

## Therapeutic Class Overview Ophthalmic Prostaglandin Analogues

### Therapeutic Class

- Overview/Summary:** Glaucoma is an optic neuropathy that causes gradual degeneration of the cells making up the optic nerve. It is the leading cause of blindness and second leading cause of vision loss in the world.<sup>1</sup> Four distinct types of glaucoma include primary open-angle, acute angle-closure, secondary and congenital. Patients with open-angle glaucoma initially experience peripheral visual field loss, followed by central field loss, which may progress to irreversible blindness if untreated. The exact etiology of open-angle glaucoma is unknown. Major risk factors for developing open-angle glaucoma include advanced age, African or Hispanic/Latino descent, elevated intraocular pressure (IOP), family history of glaucoma or a central corneal thickness of less than 545 micrometers.<sup>2-3</sup> Other possible risk factors that have been investigated include low ocular systolic perfusion pressure, low systolic blood pressure, cardiovascular disease, hypertension, diabetes mellitus and hypothyroidism.<sup>1,3-6</sup>
- IOP is the one major risk factor for glaucoma that is treatable. Available evidence suggests that lowering IOP inhibits or reduces the progression of optic nerve damage.<sup>1-3,7</sup> Treatment may be initiated in patients with a raised IOP despite having no visual field loss or optic nerve damage. An IOP greater than 22 mm Hg is generally considered to be elevated and would be treated by most clinicians; however, this number varies according to screening methods, risk factors and disease progression.<sup>7</sup> The target IOP should be individualized based on their response to therapy and disease progression. There is no consensus target IOP below which further visual loss and optic nerve damage will be prevented.<sup>2,3</sup>

**Table 1. Current Medications Available in the Therapeutic Class<sup>9-14</sup>**

Generic (Trade Name)	Food and Drug Administration Approved Indications	Dosage Form/Strength	Generic Availability
Bimatoprost (Lumigan <sup>®</sup> )	Reduction of elevated intraocular pressure in patients with open-angle glaucoma or ocular hypertension	Ophthalmic solution: 0.01% (2.5, 5, 7.5 mL) 0.03% (2.5, 5, 7.5 mL)	-
Latanoprost (Xalatan <sup>®</sup> )	Reduction of elevated intraocular pressure in patients with open-angle glaucoma or ocular hypertension	Ophthalmic solution: 0.005% (2.5 mL)	✓
Tafluprost (Zioptan <sup>®</sup> )	Reduction of elevated intraocular pressure in patients with open-angle glaucoma or ocular hypertension	Ophthalmic solution: 0.0015% (30 or 90 0.3 mL single-use containers)	-
Travoprost (Travatan Z <sup>®</sup> )	Reduction of elevated intraocular pressure in patients with open-angle glaucoma or ocular hypertension	Ophthalmic solution: 0.004% (2.5, 5 mL)	-
Unoprostone	Reduction of elevated intraocular pressure in patients with open-angle glaucoma or ocular hypertension	Ophthalmic solution: 0.015%	-

\*Available generically in one dosage form or strength.

### Evidence-based Medicine

- Many clinical trials have evaluated the safety and efficacy of the ophthalmic prostaglandin analogues for the reduction of intraocular pressure (IOP) in patients with glaucoma or ocular hypertension.<sup>18-59</sup>
- Ophthalmic bimatoprost appears to have the greatest efficacy in reducing IOP; however, trials have not consistently demonstrated a difference in IOP reduction between ophthalmic travoprost and ophthalmic latanoprost.<sup>18,20,21,25,28,30,31,35,36</sup>

- Available trials suggest that ophthalmic tafluprost may have a similar IOP-lowering effect as ophthalmic latanoprost but less than ophthalmic travoprost.<sup>49-52</sup>
- Results from one trial demonstrated a significantly lower incidence of ocular irritation/burning, tearing, itching, dry eye sensation and conjunctival hyperemia when switched from ophthalmic latanoprost to ophthalmic tafluprost as well as ophthalmic tafluprost also significantly reduced IOP compared to baseline treatment with ophthalmic latanoprost (16.4 vs 16.8 mm Hg; P=0.049).<sup>48</sup>
- A meta-analysis of 11 randomized control trials showed significant reductions in IOP with ophthalmic latanoprost compared to ophthalmic timolol (P<0.001).<sup>38</sup>
- The ophthalmic prostaglandin analogues have consistently demonstrated comparable or greater efficacy when compared to combination therapy.<sup>33,34,39-42</sup>
- The safety and efficacy of unoprostone isopropyl for lowering IOP in patients with glaucoma or ocular hypertension was established in six, six-month randomized controlled clinical studies. Patients had a mean baseline intraocular pressure of 23 mmHg, and unoprostone isopropyl lowered intraocular pressure by approximately 3 to 4 mmHg throughout the day. Unoprostone isopropyl appeared to lower intraocular pressure without affecting cardiovascular or pulmonary function.<sup>14</sup> A review of all clinical trial data suggests unoprostone may not be as efficacious as other prostanoids; however, it is effective for IOP reduction both as monotherapy and adjunctive therapy with timolol. In addition, unoprostone has decreased affinity for the prostaglandin F2 $\alpha$  receptor, which may explain its well tolerated ocular and systemic side effect profile compared with other prostanoids.<sup>59</sup>

### Key Points within the Medication Class

- According to Current Clinical Guidelines:<sup>1-3,7,8</sup>
  - The current treatment of glaucoma focuses on decreasing IOP by one of three methods: laser therapy, surgery or medical intervention.
  - Medical intervention is generally used as initial therapy prior to laser or surgical treatment. Medical intervention includes five classes of ophthalmic drugs used for the long-term management of glaucoma: alpha-2 adrenergic agonists,  $\beta$  adrenergic antagonists, carbonic anhydrase inhibitors, parasympathomimetics and prostaglandin analogues.
  - These treatments reduce IOP by either decreasing the amount of aqueous humor produced by the ciliary body or by increasing uveoscleral outflow.
  - Current guidelines by the American Academy of Ophthalmology and American Optometric Association recommend ophthalmic  $\beta$  adrenergic antagonists and prostaglandin analogues as first-line pharmacologic therapy in patients with elevated IOP. Combination or monotherapy with agents from an alternative pharmacologic class is recommended for patients that experience intolerable adverse events or who do not achieve the optimal IOP reduction with first-line agents.
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- Other Key Facts:
  - Latanoprost is the only ophthalmic prostaglandin analogue that is available generically.<sup>9</sup>
  - Tafluprost is the only preservative-free ophthalmic prostaglandin product and is only available in single-use containers.<sup>13</sup>
  - Bimatoprost and latanoprost are formulated with benzalkonium chloride, an agent associated with ocular irritation/inflammation in some patients. Travoprost is formulated with sofZia, an ionic buffer containing borate, sorbitol, propylene glycol, and zinc.<sup>9-14</sup>

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