VI.2 Elements for a public summary

VI.2.1 Overview of disease epidemiology

Ocular hypertension (OHT) is elevated eye pressure in the absence of visual field loss or glaucomatous optic nerve damage. It is estimated that 3% to 5% of those over 40 years have OHT. OHT represents a major risk for future development of chronic open angle glaucoma (COAG) with visual damage.[1]

Glaucoma is a group of ocular diseases characterized (but not defined) by elevated intraocular pressure (IOP) and possible optic nerve damage and is the leading cause of irreversible blindness in the world. The types of glaucoma are classified according to the reason for poor aqueous humor outflow into three broad categories: Open-angle glaucoma accounts for approximately 90% of all glaucoma cases, while angle-closure glaucoma and congenital glaucoma each contributes approximately 5% of cases.[2]

Four major risk factors for developing primary open-angle glaucoma include advanced age, black race, family history of glaucoma, and elevated IOP, the only risk factor amenable to therapy which can protect against further optic nerve damage and vision loss.[2]

Sixty-seven million persons globally, of whom 25 million live in Europe, are affected by glaucoma. It has been estimated that 12.3% of the worldwide population and 21.8% of European adults (including 18% of those over 50 years of age) have been diagnosed with glaucoma. Overall, glaucoma is responsible for 5.2 million cases of blindness (15% of global blindness).[3]

Childhood glaucoma is an unusual eye disease and significant cause of childhood blindness. The multiple potential causes fall into one of two categories and may be primary or secondary to some other disease process. Primary congenital glaucoma results from abnormal development of the ocular drainage system. It occurs in about 1 out of 10,000 births in the United States and is the most common form of glaucoma in infants. Secondary glaucomas result from disorders of the body or eye and may or may not be genetic. Both types may be associated with other medical diseases.[4]

VI.2.2 Summary of treatment benefits

Travoprost Zentiva contains the active substance travoprost and is available as 40 micrograms/ml eye drops, solution. Travoprost Zentiva is a 'generic medicine'. This means that it is similar to a 'reference medicine' already authorised in the European Union (EU) called Travatan.

Because Travoprost Zentiva is a generic medicine, its benefits and risks are taken as being the same as the reference medicine. Studies in people have been limited to tests to determine that it is bioequivalent to the reference medicine, Travatan. Two medicines are bioequivalent when they produce the same levels of the active substance in the body.

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[1] NICE, „Glaucoma: Diagnosis and management of chronic open angle glaucoma and ocular hypertension," 2009.
[2] Available from: http://www.thomsonhc.com/micromedex2/librarian/ND_T/evidencexpert/ND_PR/evidencexpert/CS/8E6F7E/ND_AppProduct/evidencexpert/DUPLICATIONSHIELDSYNC/3132D6/ND_PG/evidencexpert/ND_B/evidencexpert/ND_P/evidencexpert/PFActionId/evidencexpert.IntermediateToDocumentLink?docId=3053&contentSetId=50&title=DRUG+THERAPY+OF+GLAUCOMA&servicesTitle=DRUG+THERAPY+OF+GLAUCOMA&topicId=null, (accessed on 20/02/2013)
[3] Z. E. Prokofyeva E, „Epidemiology of Major Eye Diseases Leading to Blindness in Europe: A Literature Review," *Ophtalmic Research*, 2012; 47:171-188.
[4] Available from: https://www.glaucomafoundation.org/childhood_glaucoma.htm, (accessed on 14/08/2015)

VI.2.3 Unknowns relating to treatment benefits

There is a lack of data on safety and efficacy of travoprost in children below 2 months.

