

# Glucotim 0.5%

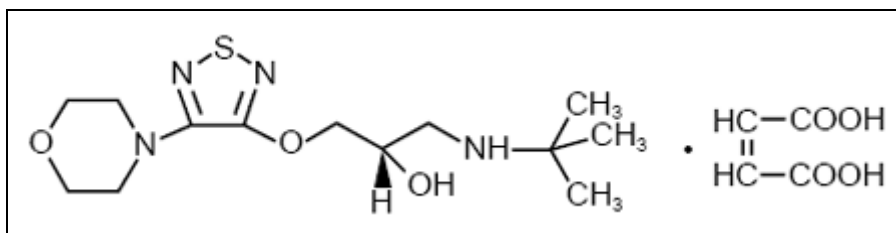
## Timolol Maleate Eye Drops IP 0.5%

STERILE EYE DROPS FOR OPHTHALMIC USE

### DESCRIPTION

Glucotim 0.5% (Timolol maleate Eye Drops) is a non-selective beta-adrenergic receptor blocking agent. Timolol maleate possesses an asymmetric carbon atom in its structure and is provided as the levo-isomer.

Its molecular formula is  $C_{13}H_{24}N_4O_3S \cdot C_4H_4O_4$  and its structural formula is:



Timolol maleate has a molecular weight of 432.49. It is a white, odorless, crystalline powder, which is soluble in water, methanol, and alcohol. Timolol maleate is stable at room temperature. Glucotim 0.5% (Timolol maleate Eye Drops) is supplied as a sterile, isotonic, buffered, aqueous solution of timolol maleate in a single strength. It has a pH of 6.5-7.5.

### COMPOSITION

Timolol Maleate IP [equivalent to Timolol]...0.5% w/v  
Benzalkonium Chloride Solution IP.....0.01% w/v  
[as preservative]  
Sterile buffered aqueous solution.....q.s.

### CLINICAL PHARMACOLOGY

#### *Mechanism of Action*

Timolol maleate is a  $\beta_1$  and  $\beta_2$  (non-selective) adrenergic receptor blocking agent that does not have significant intrinsic sympathomimetic, direct myocardial depressant, or local anesthetic (membrane-stabilizing) activity.

Glucotim 0.5% (Timolol maleate Eye Drops), when applied topically in the eye, has the action of reducing elevated as well as normal intraocular pressure, whether or not accompanied by glaucoma. Elevated intraocular pressure is a major risk factor in the pathogenesis of glaucomatous visual field loss. The higher the level of intraocular pressure, the greater the likelihood of glaucomatous visual field loss and optic nerve damage.

The precise mechanism of the ocular hypotensive action of Glucotim 0.5% (Timolol maleate Eye Drops) is not clearly established. Studies in man suggest that its predominant action may be related to reduced aqueous humor formation. However, in some studies a slight increase in outflow facility was also observed.

#### *Pharmacokinetics*

The onset of reduction in intraocular pressure following administration of Glucotim 0.5% (Timolol maleate Eye Drops) can usually be detected within half hour after a single dose. The maximum effect usually occurs in one to two hours and significant lowering of intraocular pressure can be maintained for periods as long as 24 hours

with a single dose. Repeated observations over a period of one year indicate that the intraocular pressure lowering effect of Glucotim 0.5% (Timolol maleate Eye Drops) is well maintained.

### **INDICATIONS**

Glucotim 0.5% (Timolol maleate Eye Drops) is indicated in the treatment of elevated intraocular pressure in patients with ocular hypertension or open-angle glaucoma.

### **DOSAGE & ADMINISTRATION**

One drop once or twice daily, as directed by the Physician.

### **CONTRAINDICATIONS**

Glucotim 0.5% (Timolol maleate Eye Drops) is contraindicated in patients with:

- Bronchial asthma
- Severe chronic obstructive pulmonary disease
- Sinus bradycardia
- Second or third degree atrioventricular block
- Overt cardiac failure
- Hypersensitivity to any component of this product

### **WARNINGS**

As with many 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.

### **PRECAUTIONS**

*General:* Because of potential effects of beta-adrenergic blocking agents on blood pressure and pulse, these agents should be used with caution in patients with cerebrovascular insufficiency.

*Angle-closure glaucoma:* In patients with angle-closure glaucoma, the immediate objective of treatment is to reopen the angle. This requires constricting the pupil. Timolol maleate has little or no effect on the pupil. Glucotim 0.5% (Timolol maleate Eye Drops) should not be used alone in the treatment of angle-closure glaucoma.

*Anaphylaxis:* While taking beta-blockers, patients with a history of atopy or a history of severe anaphylactic reactions to a variety of allergens may be more reactive to repeated accidental, diagnostic, or therapeutic challenge with such allergens. Such patients may be unresponsive to the usual doses of epinephrine used to treat anaphylactic reactions.

*Muscle Weakness:* Beta-adrenergic blockade has been reported to potentiate muscle weakness consistent with certain myasthenic symptoms (e.g., diplopia, ptosis, and generalized weakness). Timolol has been reported rarely to increase muscle weakness in some patients with myasthenia gravis or myasthenic symptoms.

### **PREGNANCY**

There are no adequate and well-controlled studies in pregnant women. Glucotim 0.5% (Timolol maleate Eye Drops) should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

## **LACTATION**

Timolol maleate has been detected in human milk following ophthalmic drug administration. Because of the potential for serious adverse reactions from Glucotim 0.5% (Timolol maleate Eye Drops) 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.

## **PEDIATRIC USE**

Safety and effectiveness in pediatric patients have not been established.

## **DRUG INTERACTIONS**

Although Glucotim 0.5% (Timolol maleate Eye Drops) used alone has little or no effect on pupil size, mydriasis resulting from concomitant therapy with epinephrine has been reported occasionally.

*Beta-adrenergic blocking agents:* Patients who are receiving a beta-adrenergic blocking agent orally and Glucotim 0.5% (Timolol maleate Eye Drops) should be observed for potential additive effects of beta-blockade, both systemic and on intraocular pressure. The concomitant use of two topical beta-adrenergic blocking agents is not recommended.

*Calcium antagonists:* Caution should be used in the coadministration of beta-adrenergic blocking agents, such as Glucotim 0.5% (Timolol maleate Eye Drops), and oral or intravenous calcium antagonists because of possible atrioventricular conduction disturbances, left ventricular failure, and hypotension.

*Catecholamine-depleting drugs:* 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 result in vertigo, syncope, or postural hypotension.

*Digitalis and calcium antagonists:* The concomitant use of beta-adrenergic blocking agents with digitalis and calcium antagonists may have additive effects in prolonging atrioventricular conduction time.

*Quinidine:* Potentiated systemic beta-blockade (e.g., 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.

*Clonidine:* Oral beta-adrenergic blocking agents may exacerbate the rebound hypertension, which can follow the withdrawal of clonidine. There have been no reports of exacerbation of rebound hypertension with ophthalmic timolol maleate.

## **ADVERSE REACTIONS**

The most frequently reported adverse experiences have been burning and stinging upon instillation of Glucotim 0.5% (Timolol maleate Eye Drops).

Additional events reported include: blurred vision, cataract, conjunctival injection, headache, hypertension, infection, itching and decreased visual acuity.

## **PRESENTATION**

Glucotim 0.5% (Timolol maleate Eye Drops) is available in 5ml bottles.

**STORAGE**

Store at 15-25°C (59-77°F)