INESSS
LE SAVOIR PREND FORME

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iStent® and iStent *inject*® Trabecular Bypass for Micro-invasive Glaucoma Surgery (MIGS)

English summary

Une production de l'Institut national d'excellence en santé et en services sociaux (INESSS)

Direction des services de santé et de l'évaluation des technologies

Québec

SUMMARY

Mandate

iStent® and iStent *inject*® trabecular bypasses are provided to patients with open angle glaucoma. However, access to such devices remains limited in the Quebec health system. The *Institut national d'excellence en santé et en services sociaux* (INESSS), at the request of the *Bureau de l'innovation*, assessed the pertinence of increasing access to public coverage for those devices.

Methods

To carry out this mandate and supplement the information provided by the manufacturer, INESSS conducted a systematic research of scientific literature on iStent® and iStent *inject*® trabecular bypasses. This research was complemented by a review of grey literature, contextual and experiential data gathered through consultations with an expert committee and Foundation Fighting Blindness Canada as well as the information retrieved from clinical administrative data from Quebec government databases. A model-based cost-utility analysis was conducted to evaluate the cost effectiveness of iStent® and iStent *inject*® in the perspective of the Quebec health system. Also, the potential budgetary impact of an increased access to those devices for a period of three (3) years was also performed.

Health needs

Glaucoma is described as an evolving chronic optic neuropathy that leads to irreversible visual field loss and, in certain cases, to blindness. Glaucoma is the second leading cause of blindness after cataract. Primary open-angle glaucoma (POAG) is the most common form of glaucoma. Since the incidence of glaucoma and cataract increases with age, these conditions often appear together in the elderly population. Even if glaucoma is a chronic disease, early detection and treatment can slow down its progression.

The treatment strategy aims at reducing intraocular pressure (IOP) - the easiest modifiable risk factor. IOP is the net result of aqueous humor formation in the eye and its elimination through trabecular meshwork or trabeculum. The continuum of care now being used is usually implemented in a gradual manner until the target IOP is attained. In general, medication administered at the primary level of care is followed by laser treatment. Filtration surgery – a more invasive last-line procedure – can lead to severe complications, but few patients undergo this type of intervention.

To achieve the IOP target, it is important to adhere to the pharmacotherapy treatment. But self-administration of eye drops can prove difficult for some patients (for instance, due to limitations in terms of prehension and precision, adverse effects, etc.), thus leading to lower adherence to the treatment plan. Additional therapeutic alternatives that make it possible to postpone and, in some cases, avoid the necessity to undergo more invasive surgery to attain the target IOP would be desirable.

iStent® and iStent *inject*® - Context of use

iStent® and iStent *inject*® trabecular bypasses are implantable devices designed to improve physiological aqueous humor flow through the trabecular meshwork and reduce the patient's IOP. They were approved by Health Canada in 2009 and 2015 respectively. In Canada, the use of iStent® is indicated for the management of early to moderate POAG in patients treated with hypotensive medication and undergoing cataract surgery. iStent *inject*® implantation can be used for patients suffering POAG or secondary pseudo exfoliative or pigment dispersion glaucoma and undergoing or not cataract surgery. It is common practice to combine implantation of two devices per eye with cataract surgery (phacoemulsification or phaco). According to the experts consulted, this practice would allow a reduction in surgery risk and joint and effective mobilization of medical resources.

Results – Effectiveness, safety and quality of life

To appreciate the therapeutic value of iStent® and iStent *inject*® devices, four randomized controlled studies (RCT) were selected. Separate studies were conducted for both devices, each including the following interventions and comparators, i.e.:

- Implantation of two devices per eye and phacoemulsification (phaco[1]) vs. phacoemulsification alone;
- Implantation of two devices per eye w/o phaco vs. pharmacotherapy.

In both groups, the patients who underwent intervention and cataract surgery required less medication after their surgery. The use of less medication by the control group could be explained by the hypotonic capacity of phacoemulsification. When compared 23 months after surgery, a reduction of 0,4 medication to maintain the target IOP was observed for the patients who received the device. After a 60-month follow-up period on the patients who underwent implantation alone (without phaco), nearly 80% of those who received two iStent® devices did not require medication to maintain their target IOP. On the other hand, 40% of the patients in the control group in pharmacotherapy required a second medication.

