Keep Up With Your Treatment and Keep Track of Your Eye Pressure

Get into the habit of applying your XALATAN® (latanoprost ophthalmic solution) eye drops at the same time every day

<table>
<thead>
<tr>
<th>DAY 1</th>
<th>DAY 2</th>
<th>DAY 3</th>
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<th>DAY 5</th>
<th>DAY 6</th>
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<tr>
<th>DAY 29</th>
<th>DAY 30</th>
<th>DAY 31</th>
<th>NEXT DR. VISIT</th>
<th>Notes</th>
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<tbody>
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<td>Drops</td>
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<td>Drops</td>
<td>Time:</td>
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Take this helpful chart to your next doctor appointment, so you can start keeping a record of your eye pressure at each visit.

My initial eye pressure: R ______ L ______ (R = Right Eye Pressure; L = Left Eye Pressure)

<table>
<thead>
<tr>
<th>DATE:</th>
<th>EYE PRESSURE</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>R</td>
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<tr>
<td>DATE:</td>
<td>L</td>
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</table>

XALATAN is a prescription medication for the treatment of high eye pressure/intraocular pressure (IOP) in people with open-angle glaucoma or ocular hypertension.

Important Safety Information

XALATAN is not recommended in patients with a known hypersensitivity to latanoprost, benzalkonium chloride, or any other ingredients in this product.

Visit www.XALATAN.com for more information

Please see Important Safety Information continued on next page and accompanying Full Prescribing Information.
How to Administer Your XALATAN Eye Drops

Follow these 5 steps to properly put in your eye drops:

1. Wash and dry your hands
2. Find a comfortable seat and tilt your head back slightly
3. Gently pull down your bottom eyelid
4. Use your other hand to hold the bottle and put the drop into the space between the lower lid and the eye (repeat steps 3 and 4 on your second eye)
5. Close your eyes and gently press on your tear ducts—the inner corners of the eyes—for 2 or 3 minutes; this stops the blinking action from draining the drops away. If you’re taking more than one eye drop medication, wait 5 minutes before using the second eye drop medication

To prevent infection or contamination of the solution, try not to allow the end of the bottle to make contact with the eye or anything else. And always remember to replace the bottle cap after applying the drops.

If you find it difficult to do this yourself, ask a loved one to follow these steps and administer the eye drops for you. Special devices are also available to improve administration of eye drops. Talk to your doctor or pharmacist.

Important Safety Information (continued)

XALATAN® (latanoprost ophthalmic solution) may slowly cause darkening of the eye color, darkening of the eyelid and eyelashes, and increased growth and thickness of eyelashes. Color changes may increase as long as XALATAN is administered, and eye color changes are likely to be permanent.

There have been reports of bacterial keratitis associated with the use of multiple-dose containers of topical ophthalmic products.

Contact lenses should be removed prior to the administration of XALATAN. Contact lenses can be reinserted 15 minutes following administration of XALATAN.

The most common side effects for XALATAN may include blurred vision, burning and stinging, eye redness, eye itching, the feeling of something in the eye, increased darkening of eye color, irritation of the clear front surface of the eye, or cold or flu.

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit fda.gov/medwatch or call 1-800-FDA-1088.

Please see accompanying Full Prescribing Information.
HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use XALATAN safely and effectively. See full prescribing information for XALATAN.

XALATAN® (latanoprost ophthalmic solution) 0.005%
Initial U.S. Approval: 1996

1 INDICATIONS AND USAGE
XALATAN is a prostaglandin Fα analogue indicated for the reduction of elevated intraocular pressure in patients with open-angle glaucoma or ocular hypertension. (1)

2 DOSAGE AND ADMINISTRATION
One drop in the affected eye(s) once daily in the evening. (2)

3 DOSAGE FORMS AND STRENGTHS
Ophthalmic solution containing 50 mcg/mL latanoprost. (3)

4 CONTRAINDICATIONS
Known hypersensitivity to latanoprost, benzalkonium chloride, or any other ingredients in this product. (4)

5 WARNINGS AND PRECAUTIONS

5.1 Pigmentation

5.2 Eyelash Changes

5.3 Intraocular Inflammation

5.4 Macular Edema

5.5 Herpetic Keratitis

5.6 Bacterial Keratitis

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*Sections or subsections omitted from the full prescribing information are not listed

The pigmentation change is due to increased melanin content in the melanocytes rather than to an increase in the number of melanocytes. After discontinuation of latanoprost, pigmentation of the iris is likely to be permanent, while pigmentation of the periocular tissue and eyelash changes have been reported to be reversible in some patients. Patients who receive treatment should be informed of the possibility of increased pigmentation. Beyond 5 years the effects of increased pigmentation are not known.[see Clinical Studies (14.2)].

Iris color change may not be noticeable for several months to years. Typically, the brown pigmentation around the pupil spreads concentrically towards the periphery of the iris and the entire iris or parts of the iris become more brownish. Neither nevi nor freckles of the iris appear to be affected by treatment. While treatment with XALATAN can be continued in patients who develop noticeably increased iris pigmentation, these patients should be examined regularly.[see Patient Counseling Information (17.1)].

