CADTH

CADTH COMMON DRUG REVIEW

CADTH Canadian Drug Expert Committee Recommendation

(Final)

Travoprost 0.003% (Izba — Novartis Pharmaceuticals Canada Inc. on behalf of Alcon Canada Inc.)
Indication: For the reduction of elevated intraocular pressure in patients with open-angle glaucoma or ocular hypertension.

RECOMMENDATION:

The CADTH Canadian Drug Expert Committee (CDEC) recommends that travoprost 0.003% preserved with polyquaternium-1 (PQ) be reimbursed for the reduction of elevated intraocular pressure (IOP) in patients with open-angle glaucoma (OAG) or ocular hypertension (OHT), if the following condition is met:

Condition:
The drug plan cost of treatment with travoprost 0.003% PQ should not exceed the drug plan cost of treatment with the least costly alternative prostaglandin analogue (PGA).

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Redactions: Confidential information in this document has been redacted at the request of the manufacturer in accordance with the *CADTH Common Drug Review Confidentiality Guidelines.*

About CADTH: CADTH is an independent, not-for-profit organization responsible for providing Canada's health care decision-makers with objective evidence to help make informed decisions about the optimal use of drugs, medical devices, diagnostics, and procedures in our health care system.

Funding: CADTH receives funding from Canada's federal, provincial, and territorial governments, with the exception of Quebec.

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Recommendation:

The CADTH Canadian Drug Expert Committee (CDEC) recommends that travoprost 0.003% preserved with polyquaternium-1 (PQ) be reimbursed for the reduction of elevated intraocular pressure (IOP) in patients with open-angle glaucoma (OAG) or ocular hypertension (OHT), if the following condition is met:

Condition:

The drug plan cost of treatment with travoprost 0.003% PQ should not exceed the drug plan cost of treatment with the least costly alternative prostaglandin analogue (PGA).

Reasons for the Recommendation:

1. One double-blind randomized controlled trial (RCT; Study C-11-034) concluded that travoprost 0.003% PQ was as effective as travoprost 0.004% preserved with benzalkonium chloride (BAC) in reducing mean IOP at two weeks, six weeks, and 12 weeks based on three assessments per day (8 a.m., 10 a.m., and 4 p.m.) and based on equivalence margins of ± 1.5 mm Hg and ± 1.0 mm Hg. The frequency and type of adverse events were similar for travoprost 0.003% PQ and travoprost 0.004% BAC, with the most common adverse event being ocular or conjunctival hyperemia (ranging 5.7% to 7.0% with travoprost 0.003% PQ and 7.1% to 8.1% with travoprost 0.004% BAC). A price premium compared to available PGAs in Canada is not justified as there is no evidence of any advantage to support first-line use of travoprost 0.003% PQ over other agents.

Of Note:

The BAC-preserved product is not marketed in Canada. BAC has been associated with a higher incidence of hyperemia than other preservatives. It is unknown how the safety profile of travoprost 0.003% PQ compares with travoprost 0.004% preserved with a proprietary buffered preservative system (SofZia), which is the formulation currently available in Canada. It is also unknown whether this formulation would be better tolerated in those who are unable to tolerate travoprost 0.004% preserved with SofZia.

Background:

Izba (travoprost 0.003% PQ) has a Health Canada indication for the reduction of elevated IOP in patients with OAG or OHT. It is an eye-drop solution containing 30 mcg of travoprost per millilitre of solution, preserved with PQ. It has the same therapeutic indication, contains a reduced concentration of active substance, and has a different preservative than the travoprost 0.004% solutions currently marketed in Canada. The Health Canada approved dose is one drop in the affected eye(s) once daily.

Summary of CDEC Considerations:

The Committee considered the following information prepared by the CADTH Common Drug Review: a systematic review of RCTs of Izba (travoprost 0.003% PQ) and a critique of the manufacturer's pharmacoeconomic evaluation.

Patient Input

No patient input was received for this submission.

Clinical Trials

The systematic review included one equivalence double-blind RCT (Study C-11-034) of patients with OAG or OHT (N = 864). In the study, patients were randomly assigned (1:1) to travoprost 0.003% PQ (n = 442) or travoprost 0.004% preserved with BAC (n = 422). Both medicines were given as one drop in the affected eye once a day, in the evening, for three months. The primary objective of this study was to demonstrate that the IOP-lowering efficacy of travoprost 0.003% PQ is equivalent to travoprost 0.004% BAC in patients with OAG or OHT. The primary efficacy end point in the study was the mean IOP (measured in mm Hg). Equivalence was concluded if the two-sided 95% confidence interval for the difference in mean IOP (travoprost 0.003% PQ group minus travoprost 0.004% BAC group) was within 1.5 mm Hg at each of the three time points (8 a.m., 10 a.m., and 4 p.m.) for each on-therapy visit (week 2, week 6, and month 3). A more stringent equivalence margin of ± 1.0 mm Hg was used in the equivalence testing. A key limitation of Study C-11-034 is that equivalence was determined versus BAC-preserved travoprost 0.004% instead of the SofZia-preserved travoprost 0.004% formulation available in Canada.

Outcomes

Outcomes were defined a priori in the CADTH Common Drug Review (CDR) systematic review protocol. Of these, the Committee discussed the following: changes in IOP, visual field loss as measured through best corrected visual acuity using the Early Treatment Diabetic Retinopathy Study scale, hyperemia, serious adverse events, total adverse events, and withdrawal due to adverse events. The primary outcome in Study C-11-034 was the mean IOP at week 2, week 6, and month 3, measured for each assessment time point (8 a.m., 10 a.m., and 4 p.m.). Quality-of-life outcomes were not reported in Study C-11-034.

