Professional Information

SCHEDULING STATUS

S4

1. NAME OF THE MEDICINE

OPTENSIN eye drops, solution

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

1 ml solution contains bimatoprost 0,3 mg.

Excipients with known effect:

Benzalkonium chloride 0,005 % *w/v*.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Eye drops, solution.

The solution is a clear, colourless liquid, free from particles.

pH: 6,8 – 7,8; Osmolality: 260 – 330 mOsmol/kg

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

OPTENSIN is indicated for the reduction of elevated intraocular pressure in chronic open-angle glaucoma and ocular hypertension in adults, as monotherapy or as adjunctive therapy to beta-blockers.

4.2 Posology and method of administration

Posology

Adults

The recommended dose is one (1) drop of OPTENSIN in the affected eye(s) once daily, administered in the evening, when used as monotherapy or as adjunctive therapy. The once daily dose should not be exceeded as more frequent administration may reduce the intraocular pressure lowering effect.

To prevent contamination of the dropper tip and solution, care should be taken not to touch the eyelids, surrounding areas or other surfaces with the dropper tip of the bottle during administration.

Special populations

Elderly

No dosage adjustment is required in elderly patients.

Hepatic and renal impairment

OPTENSIN should be used with caution in patients with renal and moderate to severe hepatic impairment. Bimatoprost 0,03 % has had no adverse effect on liver function over 24 months in patients with a history of mild liver disease or abnormal ALT, AST and/or bilirubin at baseline.

Paediatric population

It is not recommended to use OPTENSIN in children or adolescents, as the safety and efficacy has not been established in children aged 0 to 18 years old.

Method of administration

For ophthalmic use.

The screwcap should be removed before use.

Contact lenses should be removed before instillation of the eye drops and may be reinserted after 15 minutes (see section 4.4).

If more than one topical ophthalmic medicine is being used, the medicines should be administered at least five minutes apart.

When using nasolacrimal occlusion or closing the eyelids for 2 minutes, the systemic absorption is reduced. This may result in a decrease in systemic side effects and an increase in local activity.

4.3 Contraindications

- Hypersensitivity to the active substance(s) or to any of the excipients listed in section 6.1.

4.4 Special warnings and precautions for use

Ocular

Prior to treatment initiation, patients should be informed of the of the possibility of prostaglandin analogue periorbitopathy (PAP) and increased iris pigmentation. Some of these changes may be permanent and may result in appearance differences between the eyes when only one eye is treated (see section 4.8).

During treatment with OPTENSIN, gradual increased eyelash growth (lengthening, darkening and thickening) and darkening of the eyelid skin, with no consequent untoward ocular effects, may occur. Increased iris pigmentation (darkening) may also occur.

Increased iris pigmentation is likely to be permanent.

Cystoid macular oedema has been reported following treatment with 0,03 % bimatoprost. OPTENSIN should therefore be used with caution in patients with known risk factors for macular oedema (e.g. aphakic patients, pseudophakic patients with a torn posterior lens capsule), intraocular surgery, retinal vein occlusions, ocular inflammatory disease and diabetic retinopathy.

OPTENSIN should be used with caution in patients with active intraocular inflammation (e.g. uveitis) because the inflammation may be exacerbated.

There have been spontaneous reports of reactivation of previous corneal infiltrates or ocular infections with bimatoprost 0,3 mg/ml eye drop solution. OPTENSIN should be used with caution in patients with a history of significant ocular viral infections (e.g. herpes simplex) or uveitis/iritis.

There have been reports of bacterial keratitis linked to the use of multiple dose containers of topical ophthalmic products. These containers had been contaminated unintentionally by patients who, in most cases, had a concurrent ocular disease. Patients with disruption of the ocular epithelial surface are at greater risk of developing bacterial keratitis.

Patients should be instructed to avoid allowing the tip of the dispensing container to contact the eye or surrounding structures, to avoid eye injury and contamination of the solution.

There is no data regarding use in patients with inflammatory ocular conditions; or in the following types of glaucoma: neovascular, inflammatory, angle-closure glaucoma, congenital, or narrow-angle glaucoma.

