



Indian Health Service
National Pharmacy and Therapeutics Committee
Formulary Brief: Ophthalmic Prostaglandin Analogues
-February 2018-



Background:

The IHS National Pharmacy and Therapeutics Committee (NPTC) first reviewed the ophthalmic prostaglandin analogue (OPA) class of medications in 2008. At that time, the OPA class was added to the National Core Formulary (NCF) on the basis that this class was considered standard of care treatment for glaucoma, however no specific OPA was preferred or named. In December 2008, the NPTC added travoprost as a closed-class item to the NCF, due to significant cost advantages under a VA contract. Later, in March 2011, the FDA granted approval to five manufacturers for generic latanoprost ophthalmic solution. These generic products changed market dynamics within this class and thereby necessitated a subsequent, albeit abbreviated class re-evaluation. The NPTC, at that time, modified the NCF by removing the closed class status, allowing any OPA agent to be utilized. At the February 2018 Winter Meeting, the NPTC re-evaluated the OPA drug class. Following a glaucoma overview, a drug class review and pharmacoeconomic analysis, the **NPTC made no modifications to the NCF, thereby maintaining that any OPA agent may be used.** A brief review of the pharmacoeconomic status (i.e., pricing) of each OPA may be warranted when selecting a preferred, local agent.

Discussion:

Ophthalmic prostaglandin analogues were introduced in the late 1990's for the reduction of intraocular pressure in patients with open-angle glaucoma of ocular hypertension. There are four prostaglandin analogues currently available on the market (latanoprost, bimatoprost, travoprost, and tafluprost). Unoprostone was approved by the FDA in 2000, however it was voluntarily removed by the drug manufacturer in 2005. Therefore, it was not included in the review. Tafluprost, the newer prostaglandin analogue, received FDA approval in 2012 and was included in this NPTC review.

Prostaglandin analogues are considered first-line medical therapy in glaucoma. Recommendations vary among guidelines and some do not include specific pharmacotherapy. The following guidelines specifically describe pharmacologic options and are summarized as follows:

The American Academy of Ophthalmology (2016)

- Prostaglandin analogs are often considered as initial medical therapy. This class is the most frequently prescribed initial eye drops for lowering intraocular pressure (IOP) in patients with glaucoma due to their efficacy, tolerability, safety, and once-daily dosing.

The National Institute for Health and Care Excellence (2017)

- For medical therapy, the first choice is a generic prostaglandin analogue. If this is not tolerated, a beta-blocker is then considered. If neither of these options are tolerated, then consider other agents or a combination of treatments.

In terms of efficacy, the following randomized controlled trials conclude varying results among the prostaglandin analogues.

- Two comparative studies found bimatoprost to be superior to latanoprost in reducing IOP.^{1,2} Noecker et al. showed that bimatoprost lowered IOP significantly more than latanoprost at 6 months ($p < 0.001$). Koz et al. also concluded that bimatoprost demonstrated a greater reduction in IOP compared to both latanoprost and travoprost at 6 months ($p < 0.0001$).
- One study concluded travoprost was superior to latanoprost over a 6-week study duration ($p = 0.009$).³
- RCTs by Parrish et al. and Faridi et al. found no significant difference between latanoprost, bimatoprost and travoprost.^{4,5} Parrish evaluated participants (N=411) who were previously treated while Faridi investigated the newly-diagnosed population (N=122).

Meta-analyses have also demonstrated conflicting results.

- Aptel et al. (2008) published a meta-analysis of 8 randomized controlled trials (N=1,610).⁶ The results found the difference in absolute IOP reduction from baseline was significantly greater with bimatoprost compared to latanoprost at time points (8 am-12 pm-4 pm-8 pm). When comparing bimatoprost and travoprost, absolute IOP reduction was significantly greater with bimatoprost at two of the four time points [8 am ($p=0.004$) and 12 pm ($p=0.02$)]. No significant difference was found between latanoprost and travoprost at any time point.
- Li et al. (2006) published a meta-analysis which included 12 studies (N=3,048).⁷ The combined results found travoprost to be more effective than timolol in lowering IOP but no difference was found when comparing travoprost to bimatoprost (Mean Difference: 0.08; 95% CI: -0.62 to 0.79; $p=0.8$) or latanoprost (Mean Difference= -0.57; 95% CI: -1.18 to 0.04, $p=0.07$).
- Denis et al. (2007) performed a meta-analysis including 9 randomized controlled trials (N=1,318).⁸ Participants treated with travoprost and bimatoprost had lower IOP levels at the end of 4 months follow up of -0.98 mmHg (95% CI: -2.08 to 0.13; $p=0.08$) and -1.04 mmHg (95% CI: -2.11 to 0.04; $p=0.06$) respectively, than those treated with latanoprost. However, these results were not significant.
- Another meta-analysis published by Cheng et al. (2009) evaluated participants with chronic angle-closure glaucoma who had undergone peripheral iridotomy but still had inadequately controlled IOP (N=1,090).⁹ No significant differences were found among latanoprost, bimatoprost, or travoprost.
- More recently, a meta-analysis of 32 randomized controlled trials was published in 2014 (N=4,832).¹⁰ This analysis included the newest prostaglandin analogue, tafluprost, in the review. The results showed that all prostaglandin analogues (with the exception of tafluprost) achieved significantly greater mean IOP reductions compared to timolol. Mean IOP reductions were 8.7 mmHg for bimatoprost, 7.8 mmHg for travoprost, 7.7 mmHg for latanoprost, and 7.2 mmHg for tafluprost. All prostaglandin analogues were associated with significantly greater risk of hyperemia than timolol. The relative risks compared with timolol were 4.66, 4.34, 3.92, and 2.30 for bimatoprost, tafluprost, travoprost, and latanoprost, respectively.

Findings:

Randomized controlled trials and meta-analyses have not consistently demonstrated significant differences between the four prostaglandin analogue products. Guidelines recommend prostaglandin analogues as first-line therapy, but do not recommend any one particular product over another. The differences reported in published literature were generally small and the clinical significance of these differences remains yet to be established.

If you have any questions regarding this document, please contact the NPTC at IHSNPTC1@ihs.gov. For more information about the NPTC, please visit the [NPTC website](#).

References:

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