[DUOPHARMA (M) SDN BHD]

OPTIMOL EYE DROP 0.5%

DESCRIPTION: OPTIMOL EYE DROPS is a clear, sterile colourless solution.

COMPOSITION: OPTIMOL EYE DROPS 0.5% : Each ml contains Timolol Maleate equivalent to Timolol 0.5%.
Preservative: Benzalkonium Chloride 0.01% w/v

PHARMACODYNAMICS: Timolol maleate is a non-selective beta-adrenergic receptor blocking agent that does not give significant intrinsic sympathomimetic, direct myocardial depressant, or local anaesthetic (membrane-stabilising) activity. Timolol maleate combines reversibly with a part of the cell membrane, the beta-adrenergic receptor, and thus inhibits the usual biological response that would occur with stimulation of that receptor. This specific competitive antagonism blocks stimulation of the beta-adrenergic receptors by catecholamines having beta-adrenergic stimulating (agonist) activity, whether these originate from an endogenous or exogenous source. Reversal of this blockade can be accomplished by increasing the concentration of the agonist, which will restore the usual biological response. This extended duration of action permits control of intraocular pressure over the usual sleeping hours. Repeated observation over a period of one year indicate that the intraocular pressure lowering effect of Timolol is well maintained. The precise mechanism of action of Timolol in lowering intraocular pressure is not clearly established at this time, although a fluorescein study and tonography studies indicate that its predominant action may be related to reduced aqueous formation. However, in some studies a slight increase in outflow facility was also observed. Unlike miotics, Timolol reduces intraocular pressure with little or no effect on accommodation or pupil size. Thus, changes in visual acuity due to increased accommodation are uncommon, and dim or blurred vision and night blindness produced by miotics are not evident. In addition, in patients with cataracts, the ability to see around lenticular opacities when the pupil is constricted by miotics is avoided. When changing the patients from miotics to Timolol a refraction might be necessary when these effects of the miotic have passed. In controlled multiclinic studies in patients with untreated intraocular pressures of 22 mmHg or greater, Timolol 0.5 percent administered twice a day produced a greater reduction in intraocular pressure than 1, 2, 3 or 4 percent pilocarpine solution administered four times a day or 0.5, 1 or 2 percent adrenaline hydrochloride solution administered twice a day. In the multiclinic studies comparing Timolol with pilocarpine, 61 percent of patients treated with Timolol had intraocular pressure reduced to less than 22 mmHg compared to 32 percent of patients treated with pilocarpine. For patients completing these studies, the mean reduction in pressure at the end of the study from pre-treatment was 30.7 percent for patients treated with Timolol and 21.7 percent for patients treated with pilocarpine. In the multiclinic studies comparing Timolol with adrenaline, 69 percent of patients treated with Timolol had intraocular pressure reduced to less than 22 mmHg compared to 42 percent of patients treated with adrenaline. For patients completing these studies, the mean reduction in pressure at the end of the study from pre-treatment was 33.2 percent for patients treated with Timolol and 28.1 percent for patients treated with adrenaline. In clinical studies Timolol produced fewer and less severe side effects than either pilocarpine or adrenaline. As with the use of other antiglaucoma drugs, diminished responsiveness to Timolol after prolonged therapy has been reported in some patients. However, in one long-term study in which 96 patients have been followed for at least 3 years, no significant difference in mean intraocular pressure has been observed after initial stabilisation. Timolol has also been used in patients with glaucoma wearing conventional hard contact lenses, and has generally been studied in patients wearing lenses made with materials other than polymethylmethacrylate.

PHARMACOKINETICS: Ophthalmic beta-adrenergic blocking agents may be systemically absorbed. - Onset of action: Within 30 minutes following a single dose. - Time to peak effect: Within 1 to 2 hours following a single dose. - Duration of action: A significant lowering of intraocular pressure may be maintained for up to 24 hours following a single dose.

INDICATIONS: Timolol Ophthalmic Drops is indicated for the reduction of elevated intraocular pressure. In clinical trials it has been shown to reduce intraocular pressure in: - Patients with ocular hypertension. - Patients with chronic open-angle glaucoma.- Aphakic patients with glaucoma.

CONTRAINDICATIONS: Timolol is contraindicated in patients with: bronchospasm, bronchial asthma or with a history of bronchial asthma, or severe chronic obstructive pulmonary disease. Sinus bradycardia; second and third degree atrioventricular block; overt cardiac failure; cardiogenic shock.
Hypersensitivity to Timolol Ophthalmic Drops.

