Name of Medicine

TIMOPTOL-XE®
*timolol maleate*
0.25% and 0.5% Ophthalmic Gel Forming Solution

Presentation
A colourless to nearly colourless, slightly opalescent, slightly viscous, aqueous ophthalmic solution.

Therapeutic Class
Timolol maleate is a non-selective beta-adrenergic receptor blocking agent.

Indications
TIMOPTOL-XE is indicated for the reduction of elevated intraocular pressure in patients with:

- ocular hypertension
- chronic open-angle glaucoma
- aphakic glaucoma
- secondary glaucoma (some cases)
- narrow angles and a history of spontaneous or iatrogenically induced narrow-angle closure in the opposite eye in whom reduction of intraocular pressure is necessary (see Warnings and Precautions)

Dosage and Administration
The usual starting dose is one drop of 0.25% TIMOPTOL-XE in the affected eye(s) once a day. If the clinical response is not adequate, the dosage may be changed to one drop of 0.5% TIMOPTOL-XE in the affected eye(s) once a day. Invert the closed container and shake once before each use. It is not necessary to shake the container more than once.

If needed, concomitant therapy with other agent(s) for lowering intraocular pressure may be given with TIMOPTOL-XE. The use of two topical beta-adrenergic blocking agents is not recommended (see Warnings and Precautions). Other topically applied medications should be administered no less than 10 minutes before TIMOPTOL-XE.

How To Transfer Patients From Other Therapy
When a patient is transferred from TIMOPTOL to TIMOPTOL-XE, TIMOPTOL should be discontinued after proper dosing on one day, and treatment with the same concentration of TIMOPTOL-XE started on the following day.

When a patient is transferred from another topical ophthalmic beta-adrenergic blocking agent, that agent should be discontinued after proper dosing on one day and treatment with TIMOPTOL-XE started on the following day with 1 drop of 0.25% TIMOPTOL-XE in the affected eye once a day. The dose may be increased to one drop of 0.5% TIMOPTOL-XE once a day if the clinical response is not adequate.

When a patient is transferred from a single antiglaucoma agent, other than a topical ophthalmic beta-adrenergic blocking agent, continue the agent and add one drop of 0.25% TIMOPTOL-XE to each affected eye once a day. On the following day, discontinue the
previously used antiglaucoma agent and continue TIMOPTOL-XE. If a greater response is required, substitute one drop of 0.5% TIMOPTOL-XE for the 0.25% dosage.

**Contraindications**
TIMOPTOL-XE is contraindicated in patients with:

- reactive airway disease, bronchial asthma or other severe chronic obstructive lung disorders or a history of bronchospasm
- uncontrolled heart failure (see Warnings & Precautions)
- cardiogenic shock
- sick sinus syndrome
- grade 2 and 3 AV block and infranodal AV block
- severe bradycardia
- hypersensitivity to any component of this product
- sino-atrial block

**Warnings and Precautions**
Patients should be instructed to avoid allowing the tip of the dispensing container to contact the eye or surrounding structures.

Patients should also be instructed that 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.

Patients should also be advised that if they develop an intercurrent ocular condition (e.g. trauma, ocular surgery or infection), they should immediately seek their physician's advice concerning the continued use of the present multidose container.

There have been reports of bacterial keratitis associated with the use of multiple dose containers of topical ophthalmic products. These containers had been inadvertently contaminated by patients who, in most cases, had a concurrent corneal disease or a disruption of the ocular epithelial surface.

As with other topically applied ophthalmic agents, this agent may be absorbed systemically.

The same adverse reactions found with systemic administration of beta-adrenergic blocking agents may occur with topical administration.

**Cardio-respiratory Reactions**
Cardiac failure should be adequately controlled before beginning therapy with TIMOPTOL-XE. In patients with a history of severe cardiac disease, signs of cardiac failure should be watched for 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 complications, including death due to bronchospasm in patients with asthma, and cardiac complications, including rarely death in association with cardiac failure, have been reported following administration of beta-adrenergic blocking agents. These are potential complications of therapy with TIMOPTOL-XE.
In patients with mild/moderate chronic obstructive pulmonary disease (COPD), Timoptol XE 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.