5.2 Eyelash Changes

XALATAN may gradually change eyelashes and vellus hair in the treated eye; these changes include increased length, thickness, pigmentation, the number of lashes or hairs, and misdirected growth of eyelashes. Eyelash changes are usually reversible upon discontinuation of treatment.[see Patient Counseling Information (17.2)].

5.3 Intraocular Inflammation

XALATAN should be used with caution in patients with a history of intraocular inflammation (iritis/uveitis) and should generally not be used in patients with active intraocular inflammation because inflammation may be exacerbated.

5.4 Macular Edema

Macular edema, including cystoid macular edema, has been reported during treatment with XALATAN. XALATAN should be used with caution in aphakic patients, in pseudophakic patients with a torn posterior lens capsule, or in patients with known risk factors for macular edema.

5.5 Herpetic Keratitis

Reactivation of Herpes Simplex keratitis has been reported during treatment with XALATAN. XALATAN should be used with caution in patients with a history of herpetic keratitis. XALATAN should be avoided in cases of active herpes simplex keratitis because inflammation may be exacerbated.
5.6 Bacterial Keratitis
There have been reports of bacterial keratitis associated with the use of multiple-dose containers of topical ophthalmic products. These containers had been inadvertently contaminated by patients who, in most cases, had a concurrent corneal disease or a disruption of the ocular epithelial surface [see Patient Counseling Information (17.3)].

5.7 Use with Contact Lenses
Contact lenses should be removed prior to the administration of XALATAN, and may be reinserted 15 minutes after administration.

6 ADVERSE REACTIONS
The following adverse reactions were reported in postmarketing experience and are discussed in greater detail in other sections of the label:
- Iris pigmentation changes [see Warnings and Precautions (5.1)]
- Eyelid skin darkening [see Warnings and Precautions (5.1)]
- Eyelash changes (increased length, thickness, pigmentation, and number of lashes) [see Warnings and Precautions (5.2)]
- Intracocular inflammation (iritis/uveitis) [see Warnings and Precautions (5.3)]
- Macular edema, including cystoid macular edema [see Warnings and Precautions (5.4)]

6.1 Clinical Trials Experience
Because clinical trials are conducted under widely varying conditions, the adverse reaction rates observed in the clinical studies of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in clinical practice.

XALATAN was studied in three multicenter, randomized, controlled clinical trials. Patients received 50 mcg/mL XALATAN once daily or 5 mg/mL active-comparator (timolol) twice daily. The patient population studied had a mean age of 65±10 years. Seven percent of patients withdrew before the 6-month endpoint.

Table 1: Ocular Adverse Reactions and ocular signs/symptoms reported by 5-15% of patients receiving Latanoprost

<table>
<thead>
<tr>
<th>Symptom/Finding</th>
<th>Latanoprost (n=460)</th>
<th>Timolol (n=369)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Foreign body sensation</td>
<td>13</td>
<td>8</td>
</tr>
<tr>
<td>Punctate epithelial keratopathy</td>
<td>10</td>
<td>9</td>
</tr>
<tr>
<td>Stinging</td>
<td>9</td>
<td>12</td>
</tr>
<tr>
<td>Conjunctival hyperemia</td>
<td>8</td>
<td>3</td>
</tr>
<tr>
<td>Blurred vision</td>
<td>8</td>
<td>8</td>
</tr>
<tr>
<td>Itching</td>
<td>8</td>
<td>8</td>
</tr>
<tr>
<td>Burning</td>
<td>7</td>
<td>8</td>
</tr>
<tr>
<td>Increased pigmentation of the iris</td>
<td>7</td>
<td>0</td>
</tr>
</tbody>
</table>

Less than 1% of the patients treated with XALATAN required discontinuation of therapy because of intolerance to conjunctival hyperemia.

Table 2: Adverse Reactions that were reported in 1-5% of patients receiving Latanoprost

<table>
<thead>
<tr>
<th>Ocular Events/Signs and Symptoms</th>
<th>Latanoprost (n=460)</th>
<th>Timolol (n=369)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Excessive tearing</td>
<td>4</td>
<td>6</td>
</tr>
<tr>
<td>Lid discomfort/pain</td>
<td>4</td>
<td>2</td>
</tr>
<tr>
<td>Dry eye</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Eye pain</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Lid crusting</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Lid erythema</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>Photophobia</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Lid edema</td>
<td>1</td>
<td>3</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Systemic Events</th>
<th>Latanoprost (n=460)</th>
<th>Timolol (n=369)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Upper respiratory tract infection/cold/flu</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Muscle/joint/back pain</td>
<td>1</td>
<td>0.5</td>
</tr>
<tr>
<td>Rash/allergic skin reaction</td>
<td>1</td>
<td>0.3</td>
</tr>
</tbody>
</table>

