CADTH

CADTH COMMON DRUG REVIEW

Pharmacoeconomic Review Report

TRAVOPROST 0.003% (IZBA)

(Novartis Pharmaceuticals Canada Inc. on behalf of Icon Canada Inc.)

Indication: The reduction of intraocular pressure in patients with open-angle glaucoma or ocular hypertension.

Service Line:	CADTH Common Drug Review
Version:	Final
Publication Date:	November 2017
Report Length:	18 Pages

CADTH

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.

CADTH

Table of Contents

Abbreviations

BAC	benzalkonium chloride
CDR	CADTH Common Drug Review
CMA	cost-minimization analysis
IOP	intraocular pressure
OAG	open-angle glaucoma
ODB	Ontario Drug Benefit
PGA	prostaglandin analogue
PQ	polyquaternium-1

Drug	travoprost 0.003% ophthalmic solution (Izba)
Indication	The reduction of elevated intraocular pressure in patients with open-angle glaucoma or ocular hypertension.
Reimbursement request	As per indication
Dosage form(s)	Topical ophthalmic solution — one drop in the affected eye(s) once daily.
NOC date	23-09-2016
Manufacturer	Novartis Pharmaceuticals Canada, Inc. on behalf of Alcon Canada Inc.

Summary

Background

Polyquaternium-1–preserved travoprost 0.003% ophthalmic solution (Izba, travoprost 0.003% PQ) is a prostaglandin analogue (PGA) indicated for the reduction of intraocular pressure (IOP) among patients with open-angle glaucoma (OAG) or ocular hypertension.[1] Travoprost 0.003% PQ is available as a topical ophthalmic solution with a recommended dose of one drop in the affected eye(s) per day. The manufacturer is requesting reimbursement per indication and has submitted a market price of $20.13 per 5 mL bottle.

Summary of the Economic Analysis Submitted by the Manufacturer

The manufacturer submitted a cost comparison with the primary analysis assessing travoprost 0.003% PQ against travoprost 0.004% for the treatment of elevated IOP in adult patients with OAG or ocular hypertension.[2] Secondary analyses were conducted comparing travoprost 0.003% PQ with other PGAs (latanoprost 0.005%, bimatoprost 0.01%, and bimatoprost 0.03%). The manufacturer's analysis was conducted over a one-year time horizon from the perspective of the Canadian public health care payer. Costs included in the analysis consisted solely of drug acquisition costs (including pharmacy markup and dispensing fees). The manufacturer reported that travoprost 0.003% PQ was clinically equivalent, based on IOP lowering, to the currently available travoprost 0.004% formulations based on a phase III trial (C-11-034) comparing travoprost 0.003% PQ and benzalkonium chloride (BAC)-preserved travoprost 0.004%.[3] The assumption of similar efficacy and safety of travoprost 0.004% and other PGAs was informed by a published network meta-analysis[4] and head-to-head randomized controlled trials,[5-7] and this assumption of equivalence was extended to travoprost 0.003% PQ through study C-11-034. Drug prices were obtained from the Ontario Drug Benefit (ODB) Formulary for the comparators and from the manufacturer for the submitted product. While drug costs were based on doses recommended in the product monograph, frequency of administration and assumptions of drop volume were based on one published study.[8] All medications were

administered once daily, and treatment was assumed to be bilateral. In the manufacturer's base case, the cost of travoprost 0.003% PQ in year 1 was $152.85, including markup and dispensing fees, which is cost-neutral compared with travoprost 0.004%. Travoprost 0.003% PQ was $38.94 less expensive than latanoprost ($191.80), $139.53 less expensive than bimatoprost 0.03% ($292.38), and $204.93 less expensive than bimatoprost 0.01% ($357.78) in year 1 (Table 5).