SIDE EFFECTS: Timolol Ophthalmic solution is usually well tolerated. The following adverse reactions have been reported either in clinical trials or since the drug has been marketed. Special Senses: Signs and symptoms of ocular irritation, including burning and stinging, conjunctivitis, blepharitis, keratitis, blepharoptosis, and decreased corneal sensitivity and dry eyes. Visual disturbances, including refractive changes (due to withdrawal of miotic therapy in some cases), diplopia, ptosis, and choroidal detachment following filtration surgery (see Precautions), tinnitus. Cardiovascular: Bradycardia, arrhythmia, hypotension, syncope, heart block, cerebrovascular accident, cerebral ischaemia, congestive heart failure, palpitation, cardiac arrest, oedema, claudication, Raynaud's phenomenon, cold hands and feet. Respiratory: Bronchospasm (predominantly in patients with pre-existing bronchospastic disease), exacerbation of asthma, respiratory failure, dyspnoea, cough. Body as a Whole: Headache, asthenia, fatigue, chest pain. Integumentary: Alopecia, psoriasiform rash or exacerbation of psoriasis. Hypersensitivity: Signs and symptoms of allergic reactions including angioedema, urticaria, localised and generalised rash. Nervous System/Psychiatric: Dizziness, depression, insomnia, nightmares, memory loss, increase in signs and symptoms of myasthenia gravis, paraesthesia. Digestive: Nausea, diarrhoea, dyspepsia, dry mouth. Urogenital: Decreased libido, Peyronie's disease. Immunologic: Systemic lupus erythematosus have been reported.

WARNING AND PRECAUTIONS: As with other topically applied ophthalmic drugs, this drug may be absorbed systemically. The same adverse reactions found with systemic administration of beta-adrenergic blocking agents may occur with topical administration. Cardiac failure should be adequately controlled before beginning therapy with Timolol. In patients with a history of severe cardiac disease, signs of cardiac failure should be watched for and pulse rates should be checked. 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. Patients who are already receiving a beta-adrenergic blocking agent orally and who are given Timolol should be observed for a potential additive effect either on the intraocular pressure or on the known systemic effects of beta-blockade. In patients with angle-closure glaucoma, the immediate objective of treatment is to reopen the angle. This requires constricting the pupil with a miotic. Timolol has little or no effect on the pupil. When Timolol is used to reduce elevated intraocular pressure in angle-closure glaucoma it should be used with miotic and not alone. Choroidal detachment has been reported with administration of aqueous suppressant therapy (eg, timolol, acetazolamide) after filtration procedures.
Timolol contains the preservative benzalkonium chloride, which may be deposited in soft contact lenses; therefore, Timolol should not be used while wearing these lenses. The lenses should be removed before application of the drops and not be reinserted earlier than 15 minutes after use.
Patients should be advised that if they develop an intercurrent ocular condition (e.g. trauma, ocular surgery or infection) or any ocular reactions, particularly conjunctivitis and lid reactions they should immediately seek their physician's advice concerning the continued use of the product.

Size: 20.4cm x 11cm

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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.
Risk from Anaphylactic Reaction: While taking (-blockers, patients with a history of atopy or a history of severe anaphylactic reaction to a variety of allergens may be more reactive to repeated challenge with such allergens, either accidental, diagnostic, or therapeutic. Such patients may be unresponsive to the usual doses of epinephrine use to treat anaphylactic reactions.
Use in children: Safety and effectiveness in children have not been established by adequate and well controlled studies.

USE IN PREGNANCY & LACTATION:
Use in pregnancy: Beta-adrenergic blocking agents may cause bradycardia in the fetus and newborn infant. During the final part of pregnancy and parturition these drugs should therefore only be given after weighing the needs of the mother against the risk to the fetus. Timolol has not been studied in human pregnancy. The use of Timolol requires that the anticipated benefit be weighed against possible hazards.
Use during lactation: Because of the potential for serious adverse reactions from Timolol in nursing infants, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

