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

OCUDOR-T

Dorzolamide and Timolol Eye Drops BP

COMPOSITION
Each ml contains
Dorzolamide (as 22.26mg Dorzolamide Hydrochloride) Ph. Eur.....20 mg
Timolol (as 6.83 mg Timolol Maleate)Ph. Eur.....5 mg
Benzalkonium Chloride Ph.Eur.....0.075 mg
(As Preservative)
Aqueous Buffered Vehicle .....q.s.

DESCRIPTION
OCUDOR T (Dorzolamide and Timolol Eye drops BP) is Clear, colourless, slightly viscous solution, practically free from visible particles, filled into 5 ml low density polyethylene (LDPE) containers having blue insert cap assembly.

CLINICAL PHARMACOLOGY
PHARMACODYNAMICS / MECHANISM OF ACTION
OCUDOR T is comprised of two components: dorzolamide hydrochloride and timolol maleate. Each of these two components decreases elevated intraocular pressure by reducing aqueous humor secretion, but does so by a different mechanism of action.
Dorzolamide hydrochloride is a potent inhibitor of human carbonic anhydrase II. Inhibition of carbonic anhydrase in the ciliary processes of the eye decreases aqueous humor secretion, presumably by slowing the formation of bicarbonate ions with subsequent reduction in sodium and fluid transport. Timolol maleate is a nonselective beta-adrenergic receptor blocking agent that does not have significant intrinsic sympathomimetic, direct myocardial depressant, or local anesthetic (membrane-stabilizing) activity. The combined effect of these two agents results in additional intraocular pressure (IOP) reduction compared to either component administered alone.
Following topical administration, OCUDOR T reduces elevated intraocular pressure, whether or not associated with glaucoma. Elevated intraocular pressure is a major risk factor in the pathogenesis of optic nerve damage and glaucomatous visual field loss. The higher the level of intraocular pressure, the greater the likelihood of glaucomatous visual field loss and optic nerve damage. OCUDOR T reduces intraocular pressure without the common side effects of miotics such as night blindness, accommodative spasm and pupillary constriction.

PHARMACOKINETICS
Dorzolamide Hydrochloride
Unlike oral carbonic anhydrase inhibitors, topical administration of dorzolamide hydrochloride allows for the drug to exert its effects directly in the eye at substantially lower doses and therefore with less systemic exposure. This result in a reduction in IOP without the acid-base disturbances or alterations in electrolytes characteristic of oral carbonic anhydrase inhibitors. When topically applied, dorzolamide reaches the systemic circulation. Dorzolamide accumulates in RBCs during chronic dosing as a result of selective binding to CA-II while extremely low concentrations of free drug in plasma are maintained.
The parent drug forms a single N-desethyl metabolite that inhibits CA-II less potently than the parent drug but also inhibits a less active isoenzyme (CA-I). The metabolite also accumulates in RBCs where it binds primarily to CA-I.
Dorzolamide binds moderately to plasma proteins (approximately 33%). Dorzolamide is primarily excreted unchanged in the urine; the metabolite is also excreted in urine. After dosing ends, dorzolamide washes out of RBCs nonlinearly, resulting in a rapid decline of drug concentration initially, followed by a slower elimination phase with a half-life of about four months.

Timolol Maleate
The mean peak plasma concentration following morning dosing was 0.46 ng/mL and following afternoon dosing was 0.35 ng/mL.

INDICATION
OCUDOR T is indicated in the treatment of elevated intraocular pressure (IOP) in patients with ocular hypertension and open-angle glaucoma when concomitant therapy is appropriate.

CONTRAINDICATION
The preparation is contraindicated in patients with:
- Reactive airway disease, bronchial asthma or a history of bronchial asthma or severe chronic obstructive pulmonary disease
- Sinus bradycardia, sino-atrial block, second or third degree atrioventricular block, overt cardiac failure, cardiogenic shock
- Hypersensitivity to any component of this product
  The above are based on the components and are not unique to the combination.

DOSAGE AND ADMINISTRATION
The dose is one drop of OCUDOR T in the affected eye(s) two times daily.
When substituting OCUDOR T for another ophthalmic antiglaucoma agent(s), discontinue the other agent(s) after proper dosing on one day, and start OCUDOR T on the next day.
If another topical ophthalmic agent is being used, OCUDOR T and the other agent should be administered at least ten minutes apart.
Safety and efficacy in pediatric patients below the age of 2 years have not been established.
For information regarding use in pediatric patients ≥2 years of age see below:
The safety and efficacy of 2% dorzolamide hydrochloride ophthalmic solution has been established in a clinical study of children under the age of 6 years. In this study patients under 6 and greater than 2 years of age whose IOP was not controlled with monotherapy received OCUDOR T. In those patients OCUDOR T was generally well tolerated.
When using nasolacrimal occlusion or closing the eyelids for 2 minutes, the systemic absorption is reduced.
This may result in an increase in local activity.