Key Limitations

CADTH Common Drug Review (CDR) identified the following key limitations with the manufacturer's analysis:

Uncertainty in assumption of clinical similarity. The head-to-head trial comparing travoprost 0.003% PQ with travoprost 0.004% used a form of travoprost 0.004% that is not used in Canada. The currently available forms of travoprost 0.004% in Canada (branded and generics) use the preservative sofZia (boric acid, propylene glycol, sorbitol, and zinc chloride) instead of the preservative traditionally used (BAC), which can cause increased ocular irritation, inflammation, and hyperemia.[9,10] The impact of this difference in the comparator is uncertain. The assumption of equivalent effectiveness and safety between travoprost 0.003% PQ and bimatoprost or latanoprost was based on a naive indirect comparison, which is inappropriate. The indirect comparison[4] and one of the trials[6] cited by the manufacturer indicated that latanoprost produced fewer adverse events than travoprost 0.004%, a finding consistent with a previous CADTH rapid response comparing PGAs.[11] A higher incidence of hyperemia has been observed with travoprost 0.004% compared with latanoprost, which may affect patient compliance and thus overall effectiveness.[6,12] Previously published evidence has also suggested that bimatoprost may be more effective in lowering IOP than travoprost 0.004%, as reported in two of the clinical trials cited by the manufacturer[5,7] and CADTH's comparison of PGAs.[11] The uncertainty associated with the relative treatment effect and harms of travoprost 0.003% PQ could not be tested within the manufacturer's submitted cost-minimization analysis (CMA).

Uncertainty in number of doses per bottle. The manufacturer assumed different volume of solution supplied per drop (drop volumes) among comparator treatments, as informed by a published study[8] that measured the drop volume of branded travoprost 0.004% (Travatan and Travatan Z), bimatoprost 0.01% (Lumigan), and latanoprost 0.005% (Xalatan). The manufacturer assumed that the drop volume of generic and branded drugs was the same, and that the drop volume of travoprost 0.003% PQ was equivalent to that of travoprost 0.004%. Other published literature suggests that generic and branded travoprost[13] and latanoprost[14] have different drop volumes. Additional studies have found that drop volume is not standardized and can differ based on bottle size, dropper-tip diameter, and the physicochemical properties of the drop itself.[15-18] In particular, the latter may be expected to differ between travoprost 0.003% PQ and any of the travoprost 0.004% formulations based on differences in drug concentration and excipients, in addition to bottle and dropper-tip features. Further, studies (including the one used by the manufacturer to support its drop volume) have also noted that over-filling and under-filling bottles (relative to the reported volume) also occurs in practice.[8,19] Issues such as drop volume and over-filling and under-filling bottles ultimately determine the number of drops per bottle, and thus the number of bottles that are required annually. Published literature has also reported that the amount of drug contained in bottles (bottle size) did not predict the number of days between patient refills and that patients with larger bottles typically refilled sooner than drop-count studies had predicted.[20]

Inclusion of pharmacy markup and dispensing fees. Pharmacy markup and dispensing fees differ between provinces; thus, their inclusion and the assumption that Ontario values are generalizable to the other jurisdictions are not appropriate. The manufacturer undertook a sensitivity analysis of pharmacy markup and dispensing fees, and noted that the results are sensitive to the exclusion of a pharmacy markup and dispensing fees. Additionally, patients can receive multiple bottles at once; thus, assuming a dispensing fee for each bottle is unlikely to be an appropriate assumption. Latanoprost may require more claims annually than travoprost 0.003% PQ, leading to increased dispensing fees; however, this is likely to differ notably between provinces.

Issues for Consideration

Use in Canadian practice. The analyses were undertaken on the assumption that both eyes will be treated. If only one eye is treated, this will affect the magnitude of the incremental cost or cost savings.

Adherence and compliance in Canadian practice. Adherence and compliance have also been noted as potential issues with the use of these treatments in clinical practice. Perfect adherence was assumed in the CMA, which is unlikely to occur in clinical practice. Further, compliance with recommended administration for some of these treatments (e.g., different angles at which drops should be administered)[21] may not be observed in clinical practice.

Differential pricing of comparators among public drug programs. CDR noted that the published list prices differed among participating plans for the compared treatments; thus, the incremental costs or saving associated with travoprost 0.003% PQ may differ depending on the jurisdiction.