Skin

There is a potential for hair growth to occur in areas where the eye drop solution comes into contact with the skin surface repeatedly. Thus, it is important to use OPTENSIN as instructed and to avoid contact with the cheeks or other skin areas.

Respiratory disorders

There is no data regarding use in patients with compromised respiratory function. While there is limited information available on patients with a history of asthma or COPD, there have been reports of exacerbation of asthma, dyspnoea and COPD, as well as reports of asthma. The frequency of these symptoms is unknown. Patients with COPD, asthma or compromised respiratory function due to other conditions should be treated with caution.

Cardiovascular

There is no data available regarding use in patients with heart block more severe than first degree or uncontrolled congestive heart failure. There have been a limited number of spontaneous reports of bradycardia or hypotension with bimatoprost 0,3 mg/ml eye drop solution and OPTENSIN should be used with caution in patients predisposed to low heart rate or low blood pressure.

Preservative - Benzalkonium chloride

As the possibility of adverse effects on the corneal permeability, and the danger of disruption of the corneal epithelium with prolonged or repeated usage of benzalkonium chloride preserved ophthalmological preparations, cannot be excluded, regular ophthalmological examination is required.

Caution should be exercised in the use of benzalkonium chloride preserved topical

medication over an extended period in patients with extensive ocular surface disease.

Benzalkonium chloride has been reported to cause punctate keratopathy and/or toxic ulcerative keratopathy. Therefore, monitoring is required with frequent or prolonged use of OPTENSIN in dry eye patients or where the cornea is compromised.

Contact lenses

OPTENSIN contains benzalkonium chloride as a preservative, which may cause eye irritation and be absorbed by soft contact lenses. Contact lenses must be removed prior to instillation of OPTENSIN and may be reinserted 15 minutes following administration. Furthermore, benzalkonium chloride is known to discolour soft contact lenses and contact with soft contact lenses must be avoided.

Other information

It has been shown that more frequent exposure of the eye to more than one dose of bimatoprost daily may decrease the IOP-lowering effect. Patients using OPTENSIN with other prostaglandin analogues should be monitored for intraocular pressure changes.

Paediatric population

Safety and effectiveness in children have not been established.

4.5 Interactions with other medicines and other forms of interaction

No interactions are expected in humans, since systemic concentrations of bimatoprost are extremely low (less than 0,2 ng/ml) following ocular dosing.

Even though bimatoprost is biotransformed by multiple enzymes and pathways, there are no known effects on hepatic medicine metabolising enzymes.

Bimatoprost eye drops have been used concurrently with a number of different ophthalmic beta-blocking medicines without evidence of interactions.

Concurrent use of bimatoprost eye drops and antiglaucomatous medicines other than topical beta-blockers has not been evaluated during adjunctive glaucoma therapy.

There is a potential for the IOP-lowering effect of prostaglandin analogues, like OPTENSIN, to be reduced in patients with glaucoma or ocular hypertension when used with other prostaglandin analogues.

4.6 Fertility, pregnancy and lactation

Pregnancy

The safety of OPTENSIN during pregnancy has not been established and should not be used during pregnancy.

Breastfeeding

The safety of OPTENSIN during lactation has not been established. OPTENSIN should not be used by breastfeeding mothers as it is unknown whether OPTENSIN is excreted into breastmilk.

Fertility

There are no data on the effects of OPTENSIN on human fertility.

4.7 Effects on ability to drive and use machines

OPTENSIN has negligible influence on the ability to drive and operate machinery. As with any ocular treatment, if transient blurred vision occurs at instillation, the patient should wait

until their vision clears before driving or operating machinery.

It is not always possible to predict to what extent OPTENSIN may interfere with the daily activities of a patient. Patients should ensure that they do not engage in the above activities until they are aware of the measure to which OPTENSIN affects them.

