South Australian Policy Advisory Committee on Technology (SAPACT)

Health Technology Assessment (HTA) Decision Summary

Government of South Australia

SA Health

iStent inject trabecular micro-bypass system for the treatment of mild to moderate open-angle glaucoma in combination with phacoemulsification

SAPACT MEETING DATES	19th - 21st SAPACT meetings (13 September 2019, 22 November 2019 & 14 February 2020)
APPLICATION #	1911
TECHNOLOGY	iStent Inject Trabecular Micro Bypass System (Glaukos Corporation, CA, USA) The iStent inject trabecular micro-bypass stent system, contains two titanium microstents (1mm long) that are thinly coated with stearalkonium heparin and preloaded onto a single use inserter. The stents are designed to create a patent opening from the anterior chamber into the trabecular meshwork and Schlemm's Canal to enhance aqueous outflow and reduce intraocular pressure. The stent system is provided sterile.
TECHNOLOGY CLASSIFICATION	TGA class III high-risk
PATIENT INDICATION (TGA)	The iStent inject trabecular micro-bypass system is intended to reduce intraocular pressure in adult patients diagnosed with mild to moderate primary open-angle glaucoma currently treated with ocular hypotensive medication. The device can be implanted with or without cataract surgery.

SAPACT DECISION

☒ Restricted recommendation for clinical use with financial/operational restrictions and under audit conditions.

SAPACT Advisory Recommendations (21st SAPACT meeting)

SAPACT reviewed the additional information provided by the applicant, specifically on the proposed clinical algorithm, patient selection criteria, clinical outcomes, cost savings and system benefits to SA Health. SAPACT supports the applicant's clinical recommendations for the proposed fifteen iStent inject patients in the first year, subjected to appropriate CALHN funding and clinical governance approvals, including from the CALHN New Clinical Procedures, Services or Other Interventions (NCPSOI) Committee. SAPACT will be keen to review the clinical outcomes after 12 months of implementation.

SAPACT Advisory Recommendations (19th SAPACT meeting)

SAPACT recognised the evidence challenges for the safety, clinical- and cost-effectiveness of the iStent inject trabecular micro-bypass system for the treatment of mild to moderate open-angle glaucoma in combination with phacoemulsification.

The key concerns were regarding the (1) true value of the iStent inject compared to conventional medicated eye-drops which have variable non-adherence rate; (2) high risk of bias from RCTs for the evaluation of safety, clinical- and cost-effectiveness; (3) unclear patient selection criteria; and (4) unclear clinical outcomes for monitoring.

Hence, SAPACT recommends the deferment of a statewide advisory recommendation, until the applicant develops a (1) proposed clinical algorithm and well-defined patient selection criteria for the optimal use of the iStent inject, ocular hypotensive medication and other surgical procedures; and outlines a (2) 12-month clinical outcomes report (that includes progression of glaucoma, reduction in intraocular pressure and concurrent reduction in eye-drops) and (3) cost-savings and system benefits report for SAPACT to consider.

The initial local experience from the clinical outcomes report as well as any updated published evidence may assist in deciding the merits of the iStent inject (e.g. progression of glaucoma and sustainably reducing intraocular pressure with concurrent reduction in medicated eye-drops), as well as consider the transferability of the iStent inject procedure to other LHNs.

REGULATORY APPROVALS

☒ **ARTG**: 25/07/2015	☒ **US FDA**: 21/06/2018 (after FDA iStent pivotal trial)	☒ **EU CE mark**: 2010

ARTG ID: 250914 iStent Inject Trabecular Micro Bypass System (Model number G2 M IS AS) - Glaucoma shunt

QUALITY OF EVIDENCE

Quality of Evidence	Comprehensive systematic searches were conducted in 9 published scientific databases and 25 grey literature sources. The Cochrane Systematic Review (Le 2019), a meta-analysis (Fard 2019), MSAC Public Decision Summary 2017 and the NICE Guidance 2017 informed the SAPACT Review. The Cochrane review included 7 RCTs, which were all industry-sponsored and are appraised to be of high risk of bias. Four trials did not clearly reporting the method of generating the random sequence or concealing allocations. Five trials were unmasked, open-label studies.