ROUTE OF ADMINISTRATION
Ocular

OVERDOSE:
No data are available with regard to human overdosage by accidental or deliberate ingestion of OCUDOR T.
There have been reports of inadvertent overdosage with timolol maleate ophthalmic solution resulting in systemic effects similar to those seen with systemic beta-adrenergic blocking agents such as dizziness, headache, shortness of breath, bradycardia, bronchospasm, and cardiac arrest. The most common signs and symptoms to be expected with overdosage of dorzolamide are electrolyte imbalance, development of an acidotic state, and possibly central nervous system effects.
Treatment should be symptomatic and supportive. Serum electrolyte levels (particularly potassium) and blood pH levels should be monitored. Studies have shown that timolol does not dialyze readily.

ADVERSE EFFECTS
Dorzolamide hydrochloride and timolol maleate ophthamic solution is generally well tolerated; no adverse experiences peculiar to this combination drug have been observed. Adverse experiences have been limited to those that were reported previously with dorzolamide hydrochloride and/or timolol maleate. In general, common adverse experiences were mild and did not cause discontinuation.
The most frequently reported drug-related adverse effects were: ocular burning and stinging, taste perversion, corneal erosion, conjunctival injection, blurred vision, tearing, and ocular itching. Urolithiasis was reported rarely.
The following adverse reactions have been reported in post-marketing experience: dyspnea, respiratory failure, contact dermatitis, bradycardia, heart block, choroidal detachment following filtration surgery, nausea, Stevens- Johnson syndrome, toxic epidermal necrolysis.

WARNING & PRECAUTIONS
As with other topically-applied ophthalmic agents, this drug may be absorbed systemically. The timolol component is a betablocker. Therefore, the same types of adverse reactions found with systemic administration of beta-blockers may occur with topical administration.

Cardio-respiratory Reactions
Because of the timolol maleate component, cardiac failure should be adequately controlled before beginning therapy with OCUDOR T. Patients with a history of cardiovascular disease, including cardiac failure, should be watched for signs of deterioration of these diseases, and pulse rates should be checked.
Due to its negative effect on conduction time, beta-blockers should be given with caution to patients with first degree heart block.
Respiratory reactions and cardiac reactions, including death due to bronchospasm in patients with asthma and rarely death in association with cardiac failure, have been reported following administration of timolol maleate ophthalmic solution.

In patients with mild/moderate chronic obstructive pulmonary disease (COPD), OCUDOR T should be used with caution, and only if the potential benefit outweighs the potential risk.

Vascular Disorders
Patients with severe peripheral circulatory disturbance/disorders (e.g. severe forms of Raynaud's disease or Raynaud's syndrome) should be treated with caution.

Masking of Hypoglycemic Symptoms in Patients with Diabetes Mellitus
Beta-adrenergic blocking agents should be administered with caution in patients subject to spontaneous hypoglycemia or to diabetic patients (especially those with labile diabetes) who are receiving insulin or oral hypoglycemic agents. Beta-adrenergic blocking agents may mask the signs and symptoms of acute hypoglycemia.

Masking of Thyrotoxicosis
Beta-adrenergic blocking agents may mask certain clinical signs of hyperthyroidism (e.g., tachycardia). Patients suspected of developing thyrotoxicosis should be managed carefully to avoid abrupt withdrawal of beta-adrenergic blocking agents which might precipitate a thyroid storm.

Surgical Anesthesia
The necessity or desirability of withdrawal of beta-adrenergic blocking agents prior to major surgery is controversial. If necessary during surgery, the effects of beta-adrenergic blocking agents may be reversed by sufficient doses of adrenergic agonists.

Renal and Hepatic Impairment
OCUDOR T has not been studied in patients with severe renal impairment (CrCl<30milliliter/min). Because dorzolamide hydrochloride and its metabolite are excreted predominantly by the kidney, OCUDOR T is not recommended in such patients.
OCUDOR T has not been studied in patients with hepatic impairment and therefore should be used with caution in such patients.

Immunology and Hypersensitivity
As with other topically-applied ophthalmic agents, this drug may be absorbed systemically. The dorzolamide component is a sulfonamide. Therefore, the same types of adverse reactions found with systemic administration of sulphonamides may occur with topical administration, such as Stevens-Johnson syndrome and toxic epidermal necrolysis. If signs of serious reactions or hypersensitivity occur, discontinue use of this preparation.
While taking β-blockers, patients with a history of atopy or a history of severe anaphylactic reaction to a variety of allergens may be more reactive to accidental, diagnostic, or therapeutic repeated challenge with such allergens. Such patients may be unresponsive to the usual doses of epinephrine used to treat anaphylactic reactions.

Concomitant Therapy
There is a potential for an additive effect on the known systemic effects of carbonic anhydrase inhibition in patients receiving oral and topical carbonic anhydrase inhibitors concomitantly. The concomitant administration of OCUDOR T and oral carbonic anhydrase inhibitors has not been studied and is not recommended.

