South African National Essential Medicine List
Adult Hospital Level Medication Review Process
Component: Eye conditions

SUMMARY OVERVIEW:

Question: What is the comparative efficacy and safety of bimatoprost 0.01% versus bimatoprost 0.03% for the management of open angle glaucoma (OAG)

Date: 1 August 2019
Reviewer: JM Nabyoma
Affiliation: Lehurutshe hospital, NW Department of health, Lehurutshe, NW; Adult Hospital Level Committee (2017-2019).
Conflicts of interest: None declared

Background:
The tender for ophthalmic drops has recently been advertised and an ophthalmologist on behalf of Allergan Pharmaceuticals has submitted a request for a deviation from the tender specification of bimatoprost 0.01% to 0.03% to the National Department of Health. The Adult Hospital Level Committee was requested to review the evidence for this formulation.

The occurrence of adverse effects (AEs) with the use of topical agents in the management of OAG has been associated with adherence problems by the patients and thus poor clinical outcomes or discontinuation of treatment. The AEs have been associated with the preservative used in ocular eye drops benzalkonium chloride (BAK) and high concentrations of active ingredients (AI) such as bimatoprost 0.03%. The current STG/EML recommends bimatoprost 0.03% for management of OAG and IOP. Recent data shows that bimatoprost 0.01% is more tolerated in patients with increased intraocular pressure (IOP) and ocular hypertension (OHT), and has equivalent IOP lowering potential as the bimatoprost 0.03%.

Evidence search:
A search for evidence was conducted on the following data bases; pubmed, Cochrane, google scholar and medline. 1 Network meta-analysis, 2 RCTs and 1 observational study were reviewed.

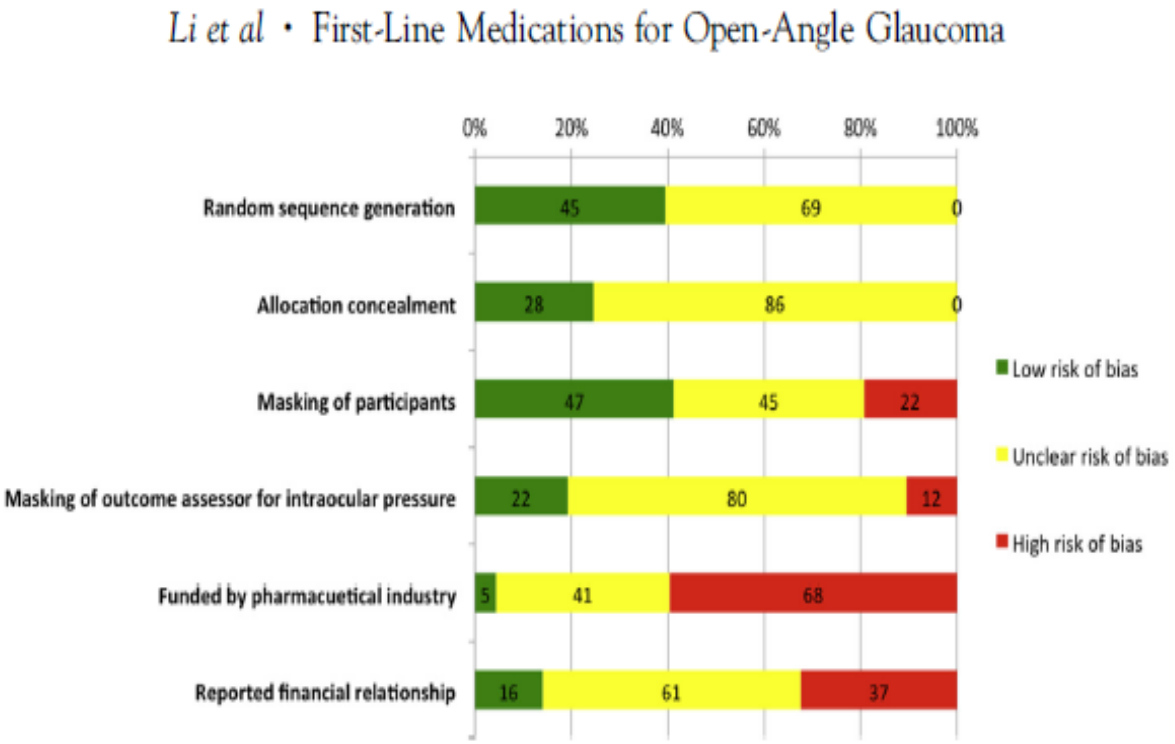
Study	Comparison	Outcomes	Conclusions	Strengths	limitations
Li *et al.*, 2016 Network meta-analysis 114 RCTs n= 20 275	Bimatoprost ***vs*** Latanoprost **or** Travoporst **or** Tafluprost	• All medicnes were more effective than placebo in lowering IOP • Prostaglandin class more efficacious than other classes although within class differences were negligible,	• Bimatoprost is not more effective than latanoprost or travoprost in lowering IOP at 3 months	• Categorisation and reporting on bias.	• Reporting bias • Indirect comparisons of agents • Industry funding of trials included in the NMA • Mean IOP between time points rather than comparing to baseline.