CLINICAL NEED

Burden of Illness	Glaucoma is a leading cause of irreversible blindness worldwide. If left untreated, glaucoma results in vision loss that is progressive, permanent and inevitable. One in 10 Australians over 80 years old will develop glaucoma. At present, 50 per cent of people with glaucoma in Australia are undiagnosed. In 2005, the Australian health care cost of glaucoma was $342 million.
Need	Conventional glaucoma medications, laser treatments and surgeries are aimed to reduce intraocular pressure to limit glaucoma development and progression. Medications are usually the first step in treating glaucoma patients and they are effective and reasonably safe. However, medications can be associated with substantial side effects, ocular surface damage, financial costs and limited effectiveness due to nonadherence in around 30 - 80% of patients. Alternatively, selective laser trabeculoplasty is modestly

	effective in reducing intraocular pressure, but its effectiveness decreases over time. Standard glaucoma surgeries such as trabeculectomy and tube shunt implantation are highly effective in reducing intraocular pressure, but they have high safety risks, including significant vision loss and the need for reoperation, that preclude their widespread use, especially in milder glaucoma cases that may not warrant the risks of such surgeries. New developments in micro-invasive glaucoma surgery, such as the iStent implant, may change the paradigm of glaucoma therapy from dependence on ocular hypotensive medications to surgical techniques that control intraocular pressure continuously.
CLINICAL BENEFIT	
Safety	The iStent inject implantation is associated with a very low incidence of intra-/post-operative complications (e.g. loss of vision) and secondary surgical interventions; no major safety events were reported.
Effectiveness	The studies did not report the outcome on the progression of glaucoma associated with the use of iStent inject. The primary clinical outcomes for most studies were the (1) reduction in intraocular pressure and the (2) reduction in the number of antiglaucoma eyedrops. The Cochrane Systematic Review (Le 2019) aimed to examine the effectiveness of iStent / iStent inject for open-angle glaucoma in comparison to conventional medical, laser, or surgical treatment. It found very low-quality evidence that treatment with iStent may result in higher proportions of participants who are drop-free or achieving better intraocular pressure control in the short, medium or long-term. None of the seven RCTs examined how the iStent affected quality of life. • Four RCTs compared iStent in combination with phacoemulsification to phacoemulsification alone. Two RCTs suggested combination group were 1.38 times more likely to be drop-free between six to 18 months. Two RCTs suggested combination group offered a small reduction in number of antiglaucoma drops (-0.42 drops). • Two RCTs compared treatment with iStent to medical therapy (one trial used the iStent inject). No meta-analysis was conducted (clinically and methodically heterogeneous). Both RCTs reported over 90% participants in the treatment groups were drop-free compared to none in the medical therapy groups at six to 18 months. • One RCT compared treatment with one versus two versus three iStents. There was no difference in terms of patients being drop-free at 36 months or less. However at longer follow-up, participants in the one iStent were less likely to be drop-free than those in two iStents or three iStents. The MSAC Public Decision Summary 2017 considered three different trabecular bypass micro-invasive glaucoma surgery (TB-MIGS) stents: the iStent, the iStent Inject and the Hydrus Microstent. MSAC agreed that there was fair evidence that TB-MIGS stent implantation in conjunction with cataract surgery was safe and effective when compared to cataract surgery alone. However, MSAC noted that the long-term clinical-effectiveness (beyond 48 months) is uncertain, including the iStent inject's impact upon disease progression and avoidance of laser trabeculoplasty or trabeculectomy. • Patients assigned to TB-MIGS stent implantation in conjunction with cataract surgery experienced a greater mean reduction in intraocular pressure (mmHg) from a medicated baseline to 12 and 24 months, compared to patients assigned cataract surgery alone. The weighted mean difference between treatment groups at both the 12 and 24 months' time points was statistically significant (p=0.04, and p=0.008, respectively). Patients in the combined TB-MIGS stent/cataract surgery group were also more likely to achieve an intraocular pressure reduction of ≥ 20% from baseline at 12 months follow-up (p=0.003). • The mean difference in the number of ocular medications was significantly greater for subjects who underwent TB-MIGS stent implantation in conjunction with cataract surgery at 12 and 24 months follow-up (p < 0.00001 and p=0.03, respectively). The NICE Guidance 2017 found that the evidence on efficacy was adequate in quality and quantity for iStent inject. The key efficacy outcomes were intraocular pressure reduction, glaucoma medication use, and quality of life. • In a systematic review and meta-analysis of 2143 patients in 32 studies examining stent insertion combined with phacoemulsification compared to phacoemulsification alone, there were: o Statistically significant reduction in intraocular pressure in combined group vs phacoemulsification-only group (p=0.128); o Statistically significant reduction in number of topical glaucoma medications per patient (p=0.092). • In 5 studies with stent insertion alone, there was statistically significant reduction in intraocular pressure after implantation of 1 or 3 stent(s) (p=0.000). Implantation of 2 stents did not show significant reduction in intraocular pressure at 6 to 12 months (p=0.000). • In an RCT (100 patients, n=50), stent implantation success rate was 96%. The meta-analysis Fard 2019 aimed to compare the overall intraocular pressure lowering effect of iStent or CyPass as isolated procedures or in combination with cataract extraction. The conclusion was that both iStent and CyPass either in combination with cataract extraction or as isolated procedures effectively decreases intraocular pressure. The effect is greatest with isolated implantation of CyPass followed by multiple iStents and then single iStent implantation and last up to 2 years. The CyPass was voluntarily removed from the market by the manufacturer upon noting increased endothelial cell loss with CyPass implantation.
SUITABILITY OF PATIENT GROUP	
Suitability of Patient Group	SAPACT members were concerned about the lack of clearly defined patient selection criteria. At this time, the iStent inject should not be used in a stand-alone procedure, but for the treatment of mild to moderate open-angle glaucoma in combination with phacoemulsification.
FINANCIAL CONSIDERATION	
Device costs	Each set of iStent inject dual stents and an injector costs around [redacted] per injection procedure. Approval is sought for 15 iStent inject treatments per year at the RAH Ophthalmology Department, hence with a total of around [redacted].