VI.2.4 Summary of safety concerns

Important identified risks

Risk	What is known	Preventability
Swelling of a yellow central area of the retina (Macular oedema)	Travoprost treatment may cause swelling of a yellow central area of the retina.	In patients with absence of the lens of the eye or in patients with known risk factors for swelling of the yellow central area of the retina, Travoprost can be used with caution.
Darkening of an area of the skin or coloured part of the eye (Hyperpigmentation)	Travoprost may change the colour of iris (the coloured part of the eye). This change may be permanent. A change in the colour of the skin around the eye may also occur.	Unknown
Abnormal amount of hair/ eyelashes growth (Hypertrichosis)	Travoprost may increase the length, thickness, colour and/or number of your eyelashes. Changes in the eyelids including unusual hair growth or in the tissues around the eye have also been observed.	Unknown
Inflammation inside the eye (Iris and uveal inflammations)	Travoprost treatment may cause inflammation inside eye.	In patients with known risk factors for eye inflammation or current or previous history of an eye inflammation (iritis and uveitis), consultation with doctor is advised.
Disorders affecting activity of heart and vessels (Cardiac and vascular disorders)	Travoprost can affect the activity of heart and vessels.	After using the medicine, patients are advised to press a finger into the corner of the eye, by the nose. This helps to stop the medicine getting into the rest of the body.
Disorders affecting breathing (Respiratory disorders)	Travoprost may rarely cause breathlessness or wheezing or increase the symptoms of asthma.	After using the medicine, patients are advised to press a finger into the corner of the eye, by the nose. This helps to stop the medicine getting into the rest of the body.
Increased allergic symptoms (Hypersensitivity reactions)	Travoprost drops contain a preservative (benzalkonium chloride) that has been reported to cause increased allergic	Patient should avoid the use of the medicine when allergic to the active substance or to any of the excipients.

Risk	What is known	Preventability
	symptoms. Also some other ingredients of the medicine can cause irritation.	

Important potential risks

Risk	What is known (Including reason why it is considered a potential risk)
Cancer of the dark pigment producing cells located in eye and skin (Melanoma)	The long term effects of Travoprost on the cells producing dark pigment in the eye and in the skin are currently unknown.
Corneal damage due to use of preserved eye drops (Corneal damage due to use of preserved eye drops)	There is a preservative in this medicine (benzalkonium chloride) that has been reported to cause corneal damage due to long term use.
Use during pregnancy and breast-feeding (Use during pregnancy and lactation)	Travoprost has harmful effects on pregnancy and/or the foetus/new-born child and should not be used during pregnancy unless clearly necessary. Travoprost must not be used in woman of child bearing potential unless adequate contraceptive measures are in place. Travoprost is not recommended for mothers who are breast-feeding, because no information is available about its safety profiles during breast-feeding

Missing information

Risk	What is known
Use in children below the age of 2 months	There is lack of knowledge whether the use of travoprost is safe and effective in children below the age of 2 months.
Influence on together administered drugs (Potential interactions)	There is no information whether administration of other medicinal products has harmful effect on the patient.

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.

<u>This medicine has no additional risk minimisation measures</u>

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	Comment
1.0	21/ 02/ 2013	Important identified risks: - Eye pigmentation Important potential risks: - Punctate keratopathy and/or toxic ulcerative keratopathy Missing information: - Safety in patients below age of 18 years	Initial version of the RMP
2.0	11/07/2013	The same as in version 1.0	Update due to comments that resulted from the procedure DK/H/2287/001/DC - Travoprost. Based on assessor comments part VI 2.2 of RMP was rewritten in layman language.
2.0A	06/01/2014	The same as in version 1.0	Update due to comments that resulted from the procedure DK/H/2287/001/DC - Travoprost. Based on assessor comments part VI 2.2 of RMP was rewritten in layman language.
3.0	26/02/2014	Important identified risks: - Macular oedema - Hyperpigmentation - Hypertrichosis - Iris and uveal inflammation - Cardiac and vascular disorders - Respiratory disorders Important potential risks: - Corneal damage and hypersensitivity due to long term use of preserved eye drops - Ocular and skin melanomas - Use during pregnancy and lactation	Update due to comments that resulted from the procedure DK/H/2287/001/DC - Travoprost. Harmonisation of safety concerns with the reference product (Travatan).

Version	Date	Safety Concerns	Comment
		Missing information: - Potential interactions	
4.0	19/08/2015	Important identified risks: - Macular oedema - Hyperpigmentation - Hypertrichosis - Iris and uveal inflammations - Cardiac and vascular disorders - Respiratory disorders - Hypersensitivity reactions Important potential risks: - Melanoma - Corneal damage due to use of preserved eye drops - Use during pregnancy and lactation Missing information: - Use in children below the age of 2 months - Potential interactions	Extension of indication on paediatric population: Decrease of elevated intraocular pressure in paediatric patients aged 2 months to < 18 years with ocular hypertension or paediatric glaucoma. Harmonisation of safety concerns with the reference product (Travatan).
4.1	19/10/2015	Same as in version 4.0	Correction of RA data in Product overview