noted that the estimated financial impact to the MBS included costs of reoperation at a rate of 6.9%. However, as noted previously, the rates of reoperation from the available studies were highly variable. ESC noted that, at the highest reoperation rate of 38%, the net cost to the MBS would be $274,637–$429,829 over 5 years, significantly higher than the base case estimates of $19,937-$31,219. Overall, ESC considered the utilisation and estimated financial impact to the MBS to be uncertain.

15. Other significant factors

Nil

16. Applicant comments on MSAC's Public Summary Document

The applicant looks forward to addressing the concerns in this report in a future submission.

17. Further information on MSAC

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