With the data available, however, it was not possible to point out the effects on visual acuity and visual field and the use of more invasive interventions. This will require long-term follow-up data. Moreover, none of the RCTs evaluated the patients' quality of life, despite the fact it is an important determinant in estimating the value of this technology. With respect to post-implantation innocuity, the results reveal a moderate number of adverse events – of low severity in most cases – similar to that observed in patients undergoing cataract surgery.

It is important to remember that the RCT specifications analysed have some weaknesses, particularly in terms of random allocation of participants (randomization), patient selection, and measurement of medication and IOP parameters. It is noteworthy to mention, however, that it may be difficult to mask surgical interventions. Interpretation

1. Specific procedure used in cataract surgery. It consists in emulsifying the blurred crystalline lens by performing an incision in the cornea and replacing it *ab interno* with an ocular implant.

of RCT results must also consider the controlled setting during clinical tests in which patients participate on a volunteer and cooperative basis. The level of adherence to treatment provided in a clinical context may differ in an actual healthcare context.

Cost utility analysis

This economic evaluation concluded to an incremental cost-utility ratio (ICUR) of approximately CAN$112,000/QALY (*quality-adjusted life year)* when two devices are used concurrently with phacoemulsification vs. phacoemulsification alone – implantation and phacoemulsification performed together is common practice for the use of these devices (more than 89% of the cases). Regarding the comparison between the implantation of two devices without phacoemulsification vs. pharmacotherapy, the ICUR is about CAN$26,000/QALY. This result must be qualified, for its absence of planned phacoemulsification surgery over a relevant time-horizon of 15 years. Moreover, it is important to stress that the estimated gain in QALY is quite low.

Considering the short follow-up period for RCTs and the potential for bias in the studies available, there remains uncertainty as to whether the lower IOP level and reduction in medication intake can be maintained over time. In a scenario where benefits would not last beyond the follow-up data available, the ICUR could rise to as much as CAN$503,000/QALY (w. phaco) and to as much as CAN$111,000/QALY (w/o phaco).

Potential budget impact

According to the base scenario used for the budget impact analysis (BIA) conducted by the INESSS, access to public coverage for those devices for patients with POAG may lead to an estimated budget cost increase of some CAN$29 M in the first three (3) years.

In scenarios where the market shares of the devices vary from 1% to 100% in patients with POAG necessitating cataract surgery, the budget cost increase over a time-horizon of three (3) years would range from CAN$4,9 M to CAN$95,8 M respectively vs the case of no access to public coverage.

SUMMARY OF THE DECISIONS AND RECOMMENDATIONS

In the light of the available data, the members of the comité d'excellence clinique en santé (CEC – santé) recognize the therapeutic value of iStent® and iStent *inject*® devices. However, the cost/benefit ratio is considered to be too high and uncertain. The members feel that public coverage for iStent® and iStent *inject*® devices at the proposed price would not be a fair allocation of the Quebec health system's resources.

Reasons for the members' unanimous position

- iStent® and iStent *inject*® devices are already being used by the Quebec health system as complementary treatment in the glaucoma care continuum.
- The members have recognized that the efficiency results of these devices show a reduction in pharmacotherapy once the target IOP is attained. However, the results indicate that the magnitude of clinical benefits seems modest and difficult to determine because of the low level of evidence.
- Overall, the safety of the devices seems acceptable and their adverse events considered to be minor.
- The incremental cost-utility ratio was deemed to be high and present a wide margin of uncertainty.
- However, the committee members recognized that some patients whose health needs remain unmet could benefit from these devices.
- The members recognize the importance to determine the place of these devices in the continuum of care for primary open-angle glaucoma for optimal use.

