



# VERDICT & SUMMARY

## Latanoprost

(Xalatan®)

For the management of glaucoma and ocular hypertension

Committee's Verdict: **CATEGORY B (Q1)**

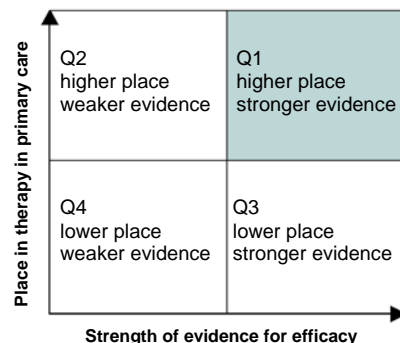
BNF: 6.6.2

**Treatment with latanoprost should be initiated by a specialist. It is then appropriate for GPs to prescribe latanoprost over the long term. Patients with ocular hypertension and glaucoma require regular specialist monitoring.**

**Category B:** suitable for restricted prescribing under defined conditions

**Q1 rating:** The evidence for the comparative efficacy and safety of latanoprost was considered to be relatively strong. Twelve double-blind RCTs showed that latanoprost is as effective as timolol or a fixed combination of timolol and dorzolamide and more effective than timolol, dorzolamide, brimonidine or betaxolol, in lowering the intraocular pressure. A fixed combination of latanoprost and timolol was more effective than latanoprost monotherapy. Well established use has given latanoprost a high place in therapy.

**The Q rating relates to the drug's position on the effectiveness indicator grid.** The strength of the evidence is determined by the quality and quantity of studies that show significant efficacy of the drug compared with placebo or alternative therapy. Its place in therapy in primary care takes into account safety and practical aspects of using the drug in primary care, alternative options, relevant NICE guidance, and the need for secondary care input.



MTRAC updated its review of this drug as part of an update of all prostaglandin analogues.

### Licensed indication

Reduction of elevated intra-ocular pressure in patients with open angle glaucoma and ocular hypertension.<sup>1</sup>

### Background information

Glaucoma is characterised by a loss of peripheral visual field associated with optic nerve damage. While glaucoma is generally associated with raised intra-ocular pressure (IOP), i.e. higher than about 21 mm Hg, it can occur when the IOP is in the normal range. Glaucoma, which can lead to blindness if left untreated, occurs in approximately 1 to 2% of the population over 40, rising to 5% at 70 years. Primary open-angle glaucoma (POAG) is the most prevalent form. It is caused by chronic obstruction of the outflow of aqueous humour within the trabecular meshwork. Ocular hypertension (OH) is defined as a raised IOP that has not resulted in demonstrable peripheral visual field defects.

Current treatments for POAG are designed to lower IOP in order to prevent further damage to nerve fibres and arrest progression of visual field loss. The extent of the reduction depends on individual risk factors but should be at least 20%, and for the majority of patients the target IOP is below 15 mm Hg.<sup>2</sup> Treatment options include the use of drugs, laser trabeculectomy or surgery.<sup>2</sup> The IOP can be modified

by drug treatment by decreasing the production of aqueous humour (e.g. by using topical carbonic anhydrase inhibitors or beta-blockers), or by increasing its outflow (e.g. prostaglandin analogues, brimonidine, pilocarpine).

Eye drops of first choice are usually prostaglandin analogues or beta-blockers, with carbonic anhydrase inhibitors and alpha agonists being used as second-choice or adjunctive agents.<sup>2</sup>

Latanoprost was the first topical prostaglandin F<sub>2α</sub> analogue.

