6.1. ELEMENTS FOR A PUBLIC SUMMARY

6.1.1. Overview of Disease Epidemiology

Glaucoma is the second leading cause of blindness worldwide, and affects about 66.8 million people worldwide[i,ii]. Glaucoma can affect individuals at any age, but it is more common with increasing age, black or Hispanic ethnicity (compared with white ethnicity), and females more than males in the adult form of the condition[iii]. The estimated incidence of open angle glaucoma (a form of glaucoma) is 1/1000 per year in white individuals, and 5.5/1000 per year in black individuals[iv,v]. In its infantile form, more males are affected by this condition than females[vi].

Paediatric or childhood glaucomas constitute a rare, varied group of conditions which can present at different ages during childhood.[vii] The incidence of paediatric glaucoma varies considerably across the world.[viii] Data from studies in Western countries suggest that the incidence of infantile primary glaucoma ranges from 1:10,000 to 20,000 live births.

6.1.2. Summary of Treatment Benefits

Latanoprost belongs to a group of medicines known as prostaglandin analogues. It works by increasing the natural outflow of fluid from inside the eye into the bloodstream. Latanoprost is used to treat conditions known as open angle glaucoma and ocular hypertension in adults. Both of these conditions are linked with an increase in the pressure within the eye, eventually affecting eye sight. Latanoprost is also used to treat increased eye pressure and glaucoma in all ages of children and babies.

The safety and efficacy of latanoprost in adult patients with elevated eye pressure is supported by more than 13 years of clinical experience. The efficacy of latanoprost has been demonstrated across multiple ethnic groups, including African American patients. Latanoprost has also been demonstrated to be effective in lowering eye pressure in a 3-month trial conducted in paediatric patients.

6.1.3. Unknowns Relating to Treatment Benefits

The treatment benefit of latanoprost has not been studied in the following populations/patients:

- Pregnant and breastfeeding women;
- Patients with kidney disease; and
- Patients with liver disease.

6.1.4. Summary of Safety Concerns

Important Identified Risks

Risk	What is Known	Preventability
Conjunctival hyperaemia	Redness of the eye is a very common possible side effect, likely to affect more than 1 in 10 patients.	This side effect is not preventable. However, the product label warns about the risk of conjunctival hyperaemia associated with latanoprost treatment, and therefore, doctors will be able to counsel patients appropriately regarding this possible common side effect.
Eyelash and vellus hair changes	A very gradual change to the eyelashes and fine hairs around the treated eye, involving an increase in the colour (darkening), length, thickness, and number of eye lashes is a very common possible side effect, likely to affect more than 1 in 10 patients is. This has been mostly reported in Japanese patients.	This side effect is not preventable. However, the product label warns about the risk of eyelash and vellus hair changes associated with latanoprost treatment, and therefore, doctors will be able to counsel patients appropriately regarding this possible common side effect. Also, proper application of the eyedrops (as specified in the patient information leaflet), and wiping any excess eye drop fluid from the skin may reduce the occurrence of vellus hair changes.
Periorbital skin discolouration	Darkening of the skin of the eyelids is a rare possible side effect, likely to affect less than 1 in every 1000 patients.	This side effect is not preventable. However, the product label warns about the risk of periorbital skin discolouration associated with latanoprost treatment, and therefore, doctors will be able to counsel patients appropriately regarding this possible rare side effect. Also, proper application of the eyedrops (as specified in the patient information leaflet), and wiping any excess eye drop fluid from the skin may reduce the occurrence of periorbital skin discolouration.
Iris hyperpigmentation	A gradual increase in the amount of brown pigment in the coloured part of the eye known as the iris is a very common possible side effect, likely to affect more than 1 in 10 patients is. This change occurs more commonly in mixed-colour eyes than in eyes of one colour.	This side effect is not preventable. However, the product label warns about the risk of iris hyperpigmentation associated with latanoprost treatment, and therefore, doctors will be able to counsel patients appropriately regarding this possible

		common side effect.
Keratitis herpetic	Developing a viral infection with the herpes simplex virus is a possible side effect.	This side effect is not preventable. However, the product label warns about the risk of keratitis herpetic associated with latanoprost treatment, and therefore, doctors will be able to counsel patients appropriately regarding this possible side effect.

Important Potential Risks

Risk	What is Known
Cystoid macular oedema	There is a possible risk of patients developing cystoid macular oedema, which is the development of a fluid within the layers of the retina.
Aggravation of asthma	In rare cases (likely affecting less than 1 in every 1000 patients), there is a possible risk of patients experiencing a worsening of asthma or shortness of breath.
Ocular and cutaneous melanoma	Cancers of the eye and skin have been reported in patients treated with latanoprost. However, no causal relationship has been established between the use of latanoprost ad these cancers. Also, no potential for causing cancer has been observed in animal studies performed with latanoprost.