6.2 Postmarketing Experience
The following reactions have been identified during postmarketing use of XALATAN in clinical practice. Because they are reported voluntarily from a population of unknown size, estimates of frequency cannot be made. The reactions, which have been chosen for inclusion due to either their seriousness, frequency of reporting, possible causal connection to XALATAN, or a combination of these factors, include:
- Nervous System disorders: dizziness, headache, and toxic epidermal necrolysis
- Eye Disorders: eyelash and vellus hair changes (increased length, thickness, pigmentation, and number); keratitis; corneal edema and erosions; intracocular inflammation (iritis/uveitis); macular edema, including cystoid macular edema; misdirected eyelashes sometimes resulting in eye irritation; periorbital and lid changes resulting in deepening of the eyelid sulcus

7 DRUG INTERACTIONS
In vitro studies have shown that precipitation occurs when eye drops containing thimerosal are mixed with XALATAN. If such drugs are used, they should be administered at least five (5) minutes apart. The combined use of two or more prostaglandins, or prostaglandin analogs including XALATAN is not recommended. It has been shown that administration of these prostaglandin drug products more than once daily may decrease the IOP lowering effect or cause paradoxical elevations in IOP.

8 USE IN SPECIFIC POPULATIONS
8.1 Pregnancy
Teratogenic Effects: Pregnancy Category C
Reproduction studies have been performed in rats and rabbits. In rabbits, an incidence of 4 of 16 dams had no viable fetuses at a dose that was approximately 80 times the maximum human dose, and the highest nonembryocidal dose in rabbits was approximately 15 times the maximum human dose.

There are no adequate and well-controlled studies in pregnant women. XALATAN should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

8.3 Nursing Mothers
It is not known whether this drug or its metabolites are excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when XALATAN is administered to a nursing woman.

8.4 Pediatric Use
Safety and effectiveness in pediatric patients have not been established.

8.5 Geriatric Use
No overall differences in safety or effectiveness have been observed between elderly and younger patients.

10 OVERDOSAGE
Intravenous infusion of up to 3 mcg/kg in healthy volunteers produced mean plasma concentrations 200 times higher than during clinical treatment and no adverse reactions were observed. Intravenous dosages of 5.5 to 10 mcg/kg caused abdominal pain, dizziness, fatigue, hot flushes, nausea, and sweating.

If overdosage with XALATAN occurs, treatment should be symptomatic.

11 DESCRIPTION
Latanoprost is a prostanoid F₂₁₄₆ analogue. Its chemical name is isopropyl-[(Z)-7[(1R,2R,3R,5S)-3,5-dihydroxy-2-[(3R)-3-hydroxy-5-phenylpentyl]cyclopentyl]-5-heptenoate. Its molecular formula is C₁₉H₂₄O₃ and its chemical structure is:

\[
\text{M.W. 432.58}
\]

Latanoprost is a colorless to slightly yellow oil that is very soluble in acetone and freely soluble in acetone, ethanol, ethyl acetate, isopropanol, methanol, and octanol. It is practically insoluble in water.

XALATAN (latanoprost ophthalmic solution) 0.005% is supplied as a sterile, isotonic, buffered aqueous solution of latanoprost with a pH of approximately 6.7 and an osmolality of approximately 267 mOsmol/kg. Each mL of XALATAN contains 50 micrograms of latanoprost. Benzalkonium chloride, 0.02% is added as a preservative. The inactive ingredients are: sodium chloride, sodium dithionite phosphate monohydrate, disodium hydrogen phosphate anhydrous, and water for injection. One drop contains approximately 1.5 mcg of latanoprost.

12 CLINICAL PHARMACOLOGY
12.1 Mechanism of Action
Latanoprost is a prostaglandin selective FP receptor agonist that is believed to reduce the intraocular pressure (IOP) by increasing the outflow of aqueous humor. Studies in animals and man suggest that the main mechanism of action is increased uveoscleral outflow. Elevated IOP represents a major risk factor for glaucomatous field loss. The higher the level of IOP, the greater the likelihood of optic nerve damage and visual field loss.

12.2 Pharmacodynamics
Reduction of the IOP in man starts about 3-4 hours after administration and maximum effect is reached after 8-12 hours. IOP reduction is present for at least 24 hours.

12.3 Pharmacokinetics
Absorption
Latanoprost is absorbed through the cornea where the isopropyl ester prodrug is hydrolyzed to the acid form to become biologically active.
XALATAN is a clear, isotonic, buffered, preserved colorless solution of latanoprost 0.005% (50 mcg/mL). It is supplied as a 2.5 mL solution in a 5 mL clear low density polyethylene bottle with a clear polyethylene dropper tip, a turquoise high density polyethylene screw cap, and a tamper-evident clear low density polyethylene overcap.

2.5 mL fill, 0.005% (50 mcg/mL): Package of 1 bottle: NDC 0013-8303-04
2.5 mL fill, 0.005% (50 mcg/mL): Multi-pack of 3 bottles: NDC 0013-8303-01

Storage: Protect from light. Store unopened bottle(s) under refrigeration at 2° to 8°C (36° to 46°F). During shipment to the patient, the bottle may be maintained at temperatures up to 40°C (104°F) for a period not exceeding 8 days. Once a bottle is opened for use, it may be stored at room temperature up to 25°C (77°F) for 6 weeks.