For the use of a Registered Medical Practitioner or a Hospital or a Laboratory

Duobrim®-T

Eye Drops

(Brimonidine Tartrate & Timolol Maleate Eye Drops)

COMPOSITION:

Brimonidine Tartrate IP…….. 0.2% w/v
Timolol Maleate IP equivalent to Timolol…..... 0.5% w/v
Benzalkonium Chloride Solution IP…….. 0.02% v/v
(as preservative)
Water for Injections IP…..q.s.

Pharmacological Action

Eye drop consists of two active substances: Brimonidine Tartrate and Timolol Maleate. These two components decrease elevated Intraocular Pressure (IOP) by complementary mechanisms of action and the combined effect results in additional IOP reduction compared to either compound administered alone. Eye drop has a rapid onset of action.

Brimonidine Tartrate is an alpha-2 adrenergic receptor agonist that is 1000-fold more selective for the alpha-2 adrenoceptor than the alpha-I adrenoreceptor. This selectivity results in no mydriasis and the absence of vasoconstriction in microvessels associated with human retinal xenografts. It is thought that brimonidine tartrate lowers IOP by enhancing uveoscleral outflow and reducing aqueous humour formation.

Timolol is a ßl and ß2 non-selective adrenergic receptor-blocking agent that does not have significant intrinsic sympathomimetic, direct myocardial depressant, or local anaesthetic (membrane-stabilizing) activity. Tmolol lowers IOP by reducing aqueous humour formation. The precise mechanism of action is not clearly established, but inhibition of the increased cyclic AMP synthesis caused by endogenous beta-adrenergic stimulation is probable.

The IOP-lowering effect of this fixed dose combination has been shown to be maintained in double-masked studies of up to 12 months.

Pharmacokinetics

Plasma Brimonidine and Timolol concentrations were determined in a crossover study comparing the monotherapy treatments to brimonidine — timolol fixed combination treatment in healthy subjects There were no statistically significant differences in Brimonidine or Timolol AUC between the fixed combination and the respective monotherapy treatments. Mean plasma Cmax values for Brimonidine and Timolol following dosing with fixed combination of Brimonidine and Timolol were 0.0327 and 0.406 mg/ml respectively.

Brimonidine: After ocular administration of 0.2% eye drops solution in humans, plasma Brimonidine concentrations are low. Brimonidine is not extensively metabolized in the human eye and human plasma protein binding is approximately 29%. The mean apparent half-life in the systemic circulation was approximately 3 hours after topical dosing in man.

Following oral administration to man, Brimonidine is well absorbed and rapidly eliminated. The major part of the dose (around 74% of the dose) was excreted as metabolites in urine within five days; no unchanged drug was detected in urine. In vitro studies, using animal and human liver, indicate that the metabolism is mediated largely by aldehyde oxidase and cytochrome P450. Hence, the systemic elimination seems to be primarily hepatic metabolism.

Brimonidine binds extensively and reversibly to melanin in ocular tissues without any untoward effects. Accumulation does not occur in the absence of melanin.

Brimonidine is not metabolized to a great extent in human eyes. After instillation of Brimonidine Tartrate 0.2% eye drops to the rabbit, peak drug concentration was 0.647 mg/ml in the aqueous humour within 1 hour post-dose. Brimonidine concentrations declined subsequently in a biphasic manner with an initial half-life of 1 hour, followed by a slower terminal elimination phase from 6 to 24 hours post dose.

Timolol:

After ocular administration of a 0.5% eye drops solution in humans undergoing cataract surgery, peak timolol concentration was 898 ng/ml in the aqueous humour at one hour post-dose. Part of the dose is absorbed systemically where it is extensively metabolized in the liver. The half-life of timolol in plasma is about 7 hours. Timolol is partially metabolized by the liver with timolol and its metabolites excreted by the kidney. Tmolol is not extensively bound to plasma.

Indications

Brimonidine-Timolol fixed combination is indicated for reduction of Intraocular Pressure (IOP) in patients with chronic open-angle glaucoma or ocular hypertension who are insufficiently responsive to topical beta-blockers.

Dosage and Administration

Recommended dosage in adults (including the elderly) The recommended dose in adults is one drop of Eye drop in the affected eye(s) twice daily, approximately 12 hours apart. If more than one topical ophthalmic product is to be used, the different products should be instilled at least 5 minutes apart.

Contraindications

Brimonidine-Timolol fixed combination is contraindicated in the following conditions reactive airway disease including bronchial asthma or a history of bronchial asthma, severe chronic obstructive pulmonary disease. Sinus bradycardia, second or third degree atrioventricular block, overt cardiac failure, cardiogenic shock.

STORAGE:

Keep in a cool place. Use the solution within one month after opening the container.

Protect from light.

KEEP OUT OF REACH OF CHILDREN

NOT FOR INJECTION

FOR EXTERNAL USE ONLY

PRESENTATION:

Duobrim-T is a sterile solution supplied in plastic opaque dropper bottle with a cap, containing 5ml of the solution.

Directions for use :

Turn the tamper proof cap anti-clockwise to break the seal.

Remove the cap, dispense drops with gentle pressure.

Replace the cap immediately after every use.

Manufactured in INDIA by :

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