Other

Patients who are already receiving a beta-adrenergic blocking agent systemically and who are given TIMOPTOL-XE 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.

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 maleate has little or no effect on the pupil. Should TIMOPTOL-XE be used to reduce elevated intraocular pressure in angle-closure glaucoma, it should be used with a miotic and not alone.

Choroidal detachment has been reported with administration of aqueous suppressant therapy (e.g. timolol, acetazolamide) after filtration procedures.

TIMOPTOL-XE has not been studied in patients wearing contact lenses. In a clinical study, the time required to eliminate 50% of the gellan solution from the eye was up to 30 minutes.

Risk from Anaphylactic Reaction

While taking beta-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 used to treat anaphylactic reactions.

Use in Pregnancy
TIMOPTOL-XE has not been studied in human pregnancy. The use of TIMOPTOL-XE requires that the anticipated benefit be weighed against possible hazards.

Nursing Mothers
Timolol is detectable in human milk. Because of the potential for serious adverse reactions from TIMOPTOL-XE in infants, a decision should be made whether to discontinue nursing or to discontinue the medicine, taking into account the importance of the medicine to the mother.

Use in Children
Timolol maleate ophthalmic solution has been shown to be efficacious and well tolerated in children; however, the formulation of timolol maleate found in TIMOPTOL-XE has not been studied in the paediatric age group.
Systemic Effects of Beta-Adrenergic Blocking Agents

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 a 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. At the first sign or symptom of cardiac failure TIMOPTOL-XE should be discontinued.

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 such as isoproterenol, dopamine, dobutamine or levarterenol (See ADDITIONAL OVERDOSAGE INFORMATION).

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

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.

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

General
Because of potential effects of beta-adrenergic blocking agents relative to 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 TIMOPTOL-XE, alternative therapy should be considered.

Patients with bronchial asthma, a history of bronchial asthma, severe chronic obstructive pulmonary disease, sinus bradycardia, second or third degree atrioventricular block, or cardiac failure should be advised not to take this product (see Contraindications).

Animal Toxicology
No adverse ocular effects were observed in monkeys and rabbits administered TIMOPTOL-XE topically in studies lasting 12 months and one month, respectively. The oral LD$_{50}$ of timolol is 1190 and 900 mg/kg in female mice and female rats, respectively. The oral LD$_{50}$ of gellan gum is greater than 5000 mg/kg in rats.
Carcinogenesis Mutagenesis, Impairment Of Fertility

In a two-year oral study of timolol maleate in rats there was a statistically significant (P<0.05) increase in the incidence of adrenal pheochromocytomas in male rats administered 300mg/kg/day (300 times* the maximum recommended human oral dose). Similar differences were not observed in rats administered oral doses equivalent to 25 or 100 times the maximum recommended human oral dose.

In a lifetime oral study in mice, there were statistically significant (P<0.05) increases in the incidence of benign and malignant pulmonary tumours and benign uterine polyps and mammary adenocarcinoma in female mice at 500mg/kg/day (500 times the maximum recommended human dose), but not at 5 or 50mg/kg/day. In a subsequent study in female mice, in which post-mortem examinations were limited to uterus and lungs, a statistically significant increase in the incidence of pulmonary tumours was again observed at 500mg/kg/day.

The increased occurrence of mammary adenocarcinoma was associated with elevations in serum prolactin which occurred in female mice administered timolol at 500mg/kg/day, but not at doses of 5 or 50mg/kg/day. An increased incidence of mammary adenocarcinomas in rodents has been associated with administration of several other therapeutic agents, which elevate serum prolactin, but no correlation between serum prolactin levels and mammary tumours has been established in man. Furthermore, in adult human female subjects who received oral dosages of up to 60mg of timolol maleate, the maximum recommended human oral dosage, there were no clinically meaningful changes in serum prolactin.

In oral studies of gellan gum administered to rats for up to 105 weeks at concentrations up to 5% of their diet and to mice for 96-98 weeks at concentrations up to 3% of their diet, no overt signs of toxicity and no increase in the incidence of tumours was observed.