Feedback from the manufacturer indicated that the bottle currently used for travoprost 0.004% (Travatan Z) will be used for travoprost 0.003% PQ; however, the manufacturing process may result in variability in the number of drops per bottle between products.

Results/Conclusions

Given the identified limitations with the manufacturer's analysis, CDR considered the manufacturer's sensitivity analyses to be more appropriate. In these analyses, pharmacy markup and dispensing fees were excluded, and equivalent drop volume (0.030 mL) was assumed for all treatments (CDR reanalysis). In this analysis, travoprost 0.003% PQ ($100.65 in year 1) is equal in cost to travoprost 0.004% ($100.66 in year 1), cost-saving relative to bimatoprost ($230 to $290 in year 1), and more costly than latanoprost 0.005% ($86.25 in year 1) (Table 7). An additional scenario analysis was undertaken in which CDR assumed a drop volume of 0.035 mL for all treatments, which did not affect the direction of the results, but had a slight impact on the magnitude of the cost differences (Table 7).

If travoprost 0.004% is considered the appropriate comparator, no price reduction is required. If all PGAs (same drug class) are considered appropriate comparators, based on the CDR base case (combination of manufacturer sensitivity analyses) a 14% reduction in price for travoprost 0.003% PQ is required to be similar in cost to latanoprost 0.005% (Table 2); or a 4.8% price reduction based on treatment costs as derived by CDR.

When the assumptions of clinical similarity (effects and harms) and equivalent dose volume are considered appropriate, at the submitted price per bottle of $20.13, travoprost 0.003% PQ is equivalent in cost to travoprost 0.004% and is cost-saving relative to bimatoprost, but

is more costly than 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 uncertainty regarding the comparative drop volume, which affects the number of drops per bottle and the relative cost of treatments.

Cost Comparison

Clinical experts have deemed the comparator treatments presented in Table 1 to be appropriate. Comparators may be recommended (appropriate) practice versus actual practice. Comparators are not restricted to drugs but may be devices or procedures. Costs are manufacturer list prices, unless otherwise specified. Existing Product Listing Agreements are not reflected in the table and, as a result, costs given may not represent the actual costs to public drug plans.

Table 1: Cost Comparison Table for Travoprost 0.003% PQ

Drug / Comparator	Dosage Form	Strength	Price Per Bottle	Price ($/mL)	Recommended Dose	Cost Per Day ($)
Travoprost 0.003% (Izba)	**Ophthalmic solution**	**5 mL**	**$20.1300[a]**	**$4.03**	**One drop daily in each affected eye**	**$0.2301**
Prostaglandin Analogues						
Travoprost 0.004% (Travatan Z and generics)	Ophthalmic solution	5 mL	$20.1320	$4.03	One drop daily in each affected eye	$0.2301
Travoprost 0.004% (generics)	Ophthalmic solution	2.5 mL	$10.0660	$4.03	One drop daily in each affected eye	$0.2301
Latanoprost 0.005% (Xalatan and generics)	Ophthalmic solution	2.5 mL	$9.5830	$3.83	One drop daily in each affected eye	$0.2190
Bimatoprost 0.01% (Lumigan RC)	Ophthalmic solution	5 mL 7.5 mL	$58.0800 $87.1200	$11.62	One drop daily in each affected eye	$0.6638
Bimatoprost 0.03% (Vistitan)	Ophthalmic solution	3 mL 5 mL	$27.5808[b] $45.9680[b]	$9.19	One drop daily in each affected eye	$0.5253

Note: All prices are from the ODB Formulary (accessed May 12, 2017) unless otherwise indicated (price paid by the plan, not unit price) and do not include dispensing fees. It is assumed that both eyes are treated.

Note: An assumption was made that all drop sizes were the same across treatments (35 drops/mL).

[a] Manufacturer-submitted price.

[b] Calculated based on cost per millilitre reported by Ontario.