Table 1. Summary Estimates for Intraocular Pressure at 3 Months Derived from Pairwise Meta-analysis Based on Direct Comparisons from 114 Trials*

			Comparison-Specific Heterogeneity				
Column 1	Column 2	No. of Studies	*Mean Difference*†	*95% CI, Lower*	*95% CI, Upper*	*Tau-Squared*	*I-Squared*
Placebo vs.							
	Brimonidine	1	−2.30	−3.99	−0.61	NA	NA
	Betaxolol	3	−2.38	−3.78	−0.98	1.11	73%
	Levobundol	2	−7.52	−8.50	−6.50	NA	NA
	Timolol	5	−3.68	−4.72	−2.63	0.71	52%
	Levobetaxolol	1	−3.00	−4.53	−1.47	NA	NA
	Brinzolamide	2	−2.17	−3.23	−1.10	0.00	0%
	Dorzolamide	4	−1.91	−2.92	−0.90	0.51	51%
	Bimatoprost	1	−4.60	−5.60	−3.60	NA	NA
Bimatoprost vs.							
	Latanoprost	6	0.87	0.01	1.73	0.82	76%
	Travoprost	8	0.59	−0.13	1.30	0.73	74%
Latanoprost vs.							
	Travoprost	7	−0.06	−0.46	0.34	0.00	0%
	Tafluprost	1	−0.90	−3.40	1.60	NA	NA
	Unoprostone	6	3.07	2.51	3.63	0.01	2%

Bias

There is uncertainty in terms of this NMA as to the extent of the different categories within the individual studies used as seen below;



Authors	comparators	Outcome
Katz *et al.*, 2010 Efficacy trial (RCT) (n=187) RCT. efficacy measure= IOP. Safety measure = AEs & conjunctival hyperaemia.	Bimatoprost 0.01% ***vs*** Bimatoprost 0.0125% **vs** Bimatoprost 0.03%	• Baseline mean IOPs were similar among treatment groups. Differences in mean IOP between the bimatoprost 0.01% or 0.0125% groups and the bimatoprost 0.03% group were less than 0.9 mm Hg throughout follow-up. • Bimatoprost 0.01%, but not bimatoprost 0.0125%, was equivalent in efficacy to bimatoprost 0.03% based on predetermined criteria (limits of the 95% confidence interval of the between-group difference in mean IOP within +/- 1.5 mm Hg at all time points and within +/- 1 mm Hg at most time points). • The overall incidence of treatment-related adverse events was reduced significantly in the bimatoprost 0.01% and bimatoprost 0.0125% groups compared with the bimatoprost 0.03% group (P < or = .034). • The percentage of patients with a moderate to severe increase from the baseline macroscopic hyperaemia score was: bimatoprost 0.01%, 3.2%; bimatoprost 0.0125%, 9.0%; bimatoprost 0.03%, 9.1% (P = .019 for bimatoprost 0.01% vs 0.03%).
DuBiner & Hubatsch, 2014 RCT (n=81) IOP≥24 and<34mmHg	Bimatoprost 0.01% ***vs*** travoprost 0.004%	• Late day IOP lowering effect of BAK free travoprost was non infetior to bimatoprost • Both were well tolerated • Bimatoprost had a high incidence of hyperemia
Deshpande *et al.*, 2017 Observational study n=35	Bimatoprost 0.01% vs Bimatoprost 0.03%	• Similar efficacy between the two concentrations • Improved tolerability post switch(hyperaemia scores)

All the studies reviewed above were industry funded.

Recommendation: Based on this summary, the Adult Hospital Level Committee recommends that bimatoprost 0.01% as opposed to 0.03% be recommended as an example of prostaglandins for reduction of intraocular pressure in open angle glaucoma in the STG. And, therapeutic class database to be updated accordingly.
Rationale: Limited evidence of efficacy suggests that bimatoprost 0.01% comparable to 0.03% in reducing intraocular pressure in open angle glaucoma; whilst improved tolerability with lower scores of hyperaemia experienced with lower dose bimatoprost.
Level of Evidence: I RCT, Observational study

NEMLC MEETING OF 26 SEPTEMBER 2019
NEMLC accepted the evidence summary overview document and accepted the recommendation(s) proposed by the Adult Hospital Level Committee.

References

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- DuBiner, H.B. & Hubatsch, D.A. 2014. Late-day intraocular pressure-lowering efficacy and tolerability of travoprost 0.004% versus bimatoprost 0.01% in patients with open-angle glaucoma or ocular hypertension: a randomized trial. *BMC ophthalmology*, 14:151-151.
- Katz, L.J., Cohen, J.S., Batoosingh, A.L., Felix, C., Shu, V. & Schiffman, R.M. 2010. Twelve-month, randomized, controlled trial of bimatoprost 0.01%, 0.0125%, and 0.03% in patients with glaucoma or ocular hypertension. *American journal of ophthalmology*, 149(4):661-671. e661.
- Li, T., Lindsley, K., Rouse, B., Hong, H., Shi, Q., Friedman, D.S., Wormald, R. & Dickersin, K. 2016. Comparative Effectiveness of First-Line Medications for Primary Open-Angle Glaucoma: A Systematic Review and Network Meta-analysis. *Ophthalmology*, 123(1):129-140.