Missing Information

Risk	What is Known
Ocular tolerability in paediatric population	Latanoprost contains the preservative benzalkonium chloride (BAK). BAK has been reported to cause damage to the clear surface of the eye (the cornea), may cause eye irritation, and is known to discolor soft contact lenses. Patients who already have medical conditions affecting the cornea may be more susceptible to BAK irritation.
Long term safety in paediatric population	There is limited information on the long term effect of latanoprost in paediatric patients.
Limited information on drug interactions in adult and paediatric patients	No studies investigating drug interactions have been conducted in paediatric patients.
Use in pregnant and lactating women	Because latanoprost has not been studied in pregnant or breastfeeding women, there is little information on the risks to pregnant women or their newborns. No potential for reproductive or developmental toxicity has been observed for latanoprost in animal studies.

6.1.5. Summary of Risk Minimisation Measures by Safety Concern

All medicines have a Summary of Product Characteristics (SmPC) which provides physicians, pharmacists and other health care professionals with details on how to use the medicine, the risks and recommendations for minimising them. An abbreviated version of this in lay language is provided in the form of a Patient Information Leaflet. The measures in these documents are known as routine risk minimisation measures.

The SmPC and the Patient Information Leaflet for latanoprost (Latanoprost Pfizer) can be found on the European Public Assessment Report page for Latanoprost Pfizer.

6.1.6. Planned Post Authorisation Development Plan

Study/Activity (Including Study Number)	**Objectives**	**Safety Concerns /Efficacy Issue Addressed**	**Status**	**Planned Date for Submission of (Interim and) Final Results**
A6111143 A prospective, non-interventional, cohort study to evaluate the long-term safety of latanoprost treatment in pediatric populations. Phase IV	To evaluate the long-term impact of treatment with latanoprost on ocular developmental and ocular neurodegenerative diseases, changes in eyelashes and hyperpigmentation of the eye, and corneal endothelial function/corneal thickness by comparing pediatric subjects treated with latanoprost with those not treated with latanoprost or other topical PGAs.	Safety: Long-term ocular and systemic safety in the pediatric population	Ongoing (Estimated completion date: 31 January 2016)	Projected study report: January 2017
A6111144 Long-term surveillance study to monitor hyperpigmentation changes in the eye in pediatric populations Phase IV	To describe the incidence (proportion and rate) of hyperpigmentation changes in the eye over a total of 10-year follow up period by combining the data collected in the 3-year A6111143 study and the subsequent 7-year A6111144 study, among pediatric patients with glaucoma or elevated IOP who have completed the 3-year cohort study (A6111143).	Safety: Long-term ocular and systemic safety in the pediatric population	Ongoing Estimated FSFV date: 10 March 2014	Projected study report: December 2024

Study/Activity (Including Study Number)	Objectives	Safety Concerns /Efficacy Issue Addressed	Status	Planned Date for Submission of (Interim and) Final Results
A6111157 A population-based cohort study using an existing database to evaluate the association between latanoprost use and primary OM and facial CM.	The primary research objective is to evaluate whether use of latanoprost increases the risk of primary malignant OM and facial CM. The secondary research objective is to evaluate whether use of topical PGAs in general (latanoprost or other topical PGAs) increases the risk of primary malignant OM and facial CM.	<u>Safety:</u> To evaluate if the use of latanoprost and topical PGAs increases the risk of primary malignant OM and facial CM.	Planned Final protocol submitted in September 2013 to the MHRA; awaiting MHRA endorsement at the time of RMP preparation.	To be determined.

Abbreviations: CM=Cutaneous melanoma; FSFV=First Subject First Visit; IOP=Intraocular pressure; MHRA=Medicines and Healthcare products Regulatory Agency; OM=Ocular melanoma; PGAs=Prostaglandin analogues.

Studies Which are a Condition of the Marketing Authorisation

None of the above studies are conditions of marketing authorisation.

---

[i] Stamper RL, Lieberman MF, Drake MV. Introduction and classification of the glaucomas. In: Becker-Shaffer's diagnosis and therapy of the glaucomas. 8th ed. Maryland Heights, MO: Mosby Elsevier; 2009: p. 1-7.

[ii] Quigley HA. Number of people with glaucoma worldwide. Br J Ophthalmol 1996;80(5):389-93.

[iii] Allingham RR. Chapter 9. Clinical epidemiology of glaucoma. In: Damji KF, Freedman S, Moroi SE, Rhee DJ, editors. Sheilds textbook of glaucoma. 6th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2011: p. 149-67.

[iv] Mukesh BN, McCarty CA, Rait JL, Taylor HR. Five-year incidence of open-angle glaucoma. Ophthalmol 2002;109:1047-51.

[v] Leske MC, Connell AM, Wu S-Y, et al. Incidence of open-angle glaucoma. The Barbados Eye Studies. Arch Ophthalmol 2001;119:89-95.

[vi] Ulrich G, Epstein DL. Chapter 22. Principles of primary angle-closure glaucoma. In: Kahook MY, Schuman JS, editors. Chandler and Grant's glaucoma. Thorofare, NJ: Slack Incorporated; 2013: p. 239-54.

[vii] Allingham RR. Chapter 13. Childhood glaucomas: classification and examination. In: Damji KF, Freedman S, Moroi SE, Rhee DJ, editors. Sheilds

textbook of glaucoma. 6th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2011: p. 206-17.

[viii] MacKinnon JR, Giubilato A, Elder JE, et al. Primary infantile glaucoma in an Australian population. Clin Experiment Ophthalmol 2004;32(1):14-8.