1-1.3.1 Summary of Product Characteristics

1. Name of the finished pharmaceutical product

ZACOMA (BIMATOPROST OPHTHALMIC SOLUTION 0.03% W/V)

2. Qualitative and quantitative composition

Composition:
Each ml contains:
Bimatoprost.....0.03% w/v
Benzalkonium chloride BP...0.005 % w/v
(As preservative)
Aqueous buffered vehicle.....Q.s.

3. Pharmaceutical form

EYE DROPS

4. Clinical particulars

4.1 Therapeutic indications
Bimatoprost Ophthalmic Solution 0.03% is indicated for the reduction of elevated intraocular pressure in patients with open angle glaucoma or ocular hypertension.

4.2 Posology and method of administration
To avoid contamination of the eye or eye drops do not allow the dropper tip to come into contact with any surface.

The recommended dosage is one drop in the affected eye(s) once daily in the evening. Bimatoprost Ophthalmic Solution 0.03% should not be administered more than once daily since it has been shown that more frequent administration of prostaglandin analogs may decrease the intraocular pressure lowering effect.

Reduction of the intraocular pressure starts approximately 4 hours after the first administration with maximum effect reached within approximately 8 to 12 hours.

Bimatoprost Ophthalmic Solution 0.03% may be used concomitantly with other topical ophthalmic drug products to lower intraocular pressure. If more than one topical ophthalmic drug is being used, the drugs should be administered at least five (5) minutes apart.

4.3 Contraindications
Bimatoprost Ophthalmic Solution 0.03% is contraindicated in patients with hypersensitivity to bimatoprost or to any of the ingredients

4.4 Special warnings and precautions for use
Pigmentation

Bimatoprost Ophthalmic Solution has been reported to cause changes to pigmented tissues. The most frequently reported changes have been increased pigmentation of the iris, periorbital tissue (eyelid) and eyelashes. Pigmentation is expected to increase as long as

bimatoprost is administered. The pigmentation change is due to increased melanin content in the melanocytes rather than to an increase in the number of melanocytes. After discontinuation of bimatoprost, pigmentation of the iris is likely to be permanent, while pigmentation of the periorbital tissue and eyelash changes have been reported to be reversible in some patients. Patients who receive treatment should be informed of the possibility of increased pigmentation. The long term effects of increased pigmentation are not known.

Iris color change 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 of the iris become more brownish. Neither nevi nor freckles of the iris appear to be affected by treatment. While treatment with Bimatoprost Ophthalmic Solution 0.03% can be continued in patients who develop noticeably increased iris pigmentation, these patients should be examined regularly.

Eyelash Changes

Bimatoprost Ophthalmic Solution 0.03% may gradually change eyelashes and vellus hair in the treated eye. These changes include increased length, thickness, and number of lashes. Eyelash changes are usually reversible upon discontinuation of treatment.

Intraocular Inflammation

Prostaglandin analogs, including bimatoprost, have been reported to cause intraocular inflammation. In addition, because these products may exacerbate inflammation, caution should be used in patients with active intraocular inflammation (e.g., uveitis).

Macular Edema

Macular edema, including cystoid macular edema, has been reported during treatment with Bimatoprost Ophthalmic Solution. Bimatoprost Ophthalmic Solution 0.03% should be used with caution in aphakic patients, in pseudophakic patients with a torn posterior lens capsule, or in patients with known risk factors for macular edema.

Bacterial Keratitis

There have been reports of bacterial keratitis associated with the use of multiple-dose containers of topical ophthalmic products. These containers had been inadvertently contaminated by patients who, in most cases, had a concurrent corneal disease or a disruption of the ocular epithelial surface.

Contact Lens Use

Bimatoprost Ophthalmic Solution 0.03% contains benzalkonium chloride, which may be absorbed by and cause discoloration of soft contact lenses. Contact lenses should be removed prior to instillation of bimatoprost ophthalmic solution 0.03% and may be reinserted 15 minutes following its administration.

4.5 Interaction with other medicinal products and other forms of interaction
It does not contain all possible drug interactions.

4.6 Fertility, pregnancy and lactation
Pregnancy

There are no adequate and well-controlled studies of Bimatoprost Ophthalmic Solution 0.03% administration in pregnant women. There is no increase in the risk of major birth defects or miscarriages based on bimatoprost postmarketing experience.

In embryofetal developmental studies, administration of bimatoprost in pregnant mice and rats during organogenesis, resulted in abortion and early delivery at oral doses at least 33 times (mice) or 94 times (rats) the human exposure at the recommended clinical dose (based on blood area under the curve [AUC] levels). These adverse effects were not observed at 2.6 times (mice) and 47 times (rats) the human exposure at the recommended clinical dose.