Value for Money	The iStent inject may have the potential to be cost-saving if it reduces or delays surgery (laser trabeculoplasty or trabeculectomy) or it may reduce expenditure on medicated eye-drops to treat raised intraocular pressure.
Australian Funding Approvals	The Commonwealth Medical Services Advisory Committee (MSAC) reviewed and approved the public funding of the TB-MIGS stent implantation for patients with open-angle glaucoma who are also undergoing cataract surgery through the listing on the Medical Benefits Schedule (MBS) since 1 November 2018. MSAC plans to finalise the consideration of the TB-MIGS service as a standalone procedure later this year, after its review of the service including predicted vs actual utilization.
FEASIBILITY OF ADOPTION	
Organizational Feasibility	This procedure may be used provided that standard arrangements are in place for clinical governance, consent and audit by the LHN(s).
Credentialing and Competency	The iStent inject procedure should only be done by clinicians with specific training in the procedure. The clinician(s) should be appropriately credentialed and approved by the SA Health Credentialing and Scope of Practice Committee to implant the iStent inject (refer to paragraph 3.4.3 New Clinical Procedures, Technologies and Treatments of the SA Health Credentialing Policy Directive).
CONSISTENCY WITH EXPECTED SOCIETAL/ ETHICAL/ LEGAL VALUES	
Values	Consistent with expected societal, ethical and legal values at this time.
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