PROFESSIONAL INFORMATION

SCHEDULING STATUS S3

1. NAME OF THE MEDICINE

TIMOPTOL® 0,5 %

Strength

TIMOPTOL® 0,5 %: Each ml contains 5,0 mg of timolol base

Pharmaceutical form

Ophthalmic Solution

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Qualitative declaration

Timolol maleate

Quantitative declaration

TIMOPTOL® 0,5 %: Each ml contains 5,0 mg of timolol base (present as timolol maleate).

Benzalkonium chloride (0,01 % *m/v*) as preservative.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Ophthalmic Solution

Colourless to light yellow, clear aqueous solution

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

TIMOPTOL® ophthalmic solution is indicated for the reduction of elevated intraocular pressure in:

- patients with ocular hypertension
- patients with chronic open-angle glaucoma
- aphakic patients with glaucoma
- some patients with secondary glaucoma

Patients with 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 section 4.4).

TIMOPTOL® is also indicated as concomitant therapy in patients with paediatric glaucoma, who are inadequately controlled with other anti-glaucoma therapy (see section 4.4).

4.2 Posology and method of administration

Posology

The dose is one drop of 0,5 % solution in each affected eye twice a day.

If needed, concomitant therapy with other agent(s) for lowering intraocular pressure may be given with TIMOPTOL®. The use of two topical beta-adrenergic blocking agents is not recommended (see section 4.4).

Since in some patients the pressure-lowering response to TIMOPTOL® may require a few weeks to stabilise, evaluation should include a determination of intraocular pressure after approximately 4 weeks of treatment with TIMOPTOL®.

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 using nasolacrimal occlusion, or closing the eyelids for 2 minutes, the systemic absorption is reduced. This may result in an increase in local activity.

If one dose is missed, treatment should continue with the next dose as planned.

If more than one topical ophthalmic medicine is being used, they should be administered at least 5 minutes apart.

Paediatric population

The recommended dose for children above 3 years of age is one drop of 0,5 % solution in the affected eye(s) every 12 hours if necessary. Use in younger patients should only be considered when strictly indicated and under close observation.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

Sinus bradycardia, sino-atrial block, second- or third-degree atrioventricular block, overt cardiac failure, cardiogenic shock.

Reactive airway disease, bronchial asthma or with a history of bronchial asthma, or severe chronic obstructive pulmonary disease.

4.4 Special warnings and precautions for use

As the possibility of adverse effects on the permeability and the danger of disruption of the corneal epithelium with prolonged or repeated usage of benzalkonium chloride preserved ophthalmological preparations cannot be excluded, regular ophthalmological examination is

required. Caution should be exercised in the use of benzalkonium chloride preserved topical medication over an extended period in patients with extensive ocular surface disease.

Benzalkonium chloride has been reported to cause eye irritation, symptoms of dry eyes and may affect the tear film and corneal surface. Should be used with caution in dry eye patients and in patients where the cornea may be compromised. Patients should be monitored in case of prolonged use.

Particular caution should be exercised with patients suffering from the following: Asthma, bronchitis, chronic respiratory diseases, second- and third-degree heart block and sinus bradycardia less than 50 per minute, peripheral vascular diseases and Raynaud's phenomenon.

In the peri-operative period it is generally unwise to reduce the dosage.

A patient's normal tachycardiac response to hypovolaemia or blood loss may be obscured during or after surgery. Particular caution should be taken in this regard.

TIMOPTOL® ophthalmic solution may be absorbed systemically.

The same types of cardiovascular, pulmonary and other adverse reactions found with systemic administration of beta-adrenergic blocking agents may occur with topical administration. Incidence of systemic ADRs after topical ophthalmic administration is lower than for systemic administration. To reduce the systemic absorption, see section 4.2.

Cardiac disorders

TIMOPTOL® ophthalmic solution should be used with caution in patients with known contra-indications to systemic use of beta-adrenergic receptor blocking agents. These include sinus bradycardia and greater than first-degree heart block, cardiogenic shock, diabetes, especially labile diabetes.

In patients with cardiovascular diseases (e.g. coronary heart disease, Prinzmetal's angina and cardiac failure) and hypotension therapy with beta-blockers should be critically assessed and the therapy with other active substances should be considered. Patients with cardiovascular diseases should be watched for signs of deterioration of these diseases and of adverse reactions.
Cardiac failure should be adequately controlled before beginning therapy with TIMOPTOL®.
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 disorders

Respiratory reactions, including death due to bronchospasm in patients with asthma have been reported following administration of some ophthalmic beta- blockers.
In patients with mild/moderate chronic obstructive pulmonary disease (COPD), TIMOPTOL® 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.

Hypoglycaemia/diabetes

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 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.

Surgical anaesthesia

Beta-blocking ophthalmological preparations may block systemic beta-agonist effects e.g. of epinephrine (adrenaline). The anaesthesiologist should be informed when the patient is receiving timolol.

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.

Corneal diseases

Ophthalmic beta-blockers may induce dryness of eyes. Patients with corneal diseases should be treated with caution.

Other beta-blocking agents

Patients who are already receiving a beta-adrenergic receptor blocking agent systemically and who are given TIMOPTOL® should be closely 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 (see section 4.5).

There have been reports of skin rashes and/or dry eyes associated with the use of beta-adrenoreceptor blocking medicines. The reported incidence is small and in most cases the symptoms have cleared when treatment was withdrawn. Discontinuation of the medicine should be considered if any such reaction is not otherwise explicable. Cessation of therapy involving beta-blockade should be gradual.

Choroidal detachment

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

In patients with angle-closure glaucoma, the immediate objective of treatment is to reopen the angle. This requires constricting the pupil with a miotic. TIMOPTOL® has little or no effect on the pupil. When TIMOPTOL® is used to reduce elevated intraocular pressure in angle-closure glaucoma it should be used with a miotic and not alone.

Patients should 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.

TIMOPTOL® has been generally well tolerated in glaucoma patients wearing conventional hard contact lenses. TIMOPTOL® has not been studied in patients wearing lenses made with material other than polymethylmethacrylate (PMMA), which is used to make hard contact lenses.

TIMOPTOL® contains benzalkonium chloride as a preservative which may be deposited in soft contact lenses; therefore TIMOPTOL® 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.

Anaphylactic Reactions

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 (adrenaline) used to treat anaphylactic reactions.

Paediatric Population

The safety of Timoptol 0.5 % has not been established in children < 3 years of age.

Timolol solutions should generally be used cautiously in young glaucoma patients.

It is important to notify the parents of potential side effects so they can immediately discontinue the medicine therapy (see section 4.8). Signs to look for are, for example, coughing and wheezing.

Because of the possibility of apnoea and Cheyne-Stokes breathing, the medicine should be used with extreme caution in neonates, infants and younger children. A portable apnoea monitor may also be helpful for neonates on timolol.

4.5 Interaction with other medicines and other forms of interaction

No specific medicine interaction studies have been performed with timolol maleate.

Although TIMOPTOL® used alone has little or no effect on pupil size, mydriasis resulting from concomitant therapy with TIMOPTOL® and epinephrine (adrenaline) has been reported.

Potentiated systemic beta-blockade (e.g. decreased heart rate, depression) has been reported during combined treatment with CYP2D6 inhibitors (e.g. quinidine, SSRIs - including fluoxetine and paroxetine) and timolol.

The potential exists for additive effects and production of hypotension and/or marked bradycardia when TIMOPTOL® is administered together with an oral calcium entry blocker, catecholamine-depleting medicines, antiarrhythmics (including amiodarone), parasympathomimetics, digitalis glycosides, rauwolfia alkaloids, guanethidine or 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.

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.

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-channel blocker is added to the treatment regimen. The nature of any cardiovascular adverse effects 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.

Intravenous calcium channel 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.

While no side effects of the oculo-cutaneous syndrome type have been described with this product, the possibility of their development with prolonged usage has not been excluded, and regular ophthalmic examination is required.

TIMOPTOL® should be administered with care in patients suffering from myasthenia gravis. Deterioration in myasthenia has been reported after application of the ophthalmic solution.

Oral beta-adrenergic blocking agents may exacerbate the rebound hypertension which can follow the withdrawal of clonidine.

Special note

Digitalisation of patients receiving long-term TIMOPTOL® therapy may be necessary if congestive cardiac failure is likely to develop. This combination can be considered despite the potentiation of negative chronotropic effect of the two medicines. Careful control of

dosages and of the individual patient's response (and notably pulse rate) is essential in this situation.

Abrupt discontinuation of therapy may cause exacerbation of angina pectoris in patients suffering from ischaemic heart disease. Discontinuation of therapy should be gradual, and patients should be advised to limit the extent of their physical activity, during the period that the medicine is being discontinued.

Patients with phaeochromocytoma usually require treatment with an alpha-adrenergic blocker.

4.6 Fertility, pregnancy and lactation

Pregnancy

There are no adequate data for the use of timolol maleate in pregnant women.

TