VI.2 Elements for a public summary

VI.2.1 Overview of disease epidemiology

Glaucoma is a leading cause of irreversible blindness with 60 million cases worldwide and 2.2 million in the United States. Up to 50 percent of those with glaucoma are not aware they have it. Early diagnosis and treatment is critical to managing glaucoma. Regular eye exams are essential to detect glaucoma and slow irreversible vision loss. If untreated, the disease can lead to blindness. In fact, 11.2 million people are predicted to go blind from glaucoma by the year 2020, due in part to lack of access to medical treatments and providers.

The worldwide prevalence of glaucoma is increasing. This is due in part to the rapidly aging population. Vision loss from glaucoma greatly impacts the independence of many people who are part of this aging population. In addition to the impact glaucoma has on personal lives, there is an increasing economic burden on society.

Paediatric glaucoma can be present at birth (congenital), is more common in populations with a high level of blood relatives (consanguinity) and is associated with certain gene mutation types. Paediatric glaucoma levels are as high as 1 in 1250 persons in the Gypsy populations of Slovakia and as low as 1 in 18,500 to 1 in 30,000 in Western populations. Levels also tend to be higher in the developing world due to consanguinity. Paediatric glaucoma can lead to blindness if left untreated.

VI.2.2 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 your eye, eventually affecting your eye sight. Latanoprost is also used to treat increased eye pressure and glaucoma in all ages of children and babies.

Latanoprost has also been demonstrated to be effective in lowering eye pressure in short term studies conducted in paediatric patients.

The safety and efficacy of latanoprost in adult patients with elevated eye pressure is supported by more than 13 years of clinical experience.

VI.2.3 Unknowns relating to treatment benefits

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

- **Pregnant and breast-feeding women**;

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, latanoprost should not be used during pregnancy. Latanoprost and its

metabolites may pass into breast milk and latanoprost should therefore not be used in breast-feeding women or breast feeding should be stopped.

VI.2.4 Summary of safety concerns

Important identified risks

Important identified risks		
Risk	**What is known**	**Preventability**
Safety concern in lay language ***(medical term)***	**Brief summary in lay language**	**Whether risk can be minimised or mitigated, and how**
Allergic reaction *(Conjunctival hyperaemia)*	Eye irritation (a feeling of burning, grittiness, itching, stinging or the sensation of a foreign body in the eye).The ocular side effect appears to occur via a secondary, unrelated mechanism.	If you experience eye irritation severe enough to make your eyes water excessively, or make you consider stopping this medicine, talk to your doctor, pharmacist or nurse promptly (within a week). You may need your treatment to be reviewed to ensure you keep receiving appropriate treatment for your condition.
Increase of the length, thickness, colour and/or number of the eyelashes that may cause unusual hair growth on the eyelids. *(Eyelash and vellous hair changes)*	Hypertrichosis or increased lash length, pigmentation, or thickness is a relatively common side-effect of prostaglandin use. This side-effect does not have particularly deleterious pshysicological effects on the patients.	These changes are solely cosmetic in nature. However, an ophthalmologist should be consulted.
Darkening of the skin around the eyes. *(Periorbital skin discolouration)*	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 latanoprost.
Change in the colour of iris (the coloured part of the eye).	Up to 10 % of patients develop darkening of the eye. This can lead to differences in the appearance of the eyes, if only	These changes are solely cosmetic in nature, and have not posed a health risk in any form.

(Iris hyperpigmentation)	one eye is treated. A predisposing condition for this risk is a mixed iris colour. The change in eye colour is likely to be permanent.	However, an ophthalmologist should be consulted.
Inflammation or irritation of the surface of the eye. *(Keratitis herpetic)*	Latanoprost should be used with caution in patients with a history of inflammation or irritation of the surface of the eye, and should be avoided in cases of active herpetic infection and in patients with a history of recurrent herpetic infectionsspecifically associated with prostaglandin analogues.	Before prescribing antiglaucoma prostaglandin analogue the healthcare professional should take careful history of any previous herpetic infection.

Important potential risks	
Risk	**What is known (Including reason why it is considered a pote ntial risk)**
Cystoid macular oedema	Macular oedema (fluid collection under the eye) has occurred m ainly in patients with no lens in the eye , in patients withimplant ed lens, or in patients with known risk factors for cystoid macul ar oedema (such as diabetic retinopathy (damage to the eye due to diabetes) and retinal vein occlusion). Latanoprost should be u sed with caution in the above patients.
Aggravation of asthma	There is limited experience from patients with respiratory disor ders, mainly with asthma, but some cases of exacerbation of ast hma and/or dyspnoea were reported in post marketing e xperience.

Missing information	
Risk	**What is known**
Ocular tolerability in paediatric population	Latanoprost may cause eye irritation. Patients who already have medical conditions affecting the cornea may be more susceptible to develop irritation.
Long-term safety in paediatric patients (including ocular developmental and neurodegenerative events, hyperpigmentation changes in the eye, and corneal endothelial function/corneal thickness)	There is limited information on the long term effect of latanoprost in paediatric patients.

Limited information on drug interactions in adult and paediatric patients	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. *Paediatric population* Interaction studies have only been performed in adults.
Use in pregnant and lactating women	*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, latanoprost should not be used during pregnancy. *Lactation* Latanoprost and its metabolites may pass into breast milk and latanoprost should therefore not be used in breast-feeding women or breast feeding should be stopped.

VI.2.5 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 the package leaflet (PL). The measures in these documents are known as routine risk minimisation measures.

This medicine has no additional risk minimisation measures.

VI.2.6 Planned post authorisation development plan

Not applicable

VI.2.7 Summary of changes to the risk management plan over time

Version	Date	Safety concerns	Change
1.0	27.04.2017	**Important identified risks** • Hypersensitivity • Eyelash and vellus hair changes • Periorbital skin discolouration • Iris hyperpigmentation • Keratitis herpetic • Cystoid macular oedema	Initial version

		• Respiratory disorders • Cardiac disorders • Iritis/Uveitis **Important potential risks** • Ocular and cutaneous melanoma • Risk of ocular overdose • Off-label use (cosmetic use for stimulation of eyelash growth) **Missing information** • Ocular tolerability in paediatric population • Long-term safety in paediatric population • Limited information on drug interactions in adult and paediatric patients • Use in pregnant and lactating women	
1.0	29.08.2017	**Important identified risks** • Conjunctival hyperaemia • Eyelash and vellus hair changes • Periorbital skin discoloration • Iris hyperpigmentation • Keratitis herpetic **Important potential risks** • Cystoid macular oedema • Aggravation of asthma • Ocular and cutaneous melanoma **Missing information** • Ocular tolerability in paediatric population • Long term safety in paediatric patients (including ocular • developmental and neurodegenerative events, hyperpigmentation • changes in the eye, and corneal endothelial function/corneal thickness) • Limited information on drug interactions in adult and paediatric • patients • Use in pregnant and lactating women	RMP update in response to day70 RMS Asssessment report
1.0	22.03.2018	**Important identified risks** • Conjunctival hyperaemia • Eyelash and vellus hair changes	RMP update in response to day120 RMS Asssessment report

		• Periorbital skin discoloration • Iris hyperpigmentation • Keratitis herpetic **Important potential risks** • Cystoid macular oedema • Aggravation of asthma **Missing information** • Ocular tolerability in paediatric population • Long term safety in paediatric patients (including ocular • developmental and neurodegenerative events, hyperpigmentation • changes in the eye, and corneal endothelial function/corneal thickness) • Limited information on drug interactions in adult and paediatric • patients Use in pregnant and lactating women	