### Clinical efficacy

Twelve double-blind randomised controlled trials (RCTs) compared latanoprost with timolol (1 to 6 months, n = 20 to 294),<sup>3-8</sup> dorzolamide (1 month, n = 20),<sup>8</sup> betaxolol (3 months, n = 31),<sup>9</sup> brimonidine (3 to 6 months, n = 33, 303),<sup>10,11</sup> and fixed combinations of dorzolamide 2% with timolol 0.5% (n = 544),<sup>12</sup> and latanoprost 0.005% with timolol 0.5% (12 months, n = 418, 436).<sup>13,14</sup>

The trials showed that latanoprost 0.005% once daily significantly lowered IOP in patients with open angle glaucoma and ocular hypertension compared with baseline. In eight comparative studies the mean IOP reduction from baseline was significantly greater with latanoprost than with timolol,<sup>3-5,7,8</sup> dorzolamide,<sup>8</sup> betaxolol<sup>9</sup> or brimonidine.<sup>10,11</sup> In two studies

latanoprost was shown to be as effective as timolol<sup>6</sup> or a fixed combination of dorzolamide and timolol;<sup>12</sup> two studies showed that latanoprost monotherapy was less effective than a combination of latanoprost and timolol.<sup>13,14</sup> In open-label studies of up to five years duration, latanoprost maintained the IOP reduction.<sup>15,16</sup>

A further six RCTs compared latanoprost with bimatoprost (1 to 6 months, n = 64 to 289),<sup>17-20</sup> travoprost (3, 12 months, n = 787)<sup>21</sup> or both bimatoprost and travoprost (3 months, n = 411).<sup>22</sup> The studies showed that latanoprost was as effective as bimatoprost at reducing IOP in four studies<sup>17,18,20,22</sup> but not in a fifth.<sup>19</sup> Latanoprost was as effective as travoprost in two studies.<sup>21,22</sup>

### Adverse effects

Common ocular adverse effects reported with latanoprost treatment were ocular pain or stinging, changes in iris pigmentation and lengthening or darkening of the eyelashes.

A gradual increase in the brown pigment of the iris has been observed with latanoprost treatment, predominantly in patients with mixed-coloured irides.<sup>1</sup>

The most common systemic adverse events reported were headache, upper respiratory tract infection, muscle, joint or back pain and allergic skin reactions. The incidence of systemic events was, however, low compared with timolol treatment.

See the Summary of Product Characteristics for further details.<sup>1</sup>

### Additional information

Latanoprost is formulated as a 0.005% ophthalmic solution. One drop should be instilled into the affected eye(s) once daily. Optimal effect is obtained if latanoprost is administered in the evening.<sup>1</sup>

Patients should be warned before initiation of therapy that permanent changes in iris pigmentation, increased eyelash growth and darkening of the eyelid skin may occur.<sup>1</sup>

At current prices (assuming one bottle per month), the cost of a year's treatment with latanoprost is £158; bimatoprost costs £138 and travoprost costs £133 per year.

### References

1. Pharmacia. Xalatan 0.005% eye drops solution. *Summary of Product Characteristics* 2005.
2. The Royal College of Ophthalmologists. Guidelines for the management of open-angle glaucoma and ocular hypertension. 2004. London.