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). In Ames tests the highest concentrations of timolol employed, 5000 or 10,000 mcg/plate, were associated with statistically significant elevations (P<0.05) of revertants observed with tester strain TA100 (in seven replicate assays), but not in the remaining three strains. In the assays with tester strain TA100, no consistent dose-response relationship was observed, nor did the ratio of test to control revertants reach 2. A ratio of 2 is usually considered the criterion for a positive Ames test.

Gellan gum was devoid of mutagenic potential when evaluated in vivo (mouse) in the micronucleus assay using doses up to 450 mg/kg. In addition, gellan gum in concentrations up to 20 mg/ml was not detectably mutagenic in the following in vitro assays:
1. unscheduled DNA synthesis in rat hepatocytes assay
2. V-79 mammalian cell mutagenesis assay, and
3. chromosomal aberrations in Chinese hamster ovary cells assay

In Ames tests, gellan gum (in concentrations up to 1000 mcg/plate, which is its limit of solubility) did not induce a 2-fold or greater increase in revertants relative to the solvent control. It is therefore not detectably mutagenic.

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.
A two generation reproduction and fertility study in rats treated with dietary concentrations up to 5% gellan gum showed no adverse effect on male or female fertility.

* The maximum recommended oral dose is 60mg of timolol. One drop of TIMOPTOL 0.5% contains about 1/300 of this dose which is about 0.2mg.

**Pregnancy Category**

Teratogenicity studies with timolol in mice and rabbits at doses up to 50mg/kg/day (50 times the maximum recommended human oral dose) showed no evidence of foetal malformations. Although delayed foetal ossification was observed at this dose in rats, there were no adverse effects on postnatal development of offspring.

Doses of 1000 mg/kg/day (1,000 times the maximum recommended human oral dose) were maternotoxic in mice and resulted in an increased number of foetal resorptions. Increased foetal resorptions were also seen in rabbits at doses of 100 times the maximum recommended human oral dose, in this case without apparent maternotoxicity.

Teratogenicity studies in rats with 2.5, 3.8, and 5% gellan gum in their diet showed no increase in overall incidences of foetal malformations as compared to the control group values. There were no skeletal anomalies related to treatment with gellan gum.

**Adverse Effects**

TIMOPTOL-XE is usually well tolerated. The most frequent medicine-related complaint in the original clinical studies for TIMOPTOL-XE was transient blurred vision (6.0%), lasting from 30 seconds to 5 minutes, following instillation.

The following possibly, probably, or definitely medicine-related adverse reactions occurred with frequency of at least 1% in active treatment controlled clinical trials:

**Ocular:** Burning and stinging, conjunctival injection discharge, foreign body sensation, itching.

The following additional adverse reaction have been reported with ocular administration of this or other timolol maleate formulations, either in clinical trials or since the medicine has been marketed.

**Special Senses:** Signs and symptoms of ocular irritations, including conjunctivitis, blepharitis, keratitis, and decreased corneal sensitivity, and dry eyes. Visual disturbances, including refractive changes (due to withdrawal of miotic therapy in some cases), diplopia, and ptosis, choroidal detachment following filtration surgery (see Warnings and 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), 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 anaphylaxis, angioedema, urticaria, localised and generalised rash.
**Nervous System/Psychiatric**: Depression, dizziness, insomnia, nightmares, memory loss, paresthesia.

**Neuromuscular**: Increase in signs and symptoms of myasthenia gravis

**Digestive**: Nausea, diarrhoea, dyspepsia, dry mouth, abdominal pain.

**Urogenital**: Decreased libido, Peyronie’s disease, sexual dysfunction.

**Immunologic**: Systemic lupus erythematosus.

**Musculoskeletal**: Myalgia.

**Potential Adverse Effects**
Adverse effects reported in clinical experience with systemic timolol maleate may be considered potential adverse effects of ophthalmic timolol maleate.

**Adverse Effects, Causal Relationship Unknown**
The following adverse effects have been reported but causal relationship to therapy with timolol maleate has not been established: aphakic cystoid macular oedema, nasal congestion, anorexia, CNS effects (e.g. behavioural changes including confusion, hallucinations, anxiety, disorientation, nervousness, somnolence, and other psychiatric disturbances), hypertension, retroperitoneal fibrosis, and pseudopemphigoid.