Patients who are already receiving a beta-adrenergic blocking agent systemically and who are given OCUDOR T should be observed for a potential additive effect either on the intraocular pressure or on the known systemic effects of beta-blockade. The use of two topical beta-adrenergic blocking agents is not recommended.

Other
The management of patients with acute angle-closure glaucoma requires therapeutic interventions in addition to ocular hypotensive agents. OCUDOR T has not been studied in patients with acute angle-closure glaucoma.
Choroidal detachment has been reported with administration of aqueous suppressant therapy (e.g., timolol, acetazolamide, dorzolamide) after filtration procedures.
There is an increased potential for developing corneal edema in patients with low endothelial cell counts. Precautions should be used when prescribing OCUDOR T to this group of patients.

Contact Lens Use
OCUDOR T contains the preservative benzalkonium chloride, which may be deposited in soft contact lenses; therefore, OCUDOR T should not be administered while wearing these lenses. The lenses should be removed before application of the drops and not be reinserted earlier than 15 minutes afteruse.

MUTAGENESIS, CARCINOGENESIS AND IMPAIRMENT OF FERTILITY
Dorzolamide Hydrochloride
Dorzolamide showed no mutagenic potential in a series of standard assays for gene mutations, chromosomal damage and DNA damage.
There are no adverse effects of dorzolamide hydrochloride on the reproductive capacity of males or females rats at oral doses up to 15 and 7.5mg/kg/day.

Timolol Maleate
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). 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.

EFFECTS ONABILITYTO DRIVE & USE MACHINE
No studies on the effects on the ability to drive and use machines have been performed.
Possible side effects such as blurred vision may affect some patients' ability to drive and/or operate machinery.

DRUG INTERACTION
Specific drug interaction studies have not been performed with OCUDOR T. Dorzolamide hydrochloride and timolol maleate ophthamic solution has been used concomitantly with the following systemicmedications without evidence of adverse interactions: ACE-inhibitors, calcium channel blockers, diuretics, non-steroidal anti inflammatory drugs including aspirin, and hormones (e.g., estrogen, insulin, thyroxine). However, the potential exists for additive effects and production of hypotension and/or marked bradycardia when timolol maleate ophthalmic solution is administered together with oral calcium channel blockers, catecholaminedepleting drugs, antiarrhythmics, parasympathomimetics or beta-adrenergic blocking agents.
Potentiated systemic beta-blockade (e.g., decreased heart rate, depression) has been reported during combined treatment with CYP2D6 inhibitors (e.g. quinidine, SSRIs) and timolol.
The dorzolamide component of OCUDOR T is a carbonic anhydrase inhibitor and although administered topically, is absorbed systemically. Dorzolamide hydrochloride ophthalmic solution has not been associated with acid-base disturbances. However, these disturbances have been reported with oral carbonic anhydrase inhibitors and have, in some instances, resulted in drug interactions (e.g., toxicity associated with high-dose salicylate therapy). Therefore, the potential for such drug interactions should be considered in patients receiving OCUDOR T. Oral β-adrenergic blocking agents may exacerbate the rebound hypertension which can follow the withdrawal of clonidine.

PREGNANCY
There are no adequate and well-controlled studies in pregnant women. OCUDOR-T should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

NURSING MOTHERS
It is not known whether dorzolamide hydrochloride is excreted in human milk. Timolol maleate does appear in human milk. Because of the potential for serious adverse reactions on the nursing infant, a decision should be made whether to discontinue nursing or discontinue the drug, taking into account the importance of the drug to the mother.

DOSAGE FORM AND PACKING AVAILABLE
5 mL solution filled in 5 mL labeled LDPE bottle with insert-cap assembly comprising of a dark blue coloured HDPE screw cap over a LDPE nozzle with tamper-evident LDPE dust-cover sealing the vial cap. One such a bottle is packed in a carton with pack insert.

STORAGE
Before Opening: Store below 30°C, protect from light.
After Opening: Store below 25°C, and discard after 28 days after first opening.

SHELF-LIFE : 24 months

Date of Revision: October 2023

Product Registration Holder:
Unimed Sdn Bhd
53, Jalan Tembaga SD 5/2B,
Bandar Sri Damansara
52200 Kuala Lumpur.

Manufactured in India by:
FDC **FDC Limited**
B-8, MIDC Industrial Estate Waluj,
Aurangabad, Maharashtra In-431136 India.

D4

FDC Limited	LEAFLET	Minipharma Code no. **Front:1862/Back: 1861**
Size	110(L) x 380 (H) mm	
Folded Size	----------	
No. of Folds	----------	
GSM	40 gsm	
Paper	Bible paper	
Colour	Black	
Edge Code		
Artwork Code: D4		Supercedes A/W Code: D3
Location: Waluj - Malaysia		Prepared On: 02-05-2023
Reason for Change: Change in Storage Condition, Change in Dosage and Administrative Section & Added Effects On Ability To Drive & Use Machine.		

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