Latanoprost

Core Safety Profile

4.3 Contraindications

Known hypersensitivity to any component in Xalatan.

4.4 Special warnings and precautions for use

Xalatan may gradually change eye colour by increasing the amount of brown pigment in the iris. Before treatment is instituted, patients should be informed of the possibility of a permanent change in eye colour. Unilateral treatment can result in permanent heterochromia.

This change in eye colour has predominantly been seen in patients with mixed coloured irides, i.e. blue-brown, grey-brown, yellow-brown and green-brown. In studies with latanoprost, the onset of the change is usually within the first 8 months of treatment, rarely during the second or third year, and has not been seen after the fourth year of treatment. The rate of progression of iris pigmentation decreases with time and is stable for five years. The effect of increased pigmentation beyond five years has not been evaluated. In an open 5-year latanoprost safety study, 33% of patients developed iris pigmentation (see 4.8). The iris colour change is slight in the majority of cases and often not observed clinically. The incidence in patients with mixed colour irides ranged from 7 to 85%, with yellow-brown irides having the highest incidence. In patients with homogeneously blue eyes, no change has been observed and in patients with homogeneously grey, green or brown eyes, the change has only rarely been seen.

The colour change is due to increased melanin content in the stromal melanocytes of the iris and not to an increase in number of melanocytes. Typically, the brown pigmentation around the pupil spreads concentrically towards the periphery in affected eyes, but the entire iris or parts of it may become more brownish. No further increase in brown iris pigment has been observed after discontinuation of treatment. It has not been associated with any symptom or pathological changes in clinical trials to date.

Neither naevi nor freckles of the iris have been affected by treatment. Accumulation of pigment in the trabecular meshwork or elsewhere in the anterior chamber has not been observed in clinical trials. Based on 5 years clinical experience, increased iris pigmentation has not been shown to have any negative clinical sequelae and Xalatan can be continued if iris pigmentation ensues. However, patients should be monitored regularly and if the clinical situation warrants, Xalatan treatment may be discontinued.

There is limited experience of Xalatan in chronic angle closure glaucoma, open angle glaucoma of pseudophakic patients and in pigmentary glaucoma. There is no experience of Xalatan in inflammatory and neovascular glaucoma,

inflammatory ocular conditions, or congenital glaucoma. Xalatan has no or little effect on the pupil, but there is no experience in acute attacks of closed angle glaucoma. Therefore, it is recommended that Xalatan should be used with caution in these conditions until more experience is obtained.

There are limited study data on the use of Xalatan during the peri-operative period of cataract surgery. Xalatan should be used with caution in these patients.

Reports of macular oedema have occurred (see 4.8) mainly in aphakic patients, in pseudophakic patients with torn posterior lens capsule or anterior chamber lenses, or in patients with known risk factors for cystoid macular oedema (such as diabetic retinopathy and retinal vein occlusion). Xalatan should be used with caution in aphakic patients, in pseudophakic patients with torn posterior lens capsule or anterior chamber lenses, or in patients with known risk factors for cystoid macular oedema.

Xalatan should be used with caution in patients with a history of herpetic keratitis, and should be avoided in cases of active herpes simplex keratitis and in patients with a history of recurrent herpetic keratitis specifically associated with prostaglandin analogues.

In patients with known predisposing risk factors for iritis/uveitis, Xalatan can be used with caution.

There is limited experience from patients with asthma, but some cases of exacerbation of asthma and/or dyspnoea were reported in post marketing experience. Asthmatic patients should therefore be treated with caution until there is sufficient experience, see also 4.8.

Periorbital skin discolouration has been observed, the majority of reports being in Japanese patients. Experience to date shows that periorbital skin discolouration is not permanent and in some cases has reversed while continuing treatment with Xalatan.

Latanoprost may gradually change eyelashes and vellus hair in the treated eye and surrounding areas; these changes include increased length, thickness, pigmentation, number of lashes or hairs and misdirected growth of eyelashes. Eyelash changes are reversible upon discontinuation of treatment.

