VI.2 Elements for a Public Summary

[BRINZOLAMIDE] 10 mg/ml eye drops, suspension

VI.2.1 Overview of disease epidemiology

The term **ocular hypertension** usually refers to any situation in which the pressure inside the eye, called intraocular pressure, is higher than normal. Eye pressure is measured in millimeters of mercury (mm Hg). Normal eye pressure ranges from 10-21 mm Hg. Ocular hypertension is an eye pressure of greater than 21 mm Hg. Ocular hypertension should not be considered a disease by itself. Instead, ocular hypertension is a term that is used to describe individuals who should be observed more closely than the general population for the onset of glaucoma.

Recent data on people with ocular hypertension from the Ocular Hypertension Treatment Study have shown that they have an average estimated risk of 10% of developing glaucoma over 5 years. This risk may be decreased to 5% (a 50% decrease in risk) if eye pressure is lowered by medications or laser surgery. However, the risk may become even less than 1% per year because of significantly improved techniques for detecting glaucomatous damage.

Glaucoma is the second leading cause of blindness in the world (after cataracts) and the leading cause of blindness among African-Americans. **Open-angle glaucoma** is the most common type of glaucoma among populations of European or African descent, whereas angle-closure glaucoma is more common among populations of Asian descent. It is estimated that there are 44.7 million people with open-angle glaucoma worldwide in 2010, and that this number will increase to 58.6 million in 2020. It is estimated that there are 2.8 million people with open-angle glaucoma in the United States (US) in 2010, and that the number will increase to 3.4 million in 2020.

The Barbados Eye Study found ocular hypertension present more frequently in women. Mean intraocculr pressure (IOP) slowly rises with increasing age. Age older than 40 years is considered a risk factor for the development of ocular hypertension and primary open-angle glaucoma (POAG). Black subjects had almost 3 times the age-adjusted prevalence of glaucoma than white subjects.

VI.2.2 Summary of treatment benefits

[Brinzolamide] is indicated to decrease elevated intraocular pressure in:

• ocular hypertension

• open-angle glaucoma

as monotherapy in adult patients unresponsive to beta-blockers or in adult patients in whom beta-blockers are contraindicated, or as adjunctive therapy to beta-blockers or prostaglandin analogues.

Intraocular pressure can be lowered with medication, usually eye drops. Several different classes of medications are used to treat glaucoma, with several different medications in each class.

Each of these medicines may have local and systemic side-effects.

Brinzolamide is a carbonic anhydrase inhibitor. Many studies have been performed, following first marketing authorisation of brinzolamide eyes drop suspension to evaluate safety and efficacy of its use as monotherapy and/or as adjuctive treatment. Brinzolamide was primarily evaluated in concomitant administration with timolol during adjunctive glaucoma therapy.

Additionally the IOP-reducing effect of brinzolamide as adjunctive therapy to the prostaglandin analogue travoprost has been studied.

VI.2.3 Unknowns relating to treatment benefits

Brinzolamide has not been studied in patients with hepatic impairment and is therefore not recommended in such patients. The safety and efficacy of brinzolamide in infants, children and adolescents aged 0 to 17 years has not been established. Brinzolamide has not been studied in pre-term infants (less than 36 weeks gestational age) or those less than 1 week of age. Brinzolamide has not been studied in patients with narrow-angle glaucoma and its use is not recommended in these patients. Brinzolamide has not been studied in patients wearing contact lenses.

There are no or limited amount of data from the use of ophthalmic brinzolamide in pregnant women. Studies in animals have shown reproductive toxicity following systemic administration.

[Brinzolamide] is not recommended during pregnancy and in women of childbearing potential not using contraception.It is unknown whether brinzolamide/metabolites are excreted in human milk following topical ocular administration. Animal studies have shown the excretion of minimal levels of brinzolamide in breast milk following oral administration. A risk to the newborns/infants cannot be excluded. A decision must be made whether to discontinue breast-feeding or to discontinue/abstain from [Brinzolamide] therapy taking in to account the benefit of breast-feeding for the child and the benefit of therapy for the woman.

VI.2.4 Summary of safety concerns

Important identified risks

Risk	What is known	Preventability
Disease of the surface layer of the eye with sore eye and blurred vision (Corneal decompensation)	Corneal oedema is manifested by blurred vision or visual disturbances (halos or rainbows around streetlights, headlights and other bright lights at night). If corneal edema progresses, symptoms may include blisters that form on the surface of the eye. These can rupture and become painful, and also cause sensitivity to light.	Treatment should immediately discontinued and a physician should be advised as the disorder can eventually cause corneal nerves to rupture, resulting in severe pain
A condition that occurs when the body produces too much acid or when the kidneys are not removing enough acid from the body. (Metabolic acidosis)	Risk of metabolic acidosis may be increased in patients with renal impairment, diabetes and other underlying conditions.	A pH under 7.1 is an emergency, due to the risk of cardiac arrhythmias, and may warrant treatment with intravenous bicarbonate. If the acidosis is particularly severe and/or there may be intoxication, consultation with the nephrology team is considered useful, as dialysis may clear both the intoxication and the acidosis.

Important potential risks

Risk	What is known (Including reason why it is considered a potential risk)
Interaction with ocular hypotensive agents	Co-administration of brinzolamide with products used to lower intraocular pressure may increase the frequency of non-serious ocular adverse reactions (e.g. local irritation signs).
Cardiovascular disorders	Depending on the cardiovascular disorder its frequency might be uncommon (cardio-respiratory distress, bradycardia, palpitations), rare (angina pectoris, heart rate irregular) or not known (arrhythmia, tachycardia, hypertension, blood pressure increased, blood pressure decreased, heart rate increased).
Interaction with oral carbonic anhydrase inhibitors (CAIs)	There is a potential for an additive effect on the known systemic effects of carbonic anhydrase inhibition in patients receiving an oral carbonic anhydrase inhibitor and brinzolamide. The concomitant administration of brinzolamide and oral carbonic anhydrase inhibitors has not been studied and is not recommended.
Interaction with salicylates	There have been rare reports of serious drug interactions (resulting in serious problems) in people taking high-dose salicylates and oral carbonic anhydrase inhibitors. Salicylates should not be administered with carbonic anhydrase inhibitors, such as brinzolamide, being administered orally or topically

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.