# Proposal for the Introduction of New Health Technologies within the Specialist Health Service

## Important information – look at this first!

- Submitted proposals for national method assessments will be published in full. If the proposer thinks information necessary for filling out the form cannot be published, contact the secretariat (Nye Metoder) before submission.

  The proposer is aware that the form will be published in its entirety (tick): ☒

- Proposer has filled out point 17 below "Interests and, if any, conflicts of interest »(tick):☒
- This form is used to submit proposals for technology assessment at the national level in Nye Metoder. The form does not apply to proposals for research projects. A technology assessment is a type of knowledge summary, and for this to be possible, documentation is required, for example, from completed clinical studies. Lack of documentation may be one of the reasons why the Ordering Forum RHF does not assign a methodological assessment.
- If the proposal concerns a medical device, the proposer is familiar with the document «Guidance criteria for management of medical devices in the National System for Managed Introduction of New Health Technologies within the Specialist Health Service in Norway (Nye Metoder) « (link) (tick): ☒

## Contact information:

**Name of proposer** (organization / institution / company / manufacturer):

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| Glaukos Corporation |

**Contact Name:**

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**Date and Place:**

| |
|---|
| 21 June 2018 London UK |

1. Proposer's title on the proposal: *
   *This can be changed in the future as the process advances

| |
|---|
| Trabecular bypass micro-invasive glaucoma surgery (MIGS) device implantation with iStent *inject* in patients with primary open-angle glaucoma, pseudoexfoliative glaucoma or pigmentary glaucoma. |

2. Brief description of the technology proposed to be considered:

The iStent *inject* is intended to reduce intraocular pressure safely and effectively in patients diagnosed with primary open-angle glaucoma, pseudoexfoliative glaucoma or pigmentary glaucoma. The iStent *inject* can deliver two (2) stents on a single pass, through a single incision. The implant is designed to stent open a passage through the trabecular meshwork to allow for an increase in the facility of outflow and a subsequent reduction in intraocular pressure. The device is safe and effective when implanted in combination with cataract surgery in those subjects who require intraocular pressure reduction and/or would benefit from glaucoma medication reduction. The device may also be implanted in patients who continue to have elevated intraocular pressure despite prior treatment with glaucoma medications and conventional glaucoma surgery.

3. Brief description of **current standard of care (SOC)** (Which technologies(s) are currently used? Status of the technologies (whether it provide curative treatment, extended life, etc.) Will the proposed technology replace or supplement today's SOC?

The objective of glaucoma management is to provide a significant and sustained decrease in intraocular pressure (IOP) which minimises the risk of progression (i.e. visual field loss) and preserves a patient's quality of life. All glaucoma treatments have potential side effects or complications. Thus, when making the choice of a treatment or providing additional treatment, the overriding consideration must be to minimise the risks and maximise the benefits to patients. Current therapies for lowering IOP are pharmacotherapy, laser surgery, and incisional glaucoma surgery.

For the majority of patients, topical medications are used as first-line therapy in glaucoma. However, medications are not suitable for some patients due to challenges adhering to difficult regimes, difficulties with administration and side effects that may create significant hurdles to achieve adequate control of eye pressure. Non-adherence is a concern in managing IOP. Recent research has shown that up to 90% of patients after 12 months in the United States are noncompliant to their medication[1]. Non-adherence can result in large IOP fluctuations, which are associated with an increased risk for vision loss.

For patients with OAG whose medications are ineffective at maintaining target IOP or who are having difficulty adhering to their medication regimen, Selective Laser Trabeculoplasty (SLT) is often considered as an adjunct or next line of therapy. The technique uses a laser to initiate cellular and biochemical changes in the trabecular meshwork to increase aqueous outflow. Although the procedure can provide a clinically significant reduction of IOP[2] the long-term results are questionable, as failure rates have been reported to be as high as 68-74%[3]. At 1 year many patients must restart the same number of medications as before and within 5 years 30% to >50% of eyes require additional surgical treatment[4].

Trabeculectomy is an established incisional surgery that reduces pressure within the eye and thereby reduces the risk of progressive glaucoma-related sight loss. While trabeculectomy surgeries can achieve lower eye pressures with less chance of progression and less chance of needing on-going medical treatment, there are considerable risks associated with incisional procedures which is why they are reserved for refractory cases.

In patients who require cataract surgery, iStent *inject* implantation will be positioned early in the management algorithm, for patients who require IOP reduction and/or would benefit from glaucoma medication reduction. The primary comparator to iStent *inject* implantation for glaucoma patients with a cataract co-morbidity is cataract surgery with continued management of IOP with medication.

iStent *inject* implantation as a stand-alone procedure will be positioned in patients who continue to have elevated IOP despite prior treatment with glaucoma medications and conventional glaucoma surgery, such as SLT. In this population, iStent *inject* implantation will provide continuing treatment to glaucoma patients whose disease severity does not yet warrant invasive incisional surgeries. The net impact will therefore be to delay those invasive surgeries and their associated safety concerns.

1. Nordstrom BL, Friedman DS, Mozaffari E, Quigley H a, Walker AM. Persistence and adherence with topical glaucoma therapy. Am J Ophthalmol. 2005;140:598-606. doi:10.1016/j.ajo.2005.04.051.
2. Ederer F, et al. The Advanced Glaucoma Intervention Study (AGIS) 13. Comparison of treatment outcomes within race: 10 year results. Ophthalmology. 2004;111:651-664.
3. Song J, et al. J Glaucoma. 2005;14:400-408.
4. Glaukos iStent® Product Monograph https://www.accessdata.fda.gov/cdrh_docs/pdf8/P080030c.pdf

| 4. What does the proposal concern? | Yes | No |
|---|---|---|
| A brand new and innovative technology? | ☒ | ☐ |
| A new application, or a new indication for an established method? | ☐ | ☒ |
| A comparison between several methods? | ☐ | ☒ |
| Is the technology already in use? | ☒ | ☐ |
| If yes – technology used in clinical practice? | ☒ | ☐ |
| If yes – technology used in research/testing? | ☐ | ☒ |
| Re-evaluation of technology used in clinical practice? | ☐ | ☒ |
| Is the technology relevant to be phased out? | ☐ | ☒ |

No

5. What does the technology involve (Multiple ticks offs possible)?

| | |
|---|---|
| Pharmaceutical | ☐ |
| Medical device/IVD medical device that is CE-marked* | ☒ |

* If the technology is CE marked: What is it CE marked as and for which indication?

CE Marking Approved (0086)

The iStent *inject* is intended to reduce intraocular pressure safely and effectively in patients diagnosed with primary open-angle glaucoma, pseudoexfoliative glaucoma or pigmentary glaucoma. The iStent *inject* can deliver two (2) stents on a single pass, through a single incision. The implant is designed to stent open a passage through the trabecular meshwork to allow for an increase in the facility of outflow and a subsequent reduction in intraocular pressure. The device is safe and effective when implanted in combination with cataract surgery in those subjects who require intraocular pressure reduction and/or would benefit from glaucoma medication reduction. The device may also be implanted in patients who continue to have elevated intraocular pressure despite prior treatment with glaucoma medications and conventional glaucoma surgery.

| | |
|---|---|
| Medical device/IVD medical device that is <u>not</u> CE-marked | ☐ |
| Procedure | ☐ |
| Screening | ☐ |
| Highly specialized services / national offers | ☐ |
| Organizational setup of the health service | ☐ |
| Other (describe) | ☐ |

Not applicable

6. Application of the technology:

| | |
|---|---|
| Prevention | ☒ |
| Assessment and diagnostics | ☐ |
| Treatment | ☒ |
| Rehabilitation | ☐ |
| Specialist health care | ☒ |
| Primary health care | ☐ |