Xalatan contains benzalkonium chloride, which is commonly used as a preservative in ophthalmic products. Benzalkonium chloride has been reported to cause punctate keratopathy and/or toxic ulcerative keratopathy, may cause eye irritation and is known to discolour soft contact lenses. Close monitoring is required with frequent or prolonged use of Xalatan in dry eye patients, or in conditions where the cornea is compromised. Contact lenses may absorb benzalkonium chloride and these should be removed before applying Xalatan but may be reinserted after 15 minutes (see section 4.2 Posology and Method of Administration).

4.5 Interaction with other medicinal products and other forms of interaction

Definitive drug interaction data are not available.

There have been reports of paradoxical elevations in intraocular pressure following the concomitant ophthalmic administration of two prostaglandin analogues. Therefore, the use of two or more prostaglandins, prostaglandin analogues or prostaglandin derivatives is not recommended.

4.6 Pregnancy and lactation

Pregnancy
The safety of this medicinal product for use in human pregnancy has not been established. It has potential hazardous pharmacological effects with respect to the course of pregnancy, to the unborn or the neonate. Therefore, Xalatan should not be used during pregnancy.

Lactation
Latanoprost and its metabolites may pass into breast milk and Xalatan should therefore not be used in nursing women or breast feeding should be stopped.

4.7 Effects on ability to drive and use machines

In common with other eye preparations, instillation of eye drops may cause transient blurring of vision. Until this has resolved, patients should not drive or use machines.

4.8 Undesirable effects

The majority of adverse events relate to the ocular system. In an open 5-year latanoprost safety study, 33% of patients developed iris pigmentation (see 4.4). Other ocular adverse events are generally transient and occur on dose administration.
Adverse events are categorized by frequency as follows: very common (≥1/10), common (≥1/100, <1/10), uncommon (≥1/1000, <1/100), rare (≥1/10,0000, <1/1000) and very rare (<1/10,000). Not known (cannot be estimated from the available data).

Infections and Infestations:
Not known: Herpetic keratitis

Eye Disorders:
Very common: Increased iris pigmentation; mild to moderate conjunctival hyperaemia eye irritation (burning grittiness, itching, stinging and foreign body sensation); eyelash and vellus hair changes (increased length, thickness, pigmentation and number) (vast majority of reports in Japanese population).

Common: transient punctate epithelial erosions, mostly without symptoms; blepharitis; eye pain.
Uncommon: Eyelid oedema: dry eye; keratitus; vision blurred; conjunctivitis.
Rare: Iritis/uveitis (the majority of reports in patients with concomitant predisposing factors); macular oedema; symptomatic corneal oedema and erosions; periorbital oedema; misdirected eyelashes sometimes resulting in eye irritation; extra row of cilia at the aperture of the meibomian glands (distichiasis).
Not known: iris cyst

Nervous System Disorders:
Not known: Headache, Dizziness.

Cardiac Disorders:
Very rare: Aggravation of angina in patients with pre-existing disease.
Not known: Palpitations.

Respiratory, Thoracic and Mediastinal Disorders:
Rare: Asthma, asthma exacerbation and dyspnoea.

Skin and Subcutaneous Tissue Disorders:
Uncommon: Skin rash.
Rare: Localised skin reaction on the eyelids; darkening of the palpebral skin of the eyelids.

Musculoskeletal and Connective Tissue Disorders:
Not known: Myalgia; Arthralgia.

General Disorders and Administration Site Conditions:
Very rare: Chest pain.

4.9 Overdose

Apart from ocular irritation and conjunctival hyperaemia, no other ocular side effects are known if Xalatan is overdosed.

If Xalatan is accidentally ingested the following information may be useful: One bottle contains 125 micrograms latanoprost. More than 90% is metabolised during the first pass through the liver. Intravenous infusion of 3 micrograms/kg in healthy volunteers induced no symptoms, but a dose of 5.5-10 micrograms/kg caused nausea, abdominal pain, dizziness, fatigue, hot flushes and sweating. In monkeys, latanoprost has been infused intravenously in doses of up to 500 micrograms/kg without major effects on the cardiovascular system.

Intravenous administration of latanoprost in monkeys has been associated with transient bronchoconstriction. However, in patients with moderate bronchial asthma, bronchoconstriction was not induced by latanoprost when applied topically on the eyes in a dose of seven times the clinical dose of Xalatan.

If overdosage with Xalatan occurs, treatment should be symptomatic.