4.8 Undesirable effects

a. Summary of the safety profile

The most common side effects are growth of eyelashes, conjunctival hyperaemia and ocular pruritis.

b. Tabulated summary of adverse reactions

System Organ Class	Frequency	Adverse Event
Infections and infestations	Less frequent	Infection, primarily colds and upper respiratory tract infections.
Immune system disorders	Frequency unknown	Hypersensitivity reactions including signs or symptoms allergic dermatitis and eye allergy.
Nervous system disorders	Frequent	Headache.
	Less frequent	Dizziness.
Eye disorders	Frequent	Conjunctival hyperaemia, ocular pruritus, growth of eyelashes, superficial punctate keratitis, corneal erosion, ocular burning, ocular irritation, allergic conjunctivitis, blepharitis, worsening of visual acuity,

		asthenopia, cataract, conjunctival oedema, foreign body sensation, ocular dryness, eye pain, photophobia, tearing, eye discharge, visual disturbance/blurred vision, increased iris pigmentation, eyelash darkening and prostaglandin analogue periorbitopathy (PAP).
	Less frequent	Retinal haemorrhage, uveitis, cystoid macular oedema, iritis, blepharospasm, eyelid retraction, eyelid oedema and periorbital erythema.
	Frequency unknown	Ocular discomfort.
Vascular disorders	Frequent	Hypertension.
Respiratory, thoracic and mediastinal disorders	Frequency unknown	Asthma, asthma exacerbation, COPD exacerbation and dyspnoea.
Gastrointestinal disorders	Less frequent	Nausea.
Skin and subcutaneous tissue disorders	Frequent	Eyelid erythema, eyelid pruritus and blepharal pigmentation.
	Less frequent	Eyelid oedema and hirsutism.
	Frequency unknown	Periocular skin pigmentation, Abnormal hair growth

General disorders and administration site conditions	Less frequent	Asthenia and peripheral oedema.
Investigations	Frequent	Liver function test abnormal.

c. Description of selected adverse reactions

Adverse reactions reported in phosphate containing eye drops

Cases of corneal calcification have been reported rarely with the use of phosphate containing eye drops in some patients with significantly damaged corneas.

Prostaglandin analogue periorbitopathy (PAP)

Prostaglandin analogues including OPTENSIN can induce periorbital lipodystrophic changes which can lead to deepening of the eyelid sulcus, ptosis, enophthalmos, eyelid retraction, involution of dermatochalasis and inferior scleral show. Changes are typically mild, can occur as early as one month after initiation of treatment with bimatoprost, and may cause impaired field of vision even in the absence of patient recognition. PAP is also associated with periocular skin hyperpigmentation or discoloration and hypertrichosis. All changes have been noted to be partially or fully reversible upon discontinuation or switch to alternative treatments.

Iris hyperpigmentation

Increased iris pigmentation is likely to be permanent. The pigmentation change is due to increased melanin content in the melanocytes rather than to an increase in the number of melanocytes. The long-term effects of increased iris pigmentation are not known. Iris colour changes seen with ophthalmic administration of bimatoprost may not be noticeable for several months to years. Typically, the brown pigmentation around the pupil spreads concentrically towards the periphery of the iris and the entire iris or parts become more brownish. Neither naevi nor freckles of the iris appears to be affected by the treatment. At 12 months, the incidence of iris pigmentation with bimatoprost was 1,5 % (see section 4.8)

and did not increase following 3 years treatment.

Adverse reactions reported in phosphate containing eye drops

Cases of corneal calcification have been reported very rarely in association with the use of phosphate containing eye drops in some patients with significantly damaged corneas.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare providers are requested to report any suspected adverse drug reactions to SAHPRA via the Med Safety APP (Medsafety X SAHPRA) and eReporting platform (who-umc.org) found on SAHPRA website.

4.9 Overdose

No cases of overdose have been reported, and it is unlikely to occur following ocular administration or to be associated with toxicity.

In the event of overdose, treatment should be symptomatic and supportive.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

A 15.4 Ophthalmic preparations – Others.

Pharmacotherapeutic group: Ophthalmologicals, prostaglandin analogues, ATC code: S01EE03.

Mechanism of action

Bimatoprost is a potent ocular hypotensive agent. It is a synthetic prostamide that is structurally related to prostaglandin F2α and does not act through any known prostaglandin receptors. Bimatoprost selectively mimics the effects of prostamides.