**Interactions**
Although timolol maleate used alone has little or no effect on pupil size, mydriasis resulting from concomitant therapy with epinephrine has been reported occasionally. The potential for mydriasis exists from concomitant therapy with TIMOPTOL-XE and epinephrine.

The potential exists for additive effects and production of hypotension and/or marked bradycardia when TIMOPTOL-XE is administered together with a calcium-channel blocker, a catecholamine-depleting medicine, antiarrhythmics, parasympathomimetics or another beta-adrenergic blocking agents.

Close observation of the patient is recommended when a beta blocker is administered to patients receiving catecholamine-depleting medicines 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.

The potential exists for hypotension, atroventricular (AV) conduction disturbances and left ventricular failure to occur in patients receiving a beta-blocking agent when an oral calcium-channel blocker is added to the treatment regimen. The nature of any cardiovascular adverse effect tends to depend on the type of calcium-channel 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.

The concomitant use of beta-adrenergic blocking agents and digitalis with either diltiazem or verapamil may have additive effects in prolonging AV conduction time.
Oral calcium-channel 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.

Intravenous calcium-channel blockers should be used with caution in patients receiving 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.

Oral β-adrenergic blocking agents may exacerbate the rebound hypertension, which can follow the withdrawal of clonidine. If the two medicines are coadministered, the β-adrenergic blocking agent should be withdrawn several days before the gradual withdrawal of clonidine. If replacing clonidine by β-blocker therapy, the introduction of β-adrenergic blocking agents should be delayed for several days after clonidine has stopped.

**Overdosage**

There have been reports of inadvertent overdosage with TIMOPTOL 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 (see also Adverse Effects).

The following additional therapeutic measures should be considered:

- **Symptomatic Bradycardia**: Administer atropine sulphate intravenously in a dosage of 0.25 to 2 mg to induce vagal blockade. If bradycardia persists, intravenous isoproterenol hydrochloride should be administered cautiously. In refractory cases the use of a transvenous cardiac pacemaker may be considered.
- **Heart Block (second or third degree)**: Administer isoproterenol hydrochloride or insert a transvenous cardiac pacemaker.
- **Hypotension**: Use sympathomimetic pressor medicine therapy, such as dopamine, dobutamine or levarterenol. In refractory cases the use of glucagon hydrochloride has been reported to be useful.
- **Acute Cardiac Failure**: Conventional therapy with digitalis, diuretics and oxygen should be instituted immediately. In refractory cases the use of intravenous aminophylline is suggested. This may be followed if necessary by glucagon hydrochloride, which has been reported to be useful.
- **Bronchospasm**: Administer isoproterenol hydrochloride. Additional therapy with aminophylline may be considered.

Timolol does not dialyse readily.

**Actions**

TIMOPTOL-XE* (timolol maleate, MSD) Ophthalmic Gel Forming Solution is a formulation of TIMOPTOL (timolol maleate, MSD) containing a novel delivery vehicle. TIMOPTOL-XE reduces elevated and normal intraocular pressure whether or not associated with glaucoma. Elevated intraocular pressure is a major risk factor in the pathogenesis of glaucomatous visual field loss. The higher the intraocular pressure, the greater the likelihood of glaucomatous visual field loss and optic nerve damage.
TIMOPTOL-XE has a safety profile similar to that of TIMOPTOL, and both are generally well tolerated. Bradycardia was reported less frequently with TIMOPTOL-XE than with TIMOPTOL. In the three studies comparing TIMOPTOL-XE 0.5% once a day to TIMOPTOL 0.5% twice a day, TIMOPTOL-XE did not reduce mean heart rate as much as TIMOPTOL (see Warnings and Precautions). At trough (24 hours post-dose TIMOPTOL-XE, 12 hours post-dose TIMOPTOL), the mean reduction was 0.8 beats/minute for TIMOPTOL-XE and 3.6 beats/minute for TIMOPTOL; whereas at two hours post-dose, the mean reduction in heart rate was comparable (3.8 beats/minute for TIMOPTOL-XE and 5 beats/minute for TIMOPTOL). There was a higher incidence of transient blurred vision following instillation in patients administered TIMOPTOL-XE.