NA

7. Responsibility for funding

| | Yes | No |
|---|---|---|
| Does the specialized health service currently have responsibility for financing the technology today? | ☐ | ☒ |
| Is the specialized health service going to be responsible for funding the technology? | ☒ | ☐ |

NA

8. Is the technology discussed in the national guidelines or action plans prepared by the Directorate of Health?

No

9. Does the technology involve the use of radiation (ionizing/non-ionizing)?

| Yes | No |
|---|---|
| ☐ | ☒ |

NA

10. Which discipline(s) apply to the technology and which patients are affected? (Does the technology possible also affect other groups (like personnel or relatives?)

Glaucoma and cataract surgeons.

Same as cataract and glaucoma surgery: After the procedure, patient will require someone to drive patient home.

11. Which aspects are relevant to the assessment? (multiple tick-offs possible)

| | |
|---|---|
| Clinical effect | ☒ |
| Safety/Adverse effects | ☒ |
| Costs/resource use | ☒ |
| Cost-effectiveness | ☒ |
| Organizational consequences | ☐ |
| Ethical | ☐ |
| Legal | ☐ |

12. Suggest the main research question/objective for the technology assessment, as well as secondary research questions/objectives (in compliance with question 10). For those familiar with "PICO" (Patient, Intervention, Comparator, Outcome) – please include tentative suggestions for PICO

**Objective:** To assess the clinical effectiveness and cost-effectiveness of iStent *inject* for the treatment of primary open-angle glaucoma, pseudoexfoliative glaucoma or pigmentary glaucoma.

**Patients:** Patients diagnosed with primary open-angle glaucoma, pseudoexfoliative glaucoma or pigmentary glaucoma at the time of cataract surgery or as a standalone procedure

**Intervention:**

**1)** In patients in need of cataract surgery: iStent *inject* in combination with cataract surgery
**2)** In patients not in need of cataract surgery: iStent *inject* as standalone treatment

**Comparators:**

**1)** In patients in need of cataract surgery: Cataract surgery alone
**2)** In patients not in need of cataract surgery: Standard of care (glaucoma medications)

**Outcomes:** Reduction in intraocular pressure (IOP) leading to a delay in loss of visual field Reduction in medication use, reduction in secondary surgery (trabeculectomy), Quality Adjusted Life Year (QALY)

13. Give a brief explanation of why it is important that the technology assessment proposed should be conducted.

Glaucoma refers to a group of diseases in which there is progressive damage of the optic nerve. It effects approximately 60 million people worldwide and is the second leading cause of blindness globally.[1] Open-angle glaucoma (OAG), the most common form of glaucoma. It is a chronic, degenerative optic neuropathy characterized by progressive visual impairment due to damage to the optic nerve and retinal ganglion cells.[2,3] Patients diagnosed with both OAG and cataract are considered a distinct patient population within ophthalmology. Coexistent cataract and OAG is common and found primarily in the elderly population. The incidence of both OAG and cataract increases sharply with age, and these conditions are both relatively common in the elderly population.[4]

Patients with mild glaucoma may be asymptomatic, but as the disease progresses, difficulties may occur with peripheral vision. In its most severe form, glaucoma results in irreversible blindness.[5] Visual impairment may affect activities of daily living (e.g., driving, walking, and reading) and may decrease QoL and health-related quality of life (HRQoL). Vision loss may also impose a psychological burden on patients owing to fear of blindness, social withdrawal, and depression.

Treatment of OAG incurs substantial annual costs that usually increase over time as the disease progresses. Direct medical costs include medication(s), physician and hospital visits, and glaucoma-related procedures; direct nonmedical costs include transportation, guide dogs, and nursing home care.[6] Indirect costs reflect lost productivity, such as days missed from work, and the productivity costs borne by caregivers such as family members and friends.

iStent *inject* is intended to reduce IOP and the subsequent risk of glaucoma disease progression is thereby reduced. The use of glaucoma medication may also be reduced. The reduction of the medication burden in patients who are intolerant to medication or the preservatives used therein, may improve compliance and improve patient's quality of life. A decrease in disease progression may achieve a delay in the need for invasive incisional surgery such as trabeculectomy, which is associated with high complication rates and may also preserve vision.