Appendix 1: Price-Reduction Analysis

Table 2: CADTH Common Drug Review (CDR) Price-Reduction Scenarios for Travoprost 0.003% PQ, CDR Reanalysis

Scenario	Current Cost of Travoprost 0.003% PQ	Current Cost of Comparator	Price Reduction Needed for Travoprost 0.003% PQ to Equal Comparator in Year 1
Price reduction needed to equal generic latanoprost 0.005%	$4.03	$3.45	14.3%
Price reduction needed to equal generic travoprost 0.004%	$4.03	$4.03	NA
Price reduction needed to equal bimatoprost 0.01%	$4.03	$11.62	NA
Price reduction needed to equal bimatoprost 0.03%	$4.03	$9.19	NA

NA = not applicable; PQ = polyquaternium-1.

Appendix 2: Reviewer Worksheets

Table 3: Summary of Manufacturer's Submission

Drug Product	**Polyquaternium-1–preserved travoprost 0.003% ophthalmic solution (Izba)**
Treatment	Travoprost 0.003% PQ, one drop daily in each affected eye
Comparators	• Primary: Travoprost 0.004% (Travatan Z, generics) • Secondary: Other prostaglandin analogues approved in Canada (listed below) • Bimatoprost 0.01% (Lumigan RC) • Bimatoprost 0.03% (Vistitan) • Latanoprost 0.005% (Xalatan, generics)
Study Objective	"From the perspective of a Canadian Public Payer (Ministry of Health, [MoH]), what is the cost of travoprost 0.003% [PQ] relative to travoprost 0.004% [and other PGAs] in the treatment of adult patients with OAG or OHT?"
Type of Economic Evaluation	Cost comparison, presented as CMA
Target Population	Adult patients with OAG or OHT
Perspective	Canadian public drug payer
Outcome Considered	Drug costs (including pharmacy markup and dispensing fees)
Key Data Sources	
Cost	• Manufacturer's submitted price for travoprost 0.003% PQ • Ontario Drug Benefit (ODB) Formulary list prices for comparators • ODB dispensing fees and markups included in the base-case analysis
Clinical Efficacy	• Equivalent efficacy of travoprost 0.003% PQ and 0.004% was inferred from the phase III pivotal trial comparing these two formulations.[3] • Equivalency of travoprost 0.004%, bimatoprost, and latanoprost was inferred from direct comparisons[5-7] and a published network meta-analysis.[4] • Equivalent efficacy of travoprost 0.003% PQ and bimatoprost and latanoprost was assumed based on the inferred equivalency of travoprost 0.003% PQ and travoprost 0.004%.
Harms	Equivalent harms were inferred from same sources as equivalent clinical efficacy.
Drug Volume Use	Total number of bottles (or claims) per year for each product was calculated based on published and assumed drop size,[8] bottle size, and total volume of ophthalmic solution required per year (in millilitres). Equivalent compliance and adherence (100%) were assumed.
Time Horizon	One year
Results for Base Case	Relative to generic travoprost 0.004%, travoprost 0.003% PQ was a cost-neutral option. Relative to latanoprost 0.005%, travoprost 0.003% PQ resulted in $38.94 saved per patient per year. Relative to bimatoprost 0.01% and 0.03%, travoprost 0.003% PQ resulted in cost savings of $204.93 and $139.53 per patient per year, respectively.

CMA = cost-minimization analysis; OAG = open-angle glaucoma; ODB = Ontario Drug Benefit; OHT = ophthalmic hypertension; PGA = prostaglandin analogue; PQ = polyquaternium-1.

Manufacturer's Results

The manufacturer submitted a cost-minimization analysis that compared the drug costs in year 1 as well as pharmacy markup and dispensing fees. This form of analysis was chosen based on the manufacturer's assumption of equivalent efficacy, supported by the phase III trial comparing travoprost 0.003% preserved with polyquaternium-1 (PQ) with travoprost 0.004%. Given the expected clinical equivalence of travoprost 0.003% with travoprost 0.004%, bimatoprost 0.01%, bimatoprost 0.03%, and latanoprost 0.005%, and the difficulty in estimating the cost impact of the reduced side effect profile expected for travoprost 0.003% PQ compared with the other treatments, supplemental costs (e.g., physician visits, ocular tests, procedures, hospitalizations, emergency room visits, other health care professional visits, etc.) were assumed to be the same across treatments.

