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

(Timolol Maleate Ophthalmic Solution USP)

SENSOLOL®

Eye Drops

For the use of Registered Medical Practitioner only

COMPOSITION:

Timolol Maleate USP equivalent to Timolol 0.5%w/v
Benzalkonium Chloride Solution USP ..... 0.02% v/v
(as preservative)
Water for Injection USP ..... q.s.

Description:

Timolol Maleate is a non-selective beta adrenergic receptor blocking agent. Its chemical name is (-)-1-(tert Butylamino)-3-[(4-morpholin-1, 2, 5-thiadiazol-3-yl) oxy]-2-propanol maleate (1:1) (salt). Timolol maleate possesses an asymmetric carbon atom in its structure and is provided as the levo-isomer.

Timolol Maleate has a molecular weight of 432.50. It is white, odorless, crystalline powder which is insoluble in water, methanol, and alcohol. Timolol Maleate is stable at room temperature

Timolol Maleate ophthalmic solution is supplied with preservative Benzalkonium chloride.

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 symphatomimetic, direct myocardial depressant, or local anesthetic (membrane stabilizing) activity.

Beta-adrenergic receptor blockade reduces cardiac output in both healthy subjects and patients with heart disease. In patients with severe impairment of myocardial function, beta-adrenergic receptor blockade may inhibit the stimulatory effect of the sympathetic nervous system necessary to maintain adequate cardiac function.

Beta-adrenergic receptor blockade in the bronchi and bronchioles results in increased airway resistance from unopposed parasympathetic activity. Such an effect in patients with asthma or other bronchospastic conditions is potentially dangerous.

Timolol Maleate Ophthalmic solution when applied topically on the eye has the action of reducing elevated as well as normal intraocular pressure whether or not accompanied by glaucoma. Elevate intraocular pressure is a major risk factor in the pathogenesis of glaucomatous visual field loss. The higher the pressure of intraocular pressure, the greater the likelihood of glaucomatous visual field loss and optic nerve damage. The onset of reduction in intraocular pressure following administration of Timolol Maleate Ophthalmic solution can usually detected within one-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 Timolol Maleate Ophthalmic solution) is well maintained.

The precise mechanism of ocular hypotensive action of Timolol Maleate Ophthalmic solution is not clearly established at this time. Tonography and Fluorophotometry studies in man suggest that its predominant action may be related to reduced aqueous formation. However, in some studies a slight increase in outflow facility was also observed.

Pharmacokinetics

In a study of plasma drug concentration in six subjects, the systematic exposure to timolol was determined following twice daily administration of Timolol Maleate 0.5 %. The main peak plasma concentration following morning dosage was 0.46 ng/mL and the following afternoon dosing was 0.35 mg/mL.

Clinical studies

In controlled multiclinic studies in patients untreated intraocular pressures of 22 mmHg or greater. Timolol Maleate Ophthalmic solution or 0.5 percent administered twice a day produced a greater reduction in intraocular pressure than 1, 2, 3, or 4 percent philocarpine solution administered four times a day or 0.5, 1, or 2 percent epinephrine hydrochloride solution administered twice a day.

In these studies, Timolol Maleate Ophthalmic solution) was generally well tolerated and produced fewer and less severe side effects than philocarpine or epinephrine. A slight reduction of resting heart rate in some patients receiving Timolol Maleate Ophthalmic solution (mean reduction 2.9 beats/minute standard deviation 10.2) was observed.

CONTRAINDICATIONS

SENSOLOL is contraindicated in patients with (1) bronchial asthma; (2) a history of bronchial asthma; (3) severe chronic obstructive pulmonary disease: (4) sinus bradycardia; (5) second or third degree atrioventricular block; (6) overt cardiac failure; (7) cardiogenic shock; or (8) hypersensitivity to any component of this product.

WARNINGS

As with many topically applied ophthalmic drugs, this drug is observed systematically. **The same adverse reactions found with systematic administration of beta-adrenergic blocking agents may occur with topical administration. For example, severe 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 systematic or ophthalmic administration of timolol maleate (see CONTRAINDICATIONS).**

Cardiac failure

Sympathetic stimulation may be essential for support of the circulation in individuals with diminished myocardial contractility and its inhibition by beta adrenergic receptor blockade may precipitate more severe failure. In patients without the history of cardiac failure continued depression of the myocardium with beta blocking agents over a period of time can in some cases lead to cardiac failure.

ADVERSE REACTIONS

The most frequently reported adverse experiences have been burning and stinging upon instillation (approximately one in eight patients). The following additional adverse experiences have been reported less frequently with ocular administration of this or other timolol maleate formulations: BODY AS A WHOLE Headache, asthenia/fatigue, and chest pain. CARDIOVASCULAR Bradycardia, arrhythmia, hypotension, hypertension, syncope, heart block, cerebral vascular accident, cerebral ischemia, cardiac failure, worsening of angina pectoris, palpitation, cardiac arrest, pulmonary edema, edema claudication, Raynaud's phenomenon, and cold hands and feet.

DIGESTIVE: Nausea, diarrhea, dyspepsia, anorexia, and dry mouth.

IMMUNOLOGIC: Systematic lupus erythematosis.

NERVOUS SYSTEM/PSYCHIATRIC

Dizziness, increase in signs and symptoms of myasthema gravis, paresthesia, somnolence, insomnia, nightmares, behavioral changes and psychic disturbances including depression, confusion, hallucinations, anxiety, disorientation, nervousness, and memory loss.

SKIN Alopecia psoriasiform rash or exacerbation of psoriasis.

HYPERSENSITIVITY: Signs and symptoms of systematic allergic reactions including anaphylaxis, angioedema, urticaria, and localized and generalized rash.

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. If signs or symptoms suggesting reduced cerebral blood flow develop following initiation of therapy with SENSOLOL, alternative therapy should be considered. Choroidal detachment after filtration procedures has been reported with the administration of aqueous suppressant therapy (e.g. timolol)

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. SENSOLOL 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.

Storage and handling instructions:

Store between 15°C - 30°C

PROTECT FORM LIGHT

KEEP OUT OF REACH OF CHILDREN

NOT FOR INJECTION

FOR EXTERNAL USE ONLY

Shelf life

24 months from the date of Manufacture.

Presentation:

A clear colourless solution filled in 5mL Sterile Gamma-irradiated white opaque LDPE bottle sealed with Sterile Gamma-irradiated natural transparent LDPE open nozzle and Sterile Gamma-irradiated white HDPE tamp safe cap in printed carton along with leaflet.

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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