Efficacy

The on-treatment IOP values in the intention-to-treat population were similar between the travoprost 0.003% PQ and travoprost 0.004% BAC groups for all on-therapy study visits and assessment time points. In patients taking travoprost 0.003% PQ, the average IOP (measured at 8 a.m.) was 19.4 mm Hg, 19.3 mm Hg, and 19.2 mm Hg, following two weeks, six weeks, and three months on treatment. The results were similar in patients taking travoprost 0.004% BAC (19.5 mm Hg, 19.3 mm Hg, and 19.3 mm Hg). The least squares mean differences between treatment groups ranged from –0.3 mm Hg to 0.0 mm Hg, with confidence intervals ranging from –0.7 mm Hg to 0.4 mm Hg. Equivalence was met, as all nine of the assessments had confidence intervals entirely within the pre-specified ± 1.5 mm Hg margin. Further, all nine of the assessments had confidence intervals that were entirely within a ± 1.0 mm Hg margin.

The differences from baseline in best corrected visual acuity were assessed as a safety variable in Study C-11-034. In the travoprost 0.003% PQ group, [redacted] of patients had an increase, [redacted] had no change, and [redacted] had a decrease in their visual acuity score. In the travoprost 0.004% BAC group, the respective proportions were [redacted].

Harms (Safety and Tolerability)

The safety profiles of travoprost 0.003% PQ and travoprost 0.004% BAC were similar. The most common adverse event reported during the study was hyperemia of the eye (ocular or conjunctival). A numerically lower incidence of hyperemia was observed in travoprost 0.003% PQ group than in travoprost 0.004% BAC group (ocular hyperemia: 7.0% versus 8.1% and conjunctival hyperemia: 5.7% versus 7.1%, respectively), but absolute differences were small.

Cost and Cost-Effectiveness

Travoprost 0.003% PQ is available as a topical ophthalmic solution administered as one drop in the affected eye(s) per day for the treatment of elevated IOP in adult patients with OAG or OHT. The manufacturer submitted a market price of $20.13 per 5 mL bottle.

The manufacturer submitted a cost comparison of travoprost 0.003% PQ with travoprost 0.004% in a primary analysis and travoprost 0.003% PQ with other PGAs (latanoprost 0.005%, bimatoprost 0.01%, and bimatoprost 0.03%) in a secondary analysis. The analyses were conducted over a one-year time horizon from the perspective of the Canadian public health care payer. The assumption of clinical equivalency between travoprost 0.003% PQ and travoprost 0.004% was based on an RCT (Study C-11-034), while similar efficacy and safety of travoprost 0.004% and other PGAs were based on a published network meta-analysis and head-to-head RCTs; this assumption of similarity was assumed to extend to travoprost 0.003% PQ through Study C-11-034. The manufacturer considered drug acquisition costs, as well as pharmacy markup and dispensing fees. Drop volume was based on one

published study, and all medications were administered once daily in both eyes. The manufacturer reported that travoprost 0.003% PQ was similar in cost to travoprost 0.004%, and less expensive than latanoprost and bimatoprost.

CDR identified several key limitations with the manufacturer's economic submission. Firstly, there is uncertainty in the assumption of clinical similarity with the relevant comparators, given that the form of travoprost 0.004% in the RCT is not used in Canada (BAC-preserved travoprost 0.004%). As well, a naive indirect comparison was used to compare travoprost 0.003% PQ with bimatoprost and latanoprost, which is not appropriate, as published evidence indicates travoprost 0.004% may be associated with more adverse events than latanoprost. Uncertainty exists about the number of doses per bottle, as noted in several studies of drop and bottle volume, which may result in differences in the number of drops per bottle and affect cost assumptions. Additionally, the economic submission included pharmacy markup and dispensing fees, which differ among provinces.

CDR considered an analysis that excluded pharmacy markup and dispensing fees and assumed equivalent drop volume (0.030 mL) for all treatments and clinical similarity (effects and harms). At the submitted price, travoprost 0.003% PQ ($101 in year 1) is equivalent in cost to travoprost 0.004% and is cost-saving relative to bimatoprost ($230 to $290 in year 1), but is more costly than latanoprost ($86 in year 1). Based on the price per mL, a 4.8% reduction in price for travoprost 0.003% PQ is required for it to be similar in cost to latanoprost 0.005%. If dispensing fees and markups are considered, travoprost 0.003% PQ may be less costly than latanoprost in certain circumstances. CDR noted there is substantial variability regarding the comparative drop volume, which affects the number of drops per bottle and the relative cost of treatment. The uncertainty in drop volume led CDR reviewers to assume equivalence in drop volumes for all of travoprost 0.003% PQ and the comparators.

CDEC Members:

Dr. Lindsay Nicolle (Chair), Dr. James Silvius (Vice-Chair), Dr. Silvia Alessi-Severini, Dr. Ahmed Bayoumi, Dr. Bruce Carleton, Mr. Frank Gavin, Dr. Peter Jamieson, Dr. Anatoly Langer, Mr. Allen Lefebvre, Dr. Kerry Mansell, Dr. Irvin Mayers, Dr. Yvonne Shevchuk, Dr. Adil Virani, and Dr. Harindra Wijeysundera.

July 19, 2017 Meeting

Regrets:

None

October 18, 2017 Meeting

Regrets:

Two CDEC members could not attend the meeting.

Conflicts of Interest:

None