The compared treatments are supplied in different-sized bottles (Table 1); thus, the manufacturer chose to include pharmacy markups and dispensing fees based on the ODB Formulary (8% markup and $8.83 dispensing fee). The dosage regimen for each of the compared treatments is one drop in each affected eye each day. The manufacturer assumed that both eyes would be treated. The manufacturer used a drop volume based on one published study for travoprost 0.004%, bimatoprost 0.03% and latanoprost 0.005%.[8] The drop volume of travoprost 0.003% PQ was assumed to be the same as travoprost 0.004%, and the drop volume of bimatoprost 0.01% was assumed to be the same as bimatoprost 0.03% (Table 4).

Table 4: Drop-Volume Assumptions

Drug	Drop Volume (mL)
Travoprost 0.003% PQ (Izba)	**0.030**
Travoprost 0.004% (Travatan Z)	0.030
APO-travoprost 0.004%	0.030
SDZ-travoprost 0.004%	0.030
TEVA-travoprost 0.004%	0.030
Bimatoprost 0.01% (Lumigan RC)	0.031
Bimatoprost 0.03% (Vistitan)	0.031
Latanoprost 0.005% (Xalatan)	0.034
APO-latanoprost 0.005%	0.034
CO-latanoprost 0.005%	0.034
GD-latanoprost 0.005%	0.034
SDZ-latanoprost 0.005%	0.034

PQ = polyquaternium-1.

Source: adapted from manufacturer's pharmacoeconomic submission.[2]

The manufacturer's primary comparison in the cost-minimization analysis of travoprost 0.003% PQ compared with travoprost 0.004% indicated that travoprost 0.003% PQ was cost-neutral relative to currently marketed forms of travoprost 0.004%. The manufacturer reported that the total year 1 cost to treat one patient with travoprost 0.003% PQ was $152.85, which is basically equivalent to the cost of travoprost 0.004% in year 1 ($152.86) (Table 5). The secondary comparison of travoprost 0.003% PQ with other prostaglandin analogues (bimatoprost 0.01%, bimatoprost 0.03%, and latanoprost 0.005%) indicated that travoprost 0.003% PQ was between $38 and $204 less costly per patient in year 1 (Table 5).

Table 5: Manufacturer's Base-Case Results

Drug	Year 1 Drug Cost	Year 1 Drug Cost (Plus Markup and Dispensing Fees)	Incremental Costs (Savings) Travoprost 0.003% PQ Versus Comparator
Travoprost 0.003% PQ (Izba)	**$100.65**	**$152.85**	**NA**
Travoprost 0.004% (Travatan Z)	$100.66	$152.86	($0.01)
APO-travoprost 0.004%	$100.66	$152.86	($0.01)
SDZ-travoprost 0.004%	$100.66	$152.86	($0.01)
TEVA-travoprost 0.004%	$100.66	$152.86	($0.01)
Bimatoprost 0.01% (Lumigan RC)	$290.40	$357.78	($204.93)
Bimatoprost 0.03% (Vistitan)	$229.84	$292.38	($139.53)
Latanoprost 0.005% (Xalatan)	$95.83	$191.80	($38.94)
APO-latanoprost 0.005%	$95.83	$191.80	($38.94)
CO-latanoprost 0.005%	$95.83	$191.80	($38.94)
GD-latanoprost 0.005%	$95.83	$191.80	($38.94)
SDZ-latanoprost 0.005%	$95.83	$191.80	($38.94)

NA = not applicable; PQ = polyquaternium-1.

Source: manufacturer's pharmacoeconomic submission.[2]

Sensitivity analyses conducted by the manufacturer included exclusion of markup and dispensing fees; assumed equal drop volume for all prostaglandin analogues; consideration of 7.5 mL bottle size for bimatoprost 0.01%; and consideration of 2.5 mL bottle size for travoprost 0.004%. Results were robust for the equal drop size analysis and for the 7.5 mL bottle size for bimatoprost 0.01% (Table 6).