However, the prostamide receptor has not yet been structurally identified.

Bimatoprost reduces intraocular pressure (IOP) by increasing aqueous humour outflow through the trabecular meshwork and enhancing uveoscleral outflow.

Reduction of intraocular pressure starts approximately 4 hours after the first dose and the maximum effect is reached within approximately 8 to 12 hours with a duration of action of 24 hours.

Limited knowledge is available regarding the use of bimatoprost in patients with open-angle glaucoma with pseudo-exfoliative and pigmentary glaucoma, and chronic angle-closure glaucoma with patent iridotomy. Hence, no recommendation can be made.

No clinically relevant effects on heart rate and blood pressure have been observed during clinical trials.

Paediatric population

The safety and efficacy in children aged 0 to 18 years has not been established.

5.2 Pharmacokinetic properties

Absorption

Bimatoprost penetrates the human cornea and sclera well in vitro. The systemic exposure of bimatoprost is low with no accumulation over time following ocular administration.

Following once daily ocular administration of one drop of 0,03 % bimatoprost to both eyes for two weeks, blood concentrations peaks within 10 minutes after dosing and declines to below the lower limit of detection (0,025 ng/ml) within 1,5 hours after dosing.

Mean C_{max} and $AUC_{0\text{-}24hrs}$ values are similar on days 7 and 14 at approximately 0,08 ng/ml and 0,09 ng•hr/ml respectively, which indicates that a steady drug concentration is

reached during the first week of ocular dosing.

Distribution

Bimatoprost is moderately distributed into body tissues and the systemic volume of distribution in humans at steady-state is 0,67 l/kg.

Bimatoprost resides mainly in the plasma and the plasma protein binding of bimatoprost is approximately 88 %.

Biotransformation

Bimatoprost is not extensively metabolised in the human eye and is the major circulating component in the plasma once it reaches systemic circulation following ocular dosing. Subsequently, bimatoprost undergoes oxidation, N-deethylation and glucuronidation to form a diverse variety of metabolites.

Elimination

Bimatoprost is primarily eliminated by renal excretion. Up to 67 % of an intravenous dose is excreted in the urine, and 25 % of the dose is excreted via faeces. The elimination half-life, determined following intravenous administration, is approximately 45 minutes, and the total blood clearance is 1,5 l/hr/kg.

Characteristics in elderly patients

After twice daily dosing with 0,03 % bimatoprost, the mean $AUC_{0\text{-}24hr}$ value of 0,0634 ng•hr/ml bimatoprost in the elderly (subjects 65 years or older) were significantly higher than 0,0218 ng•hr/ml in young healthy adults. However, this finding is not clinically relevant as systemic exposure for both elderly and young subjects remained very low from ocular dosing. There was no accumulation of bimatoprost in the blood over time and the safety profile was similar in elderly and young patients.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Benzalkonium chloride

Citric acid monohydrate

Dibasic sodium phosphate heptahydrate

Purified water

Sodium chloride

Sodium hydroxide or hydrochloric acid (for pH adjustment)

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

Store at or below 25 ºC.

Shelf life: 3 years.

After opening of the eye drop container: 28 days (4 weeks).

6.4 Special precautions for storage

Once the bottle is opened the contents must be used within 28 days and may be stored at room temperature at or below 25 ºC.

KEEP OUT OF REACH OF CHILDREN.

6.5 Nature and contents of container

5 ml white LDPE bottles with white, tamper-proof HDPE screw cap and white LDPE dropper insert packed into a unit carton containing 1 bottle.

Each LDPE bottle contains 2,5 ml or 3 ml solution.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal of a used medicine or waste materials derived from such medicine and other handling of the product

Any unused product or waste material should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

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Sandton, 2031

South Africa.

Telephone number: +27 (0) 12 664 1965 / +27 (0) 10 594 5610.

8. MARKETING AUTHORISATION NUMBER(S)

54/15.4/0391.

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

30 June 2026.

10. DATE OF REVISION OF THE TEXT

Not applicable.