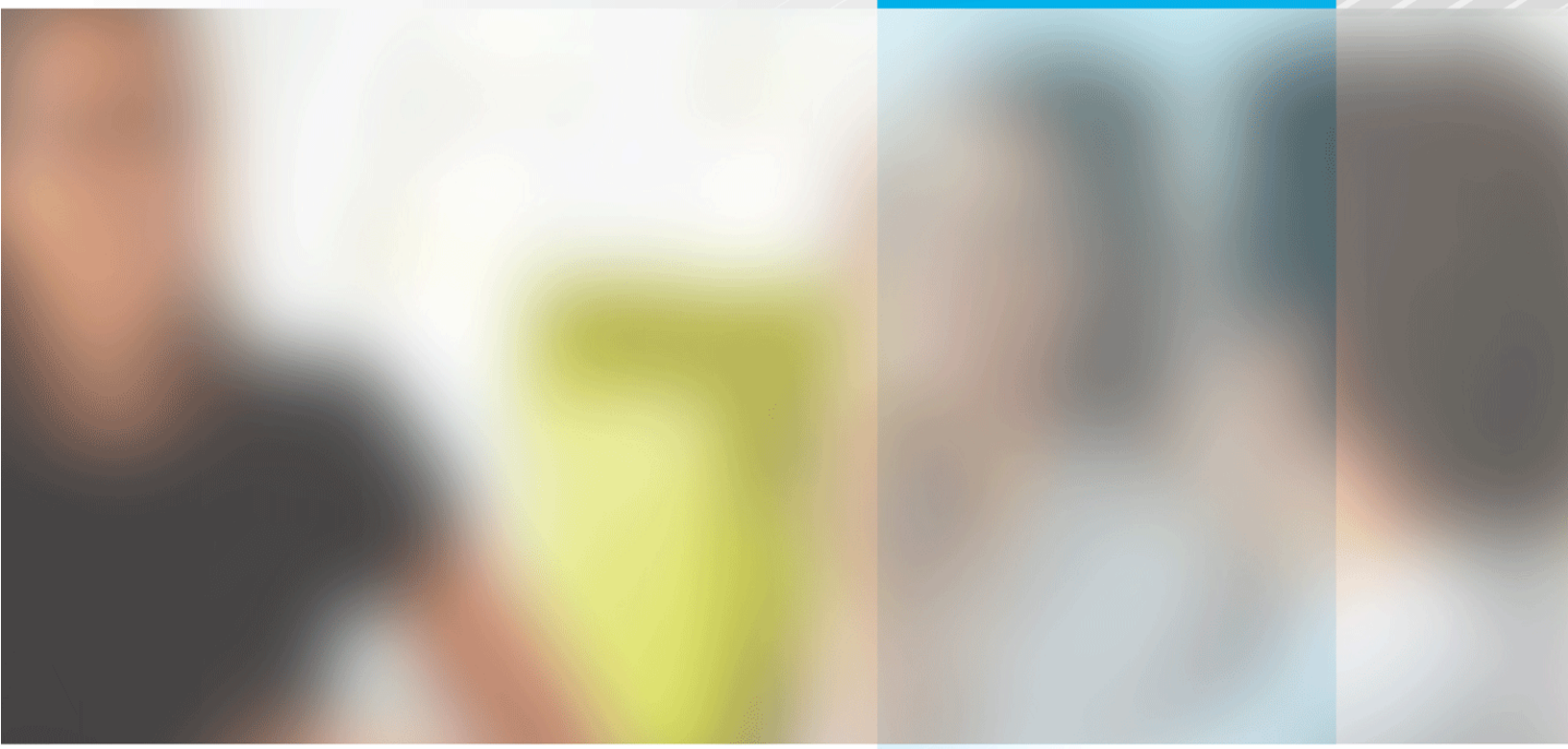
RECOMMENDATIONS

The Institut national d'excellence en santé et en services sociaux (INESSS) is of the opinion that a decision in favour of public coverage of iStent® and iStent *inject*® trabecular bypasses would be fair and reasonable if significant measures to reduce the cost were implemented and their use governed by the following criteria:

- Patients who do not respond to at least two (2) hypotonic drugs or with a documented medical condition that prevent optimal administration of eye drops.
- Poor candidates for filtration surgery.

Other considerations

1. Considering the uncertainties in terms of therapeutic value and cost-effectiveness, access to this service should be re-evaluated in light of new available data. The suggested time-horizon for a re-evaluation is three (3) years.
2. Any extension of the proposed criteria should only come to fruition in an evidence development context with the financial support of the manufacturer.



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