*1. Quigley HA, Broman AT. The number of people with glaucoma worldwide in 2010 and 2020. Br J Ophthalmol. 2006;90(3):262-267. doi:10.1136/bjo.2005.081224.*
*2. Quigley HA. Glaucoma. Lancet. 2011;377(9774):1367-1377. doi:10.1016/S0140-6736(10)61423-7.*
*3. Kwon YH, Fingert JH, Kuehn MH, Alward WL. Primary open-angle glaucoma. N Engl J Med. 2009;360(11):1113-1124. doi:10.1056/NEJMra0804630.*
*4. iStent Product Monograph. Laguna Hills, California: Glaukos Corporation; 2012.*
*5. Boland MV, Ervin AM, Friedman D, et al. Treatment for Glaucoma: Comparative Effectiveness. Rockville, MD: Agency for Healthcare Research and Quality; 2012.*
*6. Varma R, Lee PP, Goldberg I, Kotak S. An assessment of the health and economic burdens of glaucoma. Am J Ophthalmol. 2011;152(4):515-522. doi:10.1016/j.ajo.2011.06.004.*

14. Comment the technology that is proposed to be assessed with regards to the following points:

The severity of the disease/condition the technology targets

Trabecular bypass micro-invasive glaucoma surgery (MIGS) device implantation with iStent *inject* is intended for patients with mild-to-moderate open-angle glaucoma

Expected effect

**iStent *Inject* in combination with cataract surgery**

A 2-year phase III pivotal trial in patients with mild to moderate OAG on 1 to 3 medications undergoing cataract surgery were randomised to implantation with iStent *inject* (n = 387) or cataract surgery only (n = 118) was conducted.

- The primary endpoint was the proportion of eyes with ≥ 20% decrease in the 24-month medication-free mean diurnal intraocular pressure (DIOP) from baseline.
- The secondary endpoint was diurnal IOP reduction from baseline at Month 24. The diurnal IOP at 24 months for the subjects that did not meet criteria comparable to those listed above for the primary endpoint was imputed by the baseline IOP.

Both primary and secondary efficacy endpoints were achieved at 24 months. The findings from this study were presented at the American Society of Cataract and Refractive Surgery congress in Washington, D.C., US in April, 2018 and the manuscript with full results is in development.

The long-term open-label study (Arriola-Villalobos, 2016) in patients with mild to moderate OAG or ocular hypertension implanted with iStent *inject* in conjunction with cataract surgery demonstrated statistically significant differences in mean medicated IOP from medicated baseline and 1-year and 5-year mean IOP. Mean medicated IOP was reduced by 16.0% from medicated baseline (*P* = .001), and mean medication use decreased by 76.9% (*P* < .001) at 1-year postsurgery. Furthermore, 75.0% of patients (15 of 20 patients) were medication free.

**iStent *Inject* as a standalone procedure**

Fea, 2014 was a prospective, randomised trial in patients with OAG (including pseudoexfoliative and pigmentary) not controlled on one medication who underwent either implantation of two iStent *inject* devices (N=94) or received medical therapy (N=98) consisting of a FDC of latanoprost/timolol (or travoprost/timolol). Patients were followed for 1 year after treatment. Efficacy measures included percentage of subjects who achieved an IOP reduction ≥20% versus baseline unmedicated IOP, percentage of subjects who achieved an IOP ≤18 mmHg and mean reduction in IOP.

- At 12 months, 94.7% of eyes (89/94) in the iStent *inject* group reported an unmedicated IOP reduction ≥20% vs baseline unmedicated IOP, and 91.8% of eyes (88/98) in the medical therapy group reported an IOP reduction ≥20% vs baseline unmedicated IOP.
- A 17.5% between-group treatment difference in favor of the iStent *inject* group was statistically significant (P=0.02) at the >50% level of IOP reduction.

