VI.2 Elements for a Public Summary

BIMATOPROST/TIMOLOL 0.3 mg/ml + 5 mg/ml eye drops, solution

VI.2.1 Overview of disease epidemiology

Glaucoma causes irreversible defects in the visual field. This optic neuropathy is progressive and, if left untreated, can lead to vision loss or even blindness. It is a leading cause of blindness world-wide, affecting 2 % of individuals of European descent and up to 10% of individuals of sub-Saharan African descent over 50 years of age. Data from recent population-based surveys indicate that one in 40 adults older than 40 years has glaucoma with loss of visual function, which equates to 60 million people worldwide being affected and

8.4 million being bilaterally blind. As the population increases, so does the absolute number of glaucoma sufferers. In addition, with glaucoma prevalence increasing exponentially with age, glaucoma numbers are rising with the rapidly aging population. Accordingly, glaucoma patients are estimated to rise in number from 60 million in 2010 to nearly 80 million in 2020, with more than half in developed societies remaining undiagnosed.

VI.2.2 Summary of treatment benefits

Bimatoprost/Timolol 0.3 mg/ml + 5 mg/ml eye drops, solution contains two active substances, bimatoprost and timolol, which lower the pressure in the eye in different ways. Bimatoprost is a prostaglandin analogue, (a copy of the natural substance prostaglandin) that works by increasing the drainage of fluid out of the eye. Timolol is a beta-blocker that works by reducing the production of fluid within the eye. Timolol has been commonly used to treat glaucoma since the 1970's. The combination of the two active substances has an additive effect, reducing the pressure inside the eye more than either medicine alone.

VI.2.3 Unknowns relating to treatment benefits

The efficacy of bimatoprost/timolol in children below 18 years of age has not been established. There are also no adequate data from the use of the bimatoprost / timolol fixed combination in pregnant or breastfeeding women.

VI.2.4 Summary of safety concerns

Important identified risks

Risk	**What is known**	**Preventability**
Darkening of the iris (Iris hyperpigmentation)	Up to 1 % of patients develop iris darkening due to an increase in iris pigmentation. This can lead to differences in the appearance of the eyes, especially if only 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.	Treatment with the lowest therapeutically effective dose and for the shortest recommended period, if possible.
Inflammation of the cornea	Bimatoprost/Timolol can	Talk to your doctor or

with discrete opacities, without ulceration (Punctate keratitis)	cause inflammation of the cornea with discrete opacities, without ulceration. The eyes might become red, watery, and sensitive to light, and vision may somewhat decrease. Most patients recover fully.	pharmacist before using Bimatoprost/Timolol if you: • have had a cataract surgery in the past, • have dry eyes, have or have had any problems with the cornea (front transparent part of the eye), • wear contact lenses, • have had a viral infection or inflammation of the eye. Patients should not use bimatoprost if they have had to stop using eye drops in the past because of a side effect of the preservative benzalkonium chloride. If patients get any side effects, they should talk to their doctor or pharmacist.
Acute asthma and asthmatic symptoms	Breathing difficulties in patients with asthma have been reported following the administration of some beta-blockers (group of drugs that timolol belongs to) in the eye.	Bimatoprost/Timolol eye drops should not be used in patients who have or have had respiratory problems such as asthma, severe chronic obstructive bronchitis (severe lung disease which may cause wheeziness, difficulty in breathing and/ or long-standing cough).
Slow heart rate (Bradycardia)	Slow heart rate has been reported in patients who have heart and blood vessel problems.	This medicine should be given with caution in patients who have heart and blood vessel problems, as the medicine could cause further problems with the heart and blood pressure.

Important potential risks

Risk	**What is known** **(Including reason why it is considered a potential risk)**
Cardiovascular events (angina, hypotension, atrial	Patients with cardiovascular diseases (e.g. coronary heart disease, angina and cardiac failure) and those on therapy

fibrillation/arrhythmias, congestive heart failure)	with beta-blockers (e.g. bisoprolol) should be critically assessed. Patients with cardiovascular diseases should be watched for signs of deterioration and for adverse reactions. Patients with severe peripheral circulatory disturbance/disorders (i.e. severe forms of Raynaud's disease or Raynaud's syndrome) should be treated with caution.
Separation of one of the layers within the eyeball (Choroidal detachment)	Separation of one of the layers within the eyeball after surgery to reduce the pressure in the eye (choroidal detachment) has been reported with administration of aqueous suppressant therapy (e.g. timolol, acetazolamide).
Swelling of the retina within the eye leading to worsening vision (Cystoid macular oedema)	Swelling of the retina within the eye leading to worsening vision (cystoid macular oedema) is a known risk factor reported with Bimatoprost/Timolol treatment. Therefore, Bimatoprost/Timolol eye drops should be used with caution, e.g. after intraocular surgery.
Drug interaction with calcium channel blockers, guanethidine, beta-adrenergic blocking agents, para-sympathomimetcs, anti-arrhythmics, digital glycosides, mydriatic agents and CYP2D6 inhibitors	Bimatoprost/Timolol can affect or be affected by other medicines, including other eye drops for the treatment of glaucoma. Patients should be closely monitored if they are taking, have recently taken or might take any other medicines such as medicines to lower blood pressure, heart medicine, medicines to treat diabetes, quinidine (used to treat heart conditions and some types of malaria) or medicines to treat depression known as fluoxetine and paroxetine.

Missing information

Risk	**What is known**
Exposure in paediatric patients	The safety and efficacy of bimatoprost/timolol in children below 18 years of age has not been established. No data are available.

Exposure in pregnancy and lactation	There are no adequate data from the use of the bimatoprost / timolol fixed combination in pregnant women. BIMATOPROST/TIMOLOL should not be used during pregnancy unless clearly necessary. *Bimatoprost* It is not known if bimatoprost is excreted in human breast milk but it is excreted in the milk of the lactating rat. BIMATOPROST/TIMOLOL should not be used by breast-feeding women. *Timolol* Beta-blockers are excreted in breast milk. However, at therapeutic doses of timolol in eye drops it is not likely that sufficient amounts would be present in breast milk to produce clinical symptoms of beta-blockade in the infant.

VI.2.5 Summary of risk minimisation measures by safety concern

All medicines have a Summary of Product Characteristics (SPC) 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

No post-authorisation studies have been imposed or are planned.

VI.2.7 Summary of changes to the Risk Management Plan over time
Not applicable.