When markup and dispensing fees were excluded, travoprost 0.003% PQ incurred additional costs compared with latanoprost. The one-year cost of travoprost 0.003% PQ was $100.65, which was $4.82 more expensive than latanoprost ($95.83), cost-neutral compared with travoprost 0.004% ($100.66), $129.19 less expensive than bimatoprost 0.03% ($229.84), and $189.75 less expensive than bimatoprost 0.01% ($290.40) (Table 6).

When considering a 2.5 mL bottle size for travoprost 0.004%, travoprost 0.003% PQ ($152.86) resulted in cost savings of $24.46 compared with travoprost 0.004% ($177.31) (Table 6).

Table 6: Manufacturer's Sensitivity Analyses

Scenario	Travoprost 0.003% PQ Year 1 Drug Cost	Comparator Year 1 Drug Cost	Incremental Costs (Savings) Travoprost 0.003% PQ Versus Comparators
Base case	**$152.85**	**Travoprost 0.004%: $152.86** **Bimatoprost 0.01%: $357.78** **Bimatoprost 0.03%: $292.38** **Latanoprost 0.005%: $191.80**	**Travoprost 0.004%: ($0.01)** **Bimatoprost 0.01%: ($204.93)** **Bimatoprost 0.03%: ($139.53)** **Latanoprost 0.005%: ($38.94)**
Markup and dispensing fee (excluded)	$100.65	Travoprost 0.004%: $100.66 Bimatoprost 0.01%: $290.40 Bimatoprost 0.03%: $229.84 Latanoprost 0.005%: $95.83	Travoprost 0.004%: ($0.01) Bimatoprost 0.01%: ($189.75) Bimatoprost 0.03%: ($129.19) Latanoprost 0.005%: $4.82
Drop volume (assumed equal volume)	$244.56	Travoprost 0.004%: $244.58 Bimatoprost 0.01%: $572.45 Bimatoprost 0.03%: $467.80 Latanoprost 0.005%: $287.69	Travoprost 0.004%: ($0.02) Bimatoprost 0.01%: ($327.89) Bimatoprost 0.03%: ($223.24) Latanoprost 0.005%: ($43.13)
Format of bimatoprost 0.01% (7.5 mL)	$152.85	Bimatoprost 0.01%: $411.68[a]	Bimatoprost 0.01%: ($258.83)
Format of APO- and TEVA-travoprost 0.004% (2.5 mL)	$152.85	Travoprost 0.004%: $177.31[a]	Travoprost 0.004%: ($24.46)

[a] Corrections made to year 1 drug costs by CDR.

Source: adapted from manufacturer's pharmacoeconomic submission.[2]

CADTH Common Drug Review Results

The total number of bottles required per year is based on the total volume of medication required per year, which is determined by the volume of product per bottle and drop volume, and number of eyes treated. Assumptions were made to determine the number of bottles required per year, although no information was provided by the manufacturer to support these assumptions. Assuming that both eyes are treated, 21.92 mL of medication (corresponding to 4.4 bottles or five separate claims) is required, for a treatment cost of $100.65 in year 1, assuming 100% compliance. In other years, only four bottles (claims) will be required; thus, the treatment cost would be $80.52 with the same caveats. This affects the costs of the comparator products in subsequent years as well, given the different bottle sizes used.

CDR undertook the following reanalyses:

Pharmacy markup and dispensing fee should not be included in the reference case.

Pharmacy markup and dispensing fees differ among provinces; thus, their inclusion and the assumption that Ontario values are generalizable to the other jurisdictions are not appropriate. The results are sensitive to the inclusion of dispensing fees and pharmacy markups. Additionally, patients can receive multiple bottles at once; thus, assuming a dispensing fee for each bottle is unlikely to be an appropriate assumption.

The manufacturer tested this scenario in its sensitivity analyses; thus, CDR did not undertake this analysis again.

There is uncertainty associated with the number of drops per bottle for each treatment.

