SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Brand Name: GEMOLOL EYE DROPS 5 ML

Generic Name: Timolol

Pharmaceutical Dosage Form : Eye Drops (sterile)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 5 mL sterile solution contains Timolol Maleate 34.00 mg equivalent to 25.00 mg of Timolol.

For a full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

Eye Drops (sterile)

Clear transparent solution in 5 mL round ivory color plastic dropper bottle with plug and cap.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Gemolol is indicated in the treatment of elevated intraocular pressure in patients with ocular hypertension or open-angle glaucoma.

4.2 Posology and method of administration

The usual starting dose is 1 drop in the affected eye twice daily.

4.3 Contraindications

Bronchial asthma, bronchospasm, history of bronchial asthma or severe chronic obstructive pulmonary disease.

4.4 Special warnings and special precautions for use

Beta-adrenergic blocking agents should be administered with caution in patients subject to spontaneous hypoglycemia or to diabetic patients as these agents may mask the signs and symptoms of acute hypoglycemia.

4.5 Interaction with other FPPs and other forms of interaction

Possible drug interactions occur use of high doses of aspirin or related salicylates, oral beta-blockers, calcium channel blockets, oral carbonic anhydrase inhibitors, certain

antidepressants, certain medications for diabetes, digoxin, epinephrine, methyldopa, theophylline.

4.6 Fertility, pregnancy and lactation

Timolol has not been studied in human pregnancy. Beta-blockers are excreted in the milk. Breast-feeding is not recommended during treatment.

4.7 Effects on ability to drive and use machines

Gemolol has no influence on the ability to drive or use machines. However, instillation of any eye drop could result in transient blurring of vision. If this occurs, the patient should wait for the blurring to subside before driving or operating machinery or taking part in any activity where this could put themselves or others at risk.

4.8 Undesirable effects

The most frequently reported adverse experiences have been burning and stinging upon instillation.

4.9 Overdose

Not known & not likely.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Beta blocking agents, non-selective

ATC-code: C07AA06

Mechanism of action

Timolol is thought to work by decreasing the amount of fluid formed in the eye. Timolol belongs to a class of drugs known as beta blockers. The action of Timolol in lowering intraocular pressure (IOP) is usually rapid occurring approximately 20 minutes following ocular instillation. The maximum effect ofTimolol Maleate in 1 to 2 hours and significant lowering of intraocular pressure has been maintained for periods as long as 24 hours.

5.2 Pharmacokinetic properties

The onset of reduction in intra-ocular pressure can be detected within one-half hour after a single dose. The maximum effect occurs in one or two hours; significant lowering of IOP can be maintained for as long as 24 hours with a single dose.

Paediatric Population:

As already confirmed by adult data, 80% of each eye drop passes through the nasolacrimal system where it may be rapidly absorbed into the systemic circulation via the nasal mucosa, conjunctiva, nasolacrimal duct, oropharynx and gut, or the skin from tear overflow.

Due to the fact that the blood volume in children is smaller than that in adults a higher circulation concentration has to be taken into account. In addition, neonates have immature metabolic enzyme pathways and it may result in an increase in elimination half-life and potentiating adverse events.

Limited data show that plasma timolol levels in children after 0.25% greatly exceed those in adults after 0.5%, especially in infants and are presumed to increase the risk of side effects such as bronchospasm and bradycardia.

5.3 Preclinical safety data

No adverse ocular effects were observed in rabbits and dogs administered Timolol topically in studies lasting one and two years, respectively. The oral LD50 of the drug is 1,190 and 900 mg/kg in female mice and female rats, respectively.

Carcinogenesis, mutagenesis, impairment of fertility

In a two-year oral study of timolol maleate in rats there was a statistically significant ($p \leq 0.05$) increase in the incidence of adrenal phaeochromocytomas in male rats administered 300 mg/kg/day (300 times the maximum recommended human oral dose). Similar differences were not observed in rats administered oral doses equivalent to 25 or 100 times the maximum recommended human oral dose.

In a lifetime oral study in mice, there were statistically significant ($p \leq 0.05$) increases in the incidence of benign and malignant pulmonary tumours, benign uterine polyps and mammary adenocarcinoma in female mice at 500 mg/kg/day (500 times the maximum recommended human dose), but not at 5 or 50 mg/kg/day. In a subsequent study in female

mice, in which post-mortem examinations were limited to uterus and lungs, a statistically significant increase in the incidence of pulmonary tumours was again observed at 500 mg/kg/day.

The increased occurrence of mammary adenocarcinoma was associated with elevations in serum prolactin which occurred in female mice administered timolol at 500 mg/kg/day, but not at doses of 5 or 50 mg/kg/day. An increased incidence of mammary adenocarcinomas in rodents has been associated with administration of several other therapeutic agents which elevate serum prolactin, but no correlation between serum prolactin levels and mammary tumours has been established in man. Furthermore, in adult human female subjects who received oral dosages of up to 60 mg of timolol maleate, the maximum recommended human oral dosage, there were no clinically meaningful changes in serum prolactin.

Timolol maleate was devoid of mutagenic potential when evaluated in vivo (mouse) in the micronucleus test and cytogenetic assay (doses up to 800 mg/kg) and in vitro in a neoplastic cell transformation assay (up to 100 mcg/ml). In Ames tests the highest concentrations of timolol employed, 5,000 or 10,000 mcg/plate, were associated with statistically significant ($p \leq 0.05$) elevations of revertants observed with tester strain TA100 (in seven replicate assays) but not in the remaining three strains. In the assays with tester strain TA100, no consistent dose-response relationship was observed, nor did the ratio of test to control revertants reach 2. A ratio of 2 is usually considered the criterion for a positive Ames test.

Reproduction and fertility studies in rats showed no adverse effect on male or female fertility at doses up to 150 times the maximum recommended human oral dose.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Benzalkonium Chloride Solution, 50%

Sodium Dihydrogen Phosphate Dihydrate (For Sterile)

Disodium Hydrogen Phosphate Dodecahydrate (For Sterile)

Water for Injections

6.2 Incompatibilities

The product is stable up to the mentioned shelf life. So it can be assured that there is no incompatibility with active and excipients.

6.3 Shelf life

2 years (24 Months from the date of manufacturing)

6.4 Special precautions for storage

Store below 30°C (protect from direct sunlight and heat. Keep out of reach of children. Do not touch the dropper tip to surfaces since this may contaminate the solution. After one month of the opening of dropper, do not use the medicine.

6.5 Nature and contents of container

5 ml round Ivory color plastic dropper bottle with plug & cap.

The packaging material i.e container & plug material is Low Density Polyethylene(LDPE) and cap material is the combination of Low Density Polyethylene (LDPE) & High Density Polyethylene (HDPE).

6.6 Special precautions for disposal and other handling

Patients should be instructed to avoid allowing the tip of the dispensing container to contact the eye or surrounding structures.

Patients should also be instructed those ocular solutions, if handled improperly, can become contaminated by common bacteria known to cause ocular infections. Serious damage to the eye and subsequent loss of vision may result from using contaminated solutions.

Any unused medicinal product should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

GENERAL Pharmaceuticals Ltd. (Unit: 2)

Karolshurichala, Kaliakair, Gazipur, Bangladesh

E-mail :gplfactoryu2@generalpharma.com

8. MARKETING AUTHORISATION NUMBER(S)

05569/07563/REN/2020

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

16-12-2020

10. DATE OF REVISION OF THE TEXT

20-08-2023