3. Alm A *et al.* Effects on intraocular pressure and side effects of 0.005% latanoprost applied once daily, evening or morning. *Ophthalmology* 1995;**102**:1743-52.
4. Camras C. Comparison of latanoprost and timolol in patients with ocular hypertension and glaucoma. *Ophthalmology* 1996;**103**:138-47.
5. Mishima HK *et al.* A comparison of latanoprost and timolol in primary open-angle glaucoma and ocular hypertension. *Arch Ophthalmology* 1996;**114**:929-32.
6. Watson P *et al.* A six-month, randomized, double-masked study comparing latanoprost with timolol in open-angle glaucoma and ocular hypertension. *Ophthalmology* 1996;**103**:126-37.
7. Konstas AG *et al.* Comparison of 24-hour intraocular pressure reduction with two dosing regimens of latanoprost and timolol maleate in patients with primary open-angle glaucoma. *Am J Ophthalmol* 1999;**128**:15-20.
8. Orzalesi N *et al.* Effect of timolol, latanoprost, and dorzolamide on circadian IOP in glaucoma or ocular hypertension. *Invest Ophthalmol Vis Sci* 2000;**41**:2566-73.
9. Erkin EF *et al.* Effects of betaxolol and latanoprost on ocular blood flow and visual fields in patients with primary open-angle glaucoma. *Eur J Ophthalmol* 2004;**14**:211-9.
10. Stewart WC *et al.* The efficacy and safety of latanoprost 0.005% once daily versus brimonidine 0.2% twice daily in open-angle glaucoma or ocular hypertension. *Am J Ophthalmol* 2001;**131**:631-5.
11. Camras C *et al.* Latanoprost or brimonidine as treatment for elevated intraocular pressure. *J Glaucoma* 2005;**14**:161-7.
12. Fechtner R *et al.* Efficacy and tolerability of the dorzolamide 2%/timolol 0.5% combination (COSOPT TM) versus latanoprost 0.005% (XALATAN TM) in the treatment of ocular hypertension or glaucoma: results from two randomised clinical trials. *Acta Ophthalmol Scand* 2004;**82**:42-8.
13. Higginbotham E *et al.* Latanoprost and timolol combination therapy vs monotherapy. *Arch Ophthalmol* 2002;**120**:915-22.
14. Pfeiffer N. A comparison of the fixed combination of latanoprost and timolol with its individual components. *Graefes Arch Clin Exp Ophthalmol* 2002;**240**:893-9.
15. Alm A *et al.* A 5-year, multicentre, open-label, safety study of adjunctive latanoprost therapy for glaucoma. *Arch Ophthalmol* 2004;**122**:957-65.
16. Alm A *et al.* Latanoprost: experience of 2-year treatment in Scandinavia. *Acta Ophthalmol Scand* 2000;**78**:71-6.
17. DuBiner H *et al.* Efficacy and safety of bimatoprost in patients with elevated intraocular pressure: A 30-day comparison with latanoprost. *Surv Ophthalmol* 2001;**45**:S353-S360.
18. Gandolfi S *et al.* Three-month comparison of bimatoprost and latanoprost in patients with glaucoma and ocular hypertension. *Adv Ther* 2001;**18**:110-21.
19. Noecker R *et al.* A six-month randomised clinical trial comparing the intraocular pressure-lowering efficacy of bimatoprost and latanoprost in patients with ocular hypertension or glaucoma. *Am J Ophthalmol* 2003;**135**:55-63.
20. Walters TR *et al.* 24-Hour IOP control with once-daily bimatoprost, timolol gel-forming solution, or latanoprost: a 1-month, randomized, comparative clinical trial. *Surv Ophthalmol* 2004;**49** Suppl 1:S26-S35.
21. Netland P *et al.* Travoprost compared with latanoprost and timolol in patients with open angle glaucoma or ocular hypertension. *Am J Ophthalmol* 2001;**132**:472-84.
22. Parrish RK *et al.* A comparison of latanoprost, bimatoprost, and travoprost in patients with elevated intraocular pressure: a 12-week, randomised, masked-evaluator multicentre study. *Am J Ophthalmol* 2003;**135**:688-703.

Launch date: March 1997

Manufacturer: Pharmacia

PL 00032/0220

WARNING: This sheet should be read in conjunction with the Summary of Product Characteristics  
This guidance is based upon the published information available in English at the time the drug was considered. It remains open to review in the event of significant new evidence emerging.

MTRAC can be contacted at the Dept. of Medicines Management, Keele University, Keele, Staffs ST5 5BG

Tel: 01782 584131 Fax: 01782 713586 Email: mtrac@keele.ac.uk Web: [www.mtrac.co.uk](http://www.mtrac.co.uk)

RELEVANT NICE GUIDANCE WAS NOT AVAILABLE AT THE TIME OF ISSUE OF THIS VERDICT

Date: April 2006

©Midlands Therapeutics Review & Advisory Committee

VS06/09

(This Verdict & Summary sheet replaces VS02/13 and SS02/13)



KEELE  
UNIVERSITY

Faculty of health Department of medicines management