Clinical studies have shown that the intraocular pressure lowering effect of TIMOPTOL-XE administered once a day is equivalent to TIMOPTOL administered twice a day. The vehicle of TIMOPTOL-XE increases the contact time of the medicine with the eye.

Timolol maleate is a nonselective beta-adrenergic receptor blocking agent that does not have 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 biologic 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 biologic response.

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.

**Pharmacokinetics**

Maximum reduction of intraocular pressure occurs in two to four hours with TIMOPTOL-XE. Significant lowering of intraocular pressure has been maintained for 24 hours with both 0.25% and 0.5% TIMOPTOL-XE.

In a study of plasma concentration in six subjects, the systemic exposure to timolol was determined following once daily administration of TIMOPTOL-XE 0.5% in the morning. The mean peak plasma concentration following this morning dose was 0.28 ng/mL.

Onset of action of timolol maleate is usually rapid, occurring approximately 20 minutes after topical application to the eye. The precise mechanism of action of timolol maleate in lowering intraocular pressure is not clearly established.

A fluorescein study and tonography studies indicate that the predominant action may be related to reduced aqueous formation. However, in some studies a slight increase in outflow facility was also observed.

In clinical studies timolol maleate was generally effective in more patients and produced fewer and less severe adverse effects than either pilocarpine or epinephrine.
Unlike miotics, timolol maleate 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 the dim or blurred vision and night blindness produced by miotics are not evident. In addition, in patients with cataracts the inability to see around lenticular opacities when the pupil is constricted by miotics is avoided. When changing patients from miotics to TIMOPTOL-XE, refraction may be necessary after the effects of the miotic have passed.

As with other antiglaucoma agents, diminished responsiveness to timolol maleate after prolonged therapy has been reported in some patients. However, in clinical studies of TIMOPTOL in which 164 patients were followed for at least 3 years, no significant difference in mean intraocular pressure was observed after initial stabilisation. This indicates that the intraocular pressure-lowering effect of timolol maleate is well maintained.

In a study of plasma timolol concentrations, the systemic exposure to timolol was less when normal healthy volunteers received 0.5% TIMOPTOL-XE once daily than when they received 0.5% TIMOPTOL twice daily.

**Pharmaceutical Precautions**
Protect from light, store at or below 30°C. Avoid freezing.

**Medicine Classification**
Prescription Medicine.

**Package Quantities**
TIMOPTOL-XE 0.25% and 5% solution 2.5 mL

**Further Information**

**Chemistry**
(Timolol maleate is a β-adrenergic receptor blocking agent. The chemical name is (S)-1-[(1,1-dimethyllethyl)amino]-3-[[4-(4-morpholinyl)-1,2,5-thiadiazol-3-yl]oxy]-2-propanol (Z)-2-butenedioate(1:1) (salt). Timolol maleate possesses an asymmetric carbon atom in the structure and is provided as the levo isomer. The empirical formula is C_{13}H_{24}N_{4}O_{3}S•C_{4}H_{4}O_{4} and the structural formula is:

![Timolol Maleate Structural Formula](image)

Timolol maleate has a molecular weight of 432.50. It is a white, odourless, crystalline powder which is soluble in water, methanol, and alcohol. TIMOPTOL is stable at room temperature.

Gellan solution contains a highly purified anionic heteropolysaccharide derived from gellan gum. Aqueous solutions of gellan gum form a clear transparent gel in the presence of cations. The concentration of sodium cations in tears is ideally suited to cause gelation of the material when topically instilled in the conjunctival sac.
Composition
Each mL of TIMOPTOL-XE 0.25% contains 2.5 mg of timolol (3.4 mg of timolol maleate). Each mL of TIMOPTOL-XE 0.5% contains 5.0 mg of timolol (6.8 mg of timolol maleate). Inactive ingredients: gellan gum, tromethamine, mannitol, and water for injection. Benzododecinium bromide 0.012% is added as preservative.

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