INTERACTION WITH OTHER MEDICAMENTS: Although Timolol used alone has little or no effect on pupil size, mydriasis resulting from concomitant therapy with Timolol and adrenaline has been reported occasionally. Close observation of the patient is recommended when a beta-blocker is administered to patients receiving catecholamine-depleting drugs such as reserpine, because of possible additive effects and the production of hypotension and/or marked bradycardia, which may produce vertigo, syncope, or postural hypotension.
Oral calcium antagonists may be used in combination with beta-adrenergic blocking agents when heart function is normal, but should be avoided in patients with impaired cardiac function.
Potentiated systemic beta-blockade (eg, decreased heart rate) has been reported during combined treatment with quinidine and timolol, possibly because quinidine inhibits the metabolism of timolol via the P-450 enzyme, CYP2D6.
The potential exists for hypotension, AV conduction disturbances and left ventricular failure to occur in patients receiving a beta-blocking agent when an oral calcium entry blocker is added to the treatment regimen. The nature of any cardiovascular adverse effect tends to depend on the type of calcium blocker used. Dihydropyridine derivatives, such as nifedipine, may lead to hypotension, whereas verapamil or diltiazem have a greater propensity to lead to AV conduction disturbances or left ventricular failure when used with a beta-blocker.
Intravenous calcium entry blockers should be used with caution in patients receiving beta-adrenergic blocking agents.
The concomitant use of beta-adrenergic blocking agents and digitalis with either diltiazem or verapamil may have additive effects in prolonging AV conduction time.

RECOMMENDED DOSAGE: Recommended therapy is one drop of 0.25 percent solution in the affected eye twice a day.
If clinical response is not adequate, dosage may be changed to one drop of 0.5 percent solution in each affected eye twice a day.
If needed, concomitant therapy with miotics, epinephrine and systemically administered carbonic anhydrase inhibitors may be instituted. The use of two beta-adrenergic blocking agent is not recommended.
Since in some patients the pressure-lowering response to Timolol may require a few weeks to stabilise, evaluation should include a determination of intraocular pressure after approximately 4 weeks of treatment with Timolol.
If the intraocular pressure is maintained at satisfactory levels, many patients can be placed on once-a-day therapy. Because of naturally occurring diurnal variations in intraocular pressure, satisfactory response is best determined by measuring the intraocular pressure at different times during the day.
When patients are being transferred from other antiglaucoma agents, monitoring of intraocular pressure is recommended. When a patient is transferred from a single antiglaucoma agent, on the first day continue with the agent already being used and add one drop of 0.25 percent Timolol in each affected eye twice a day. On the following day, discontinue the previously used antiglaucoma agent completely and continue with Timolol. If a higher dosage of Timolol is required substitute one drop of 0.5 percent solution in the eye twice a day.
Systemic absorption of drugs from ophthalmic solutions may be minimised by pressure on the tear-duct immediately after application. When a patient is transferred from several concomitantly administered antiglaucoma agents, individualisation is required. The physician may be able to discontinue some or all of the other anti-glaucoma agents. Adjustments should involve one agent at a time.

ROUTE OF ADMINISTRATION: Ophthalmic application.

SYMPTOMS AND TREATMENT OF OVERDOSAGE: Overdosage: There have been reports of inadvertent overdosage with Timolol Maleate Ophthalmic Drops 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.
Treatment of Overdosage: Recommended treatment includes:
If an ophthalmic overdose occurs, immediately flush the eyes with warm tap water.
If an ophthalmic beta-adrenergic blocking agent is accidentally ingested, activated charcoal or gastric lavage may be appropriate to decrease further absorption.
For symptoms of systemic toxicity, the medication should be discontinued. Depending on severity of toxicity, the following supportive and symptomatic treatments should be utilised if necessary:
- For bradycardia: Atropine (0.25 to 2 mg) should be administered intravenously to induce vagal blockade. If bradycardia persists, intravenous isoproterenol hydrochloride may be administered with caution. A transvenous cardiac pacemaker may be used, if necessary.
- For hypotension: Glucagon and sympathomimetic pressor agents, such as dobutamine, dopamine, or norepinephrine, may be used.
- For bronchospasm: Isoproterenol hydrochloride should be administered. Additional therapy with a beta-2-agonist or a theophylline derivative may be used, if necessary.
- For cardiac failure, acute: Digitalis, diuretics and oxygen should be administered immediately. Intravenous aminophylline may be used in refractory cases. Also, glucagon hydrochloride may be used, if necessary.
- For heart block, second or third degree: Isoproterenol hydrochloride or a transvenous cardiac pacemaker should be used.

PACK SIZES: Content of 5ml in 10ml sterile eye drop bottle. Pack in cartons of 10.

STORAGE CONDITIONS: Store below 30˚C. Protect from light. Do not use 1 month after first opening.
KEEP OUT OF REACH OF CHILDREN. JAUHKAN DARIPADA KANAK-KANAK.

SHELF LIFE: Please refer to the outer package.

PRODUCT REGISTRATION HOLDER & MANUFACTURER: DUOPHARMA (M) SDN BHD
Lot 2599 Jalan Seruling 59 Kawasan 3, Taman Klang Jaya, 41200 Klang Selangor Darul Ehsan, MALAYSIA.

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Size: 20.4cm x 11cm