In pre/postnatal development studies, administration of bimatoprost to pregnant rats from organogenesis to the end of lactation resulted in reduced gestation length and fetal body weight, and increased fetal and pup mortality at oral doses at least 41 times the human systemic exposure at the recommended clinical dose (based on blood AUC levels). No adverse effects were observed in rat offspring at exposures estimated at 14 times the human exposure at the recommended clinical dose (based on blood AUC levels).

Because animal reproductive studies are not always predictive of human response Bimatoprost Ophthalmic Solution 0.03% should be administered during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Breastfeeding

Risk Summary

It is not known whether topical ocular treatment with Bimatoprost Ophthalmic Solution 0.03% could result in sufficient systemic absorption to produce detectable quantities in human milk. In animal studies, bimatoprost has been shown to be present in breast milk of lactating rats at an intravenous dose (i.e., 1 mg/kg) 324 times the RHOD (on a m 2g/m basis), however no animal data is available at clinically relevant doses.

The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for Bimatoprost Ophthalmic Solution, 0.03% and any potential adverse effects on the breastfed child from Bimatoprost Ophthalmic Solution, 0.03%.

4.7 Effects on ability to drive and use machines
Bimatoprost has minor influence on the ability to drive and use machines. Bimatoprost may cause transient blurring of vision, visual disturbance, fatigue and/or drowsiness which may impair the ability to drive or operate machines. The patient should wait until these symptoms have cleared before driving or using machinery.

4.8 Undesirable effects

The following adverse reactions are described elsewhere in the labeling:

- Pigmentation
- Eyelash Changes
- Intraocular Inflammation Macular Edema
- Hypersensitivity

4.9 Overdose

No information is available on overdosage in humans. If overdose with Bimatoprost Ophthalmic Solution, 0.03% occurs, treatment should be symptomatic.

In oral (by gavage) mouse and rat general toxicity studies, doses up to 100 mg/kg/day did not produce any toxicity. This dose expressed as mg/m2 is at least 70 times higher than the accidental dose of one bottle of Bimatoprost Ophthalmic Solution, 0.03% for a 10 kg child.

5. Pharmacological properties

5.1 Pharmacodynamic properties

Bimatoprost, a prostaglandin analog, is a synthetic structural analog of prostaglandin with ocular hypotensive activity. It selectively mimics the effects of naturally occurring substances, prostamides. Bimatoprost is believed to lower intraocular pressure (IOP) in humans by increasing outflow of aqueous humor through both the trabecular meshwork and uveoscleral routes. Elevated IOP presents a major risk factor for glaucomatous field loss. The higher the level of IOP, the greater the likelihood of optic nerve damage and visual field loss.

5.2 Pharmacokinetic properties

Absorption

After one drop of Bimatoprost Ophthalmic Solution 0.03% was administered once daily to both eyes of 15 healthy subjects for two weeks, blood concentrations peaked within 10 minutes after dosing and were below the lower limit of detection (0.025 ng/mL) in most subjects within 1.5 hours after dosing. Mean C max and AUC 0 to 24hr values were similar on days 7 and 14 at approximately 0.08 ng/mL and 0.09 ng•hr/mL, respectively, indicating that steady state was reached during the first week of ocular dosing. There was no significant systemic drug accumulation over time.

Distribution

Bimatoprost is moderately distributed into body tissues with a steady-state volume of distribution of 0.67 L/kg. In human blood, bimatoprost resides mainly in the plasma. Approximately 12% of bimatoprost remains unbound in human plasma.

Elimination

Metabolism

Bimatoprost is the major circulating species in the blood once it reaches the systemic circulation following ocular dosing. Bimatoprost then undergoes oxidation, N-deethylation and glucuronidation to form a diverse variety of metabolites.

Excretion

Following an intravenous dose of radiolabeled bimatoprost (3.12 mcg/kg) to six healthy subjects, the maximum blood concentration of unchanged drug was 12.2 ng/mL and decreased rapidly with an elimination half-life of approximately 45 minutes. The total blood clearance of bimatoprost was 1.5 L/hr/kg. Up to 67% of the administered dose was excreted in the urine while 25% of the dose was recovered in the feces.

5.3 Preclinical safety data
NA

6. Pharmaceutical particulars

6.1 List of excipients
As per dossier

6.2 Incompatibilities
Not applicable.

6.3Shelf life
24 months

6.4. Special precautions for storage

Store below 30°C. Protect from light and moisture.
Keep out of reach of children.

6.5 Nature and contents of container
10 ml plastic bottle

6.6. Special precautions for usage / preparation before use
NA

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MANUFACTURER DETAILS:

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