Safety (briefly describe known risk factors, safety aspects/concerns and side effects)

Trabecular micro-bypass stenting with iStent *inject* is both safe and well tolerated. In patients who were implanted with iStent *inject* in conjunction with cataract surgery, long-term safety evaluations (60 months) showed no adverse events as a result of the device or procedure (Arriola-Villalobos 2017)

In studies with iStent *inject* implantation without cataract surgery, the most frequently reported adverse events or observations in individual studies were elevated IOP and stent not visible upon gonioscopy (Fea 2014, Voskanyan 2014, Kalmann 2015); however, these were not consistent across all studies and were minimal. Complications were resolved with medications or surgical interventions. Some studies reported no complications during or after surgery.

The National Institute of Clinical Excellence (NICE) stated in its guidance (IPG575 2017) for trabecular stent bypass microsurgery for open angle glaucoma: *"Current evidence on trabecular stent bypass microsurgery for open angle glaucoma raises no major safety concerns."*

Total number of patients in Norway the technology is applicable to

It is estimated that 2,500 – 3,300 patients over the next 5 years will be eligible for iStent *inject*

Consequences for resource use in the health care sector

Reduced medications, reduced secondary surgeries and reduced follow-up appointments,

Delay in vision loss will improve quality of life and impact on depression and falls.

Need for revision of existing national guidelines or preparation of new guidelines

Yes - to include iStent *Inject* in Norwegian glaucoma treatment pathway

15. Provide references to documentation of the technology's effect and safety (i.e. previous technology assessments). (Up to 10 key references are provided, do not send attachments in this step of the process):


1. Australian MSAC TB MIGS Public Summary Document. **http://www.msac.gov.au/internet/msac/publishing.nsf/Content/65E78C5C907A914BCA2580DC007D64DD/$File/1483-Final-PSD.pdf**

2. UK NICE interventional procedures guidance on trabecular stent bypass microsurgery for open-angle glaucoma (IPG396). **https://www.nice.org.uk/guidance/ipg575**

3. American Academy of Ophthalmology Primary Open-Angle Glaucoma Preferred Practice Pattern(®) Guidelines. Prum BE, Lim MC, Mansberger SL, et al. Primary Open-Angle Glaucoma Suspect Preferred Practice Pattern® Guidelines. *Ophthalmology*. 2015;123(1):P112-P151. doi:10.1016/j.ophtha.2015.10.055.

4. Fea AM, Belda JI, Rekas M et al. Prospective unmasked randomized evaluation of the iStent Inject® versus two ocular hypotensive agents in patients with primary open-angle glaucoma. Clinical Ophthalmology 2014:8 875–882.

5. Arriola-Villalobos P, Martinez-de-la-Casa JM, Diaz-Valle D, Morales-Fernandez L, Fernandez-Perez C, and Garcia-Feijoo J. Glaukos iStent inject® trabecular micro-bypass implantation associated with cataract surgery in patients with coexisting cataract and open-angle glaucoma or ocular hypertension: a long-term study. Journal of Ophthalmology. 2016;2016:1056573. Epub 2016 Nov 1.


16. Provide the name of the manufacturer/supplier of the technology (if applicable/available):

Glaukos Corporation

17. Marketing Authorization Status (MAS) or CE-marking: When is MAS or CE marking expected? If possible provide the time of planned marketing:

CE Marking Approved (0086)

18. Additional relevant information (up to 300 words.)

19. Interests and potential conflicts of interests

Describe the proposers' relationship or activities that may affect, be influenced by, or perceived by others to be important for further management of the technology that is proposed evaluated (i.e. proposer has financial interests in the matter. Proposer has or had assignments in connection with the technology or players who have interests in the technology)

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|---|
| Glaukos Corporation, the manufacturer of iStent *inject* is the proposer |