The number of drops per bottle is a large driver of costs. In particular, if the drop volume of travoprost 0.004% is even 10% less than that of travoprost 0.003% PQ (0.027 mL per drop rather than 0.03 mL), travoprost 0.003% PQ incurs additional costs compared with travoprost 0.004%. Published literature indicates that drop volume differs between treatments and that dose volume can differ between treatments and even batches of the same treatment. Due to the uncertainty associated with the comparability of these factors, equivalent drop volume was assumed between treatments.

The manufacturer tested this scenario in its sensitivity analyses; thus, CDR did not undertake this analysis again.

CDR Base-Case Analysis

The CDR base-case analysis was undertaken based on no pharmacy markup or dispensing fees and equivalent drop volume among the treatments (0.030 mL) (Table 7).

Table 7: CADTH Common Drug Review Reanalyses

Scenario	Travoprost 0.003% PQ Year 1 Drug Cost	Comparator Year 1 Drug Cost	Incremental Range in Costs (Savings) Travoprost 0.003% PQ Versus Comparators
Manufacturer's base case	**$152.85**	**Travoprost 0.004%: $152.86** **Bimatoprost 0.01%: $357.78** **Bimatoprost 0.03%: $292.38** **Latanoprost 0.005%: $191.80**	**Travoprost 0.004%: ($0.01)** **Bimatoprost 0.01%: ($204.93)** **Bimatoprost 0.03%: ($139.53)** **Latanoprost 0.005%: ($38.94)**
CDR Base-Case Reanalysis			
Markup and dispensing fee excluded, drop volume assumed to be 0.030 mL	$100.65	Travoprost 0.004%: $100.66 Bimatoprost 0.01%: $290.40 Bimatoprost 0.03%: $229.84 Latanoprost 0.005%: $86.25	Travoprost 0.004%: ($0.01) Bimatoprost 0.01%: ($189.75) Bimatoprost 0.03%: ($129.19) Latanoprost 0.005%: $14.40
CDR Scenario Analysis			
Markup and dispensing fee excluded, drop volume assumed to be 0.035 mL	$120.78	Travoprost 0.004%: $120.79 Bimatoprost 0.01%: $348.48 Bimatoprost 0.03%: $275.81 Latanoprost 0.005%: $105.41	Travoprost 0.004%: ($0.01) Bimatoprost 0.01%: ($227.70) Bimatoprost 0.03%: ($155.03) Latanoprost 0.005%: $15.37

References

1. [Pr]Izba (travoprost ophthalmic solution) 0.003% w/v [product monograph]. Mississauga (ON): Alcon Canada Inc.; 2016 Sep 23.
2. Pharmacoeconomic evaluation. In: CDR submission: Izba (travoprost.003% w/v). Company: Novartis Pharmaceuticals Canada Inc., on behalf of Alcon Canada Inc. [**CONFIDENTIAL** manufacturer's submission]. Dorval (QC): Novartis Pharmaceuticals Canada Inc.; 2017 Feb 24.
3. Peace JH, Ahlberg P, Wagner M, Lim JM, Wirta D, Branch JD. Polyquaternium-1-preserved travoprost 0.003% or benzalkonium chloride-preserved travoprost 0.004% for glaucoma and ocular hypertension. Am J Ophthalmol. 2015 Aug;160(2):266-74.
4. Li N, Chen XM, Zhou Y, Wei ML, Yao X. Travoprost compared with other prostaglandin analogues or timolol in patients with open-angle glaucoma or ocular hypertension: meta-analysis of randomized controlled trials. Clin Exp Ophthalmol. 2006 Nov;34(8):755-64.
5. Faridi UA, Saleh TA, Ewings P, Venkateswaran M, Cadman DH, Samarasinghe RA, et al. Comparative study of three prostaglandin analogues in the treatment of newly diagnosed cases of ocular hypertension, open-angle and normal tension glaucoma. Clin Exp Ophthalmol. 2010 Oct;38(7):678-82.
6. Parrish RK, Palmberg P, Sheu WP, XLT Study Group. A comparison of latanoprost, bimatoprost, and travoprost in patients with elevated intraocular pressure: a 12-week, randomized, masked-evaluator multicenter study. Am J Ophthalmol. 2003 May;135(5):688-703.
7. Cantor LB, Hoop J, Morgan L, Wudunn D, Catoira Y, Bimatoprost-Travoprost Study Group. Intraocular pressure-lowering efficacy of bimatoprost 0.03% and travoprost 0.004% in patients with glaucoma or ocular hypertension. Br J Ophthalmol [Internet]. 2006 Nov [cited 2017 Mar 30];90(11):1370-3. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1857505
8. Rylander NR, Vold SD. Cost analysis of glaucoma medications. Am J Ophthalmol. 2008 Jan;145(1):106-13.
9. Mirza SK, Johnson SM. Efficacy and patient tolerability of travoprost BAK-free solution in patients with open-angle glaucoma and ocular hypertension. Clin Ophthalmol [Internet]. 2010 Aug 9 [cited 2017 May 26];4:877-88. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2921296
10. Committee for Medicinal Products for Human Use (CHMP). Assessment report: Izba (travoprost) [Internet]. London (GB): European Medicines Agency; 2013 Dec 19. [cited 2017 May 12]. (European public assessment report). Available from: http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Public_assessment_report/human/002738/WC500163298.pdf
11. Prostaglandin analogues for ophthalmic use: a review of the comparative clinical effectiveness and cost-effectiveness [Internet]. Ottawa: CADTH; 2015 Jul 30. [cited 2017 May 26]. (Rapid response report: summary with critical appraisal). Available from: https://www.cadth.ca/sites/default/files/pdf/htis/july-2015/RC0684-Prostaglandins-Final.pdf
12. Li T, Lindsley K, Rouse B, Hong H, Shi Q, Friedman DS, et al. Comparative effectiveness of first-line medications for primary open-angle glaucoma: a systematic review and network meta-analysis. Ophthalmology [Internet]. 2016 Jan [cited 2017 Apr 20];123(1):129-40. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4695285/
13. Wadhwani M, Mishra SK, Angmo D, Velpandian T, Sihota R, Kotnala A, et al. Evaluation of physical properties of generic and branded travoprost formulations. J Curr Glaucoma Pract [Internet]. 2016 May [cited 2017 May 8];10(2):49-55. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4981658
14. Kolko M, Koch Jensen P. The physical properties of generic latanoprost ophthalmic solutions are not identical. Acta Ophthalmol. 2017 Jun;95(4):370-3.
15. Walt J, Alexander F. Drops, drops, and more drops. In: Gunvant P, editor. Glaucoma: current clinical and research aspects [Internet]. Rijeka, Croatia: InTech; 2011 [cited 2017 May 26]. Chapter 12. Available from: http://cdn.intechweb.org/pdfs/22975.pdf
16. Mammo ZN, Flanagan JG, James DF, Trope GE. Generic versus brand-name North American topical glaucoma drops. Can J Ophthalmol. 2012 Feb;47(1):55-61.
17. Gao Y, Wu L, Li A. Daily cost of glaucoma medications in China. J Glaucoma. 2007 Oct;16(7):594-7.

18. Van Santvliet L, Ludwig A. Determinants of eye drop size. Surv Ophthalmol. 2004 Mar;49(2):197-213.
19. Angmo D, Wadhwani M, Velpandian T, Kotnal A, Sihota R, Dada T. Evaluation of physical properties and dose equivalency of generic versus branded latanoprost formulations. Int Ophthalmol. 2017 Apr;37(2):423-8.
20. Platt R, Reardon G, Mozaffari E. Observed time between prescription refills for newer ocular hypotensive agents: the effect of bottle size. Am J Ophthalmol. 2004 Jan;137(1 Suppl):S17-S23.
21. Brown D, Ford JL, Nunn AJ, Rowe PH. An assessment of dose-uniformity of samples delivered from paediatric oral droppers. J Clin Pharm Ther. 2004 Dec;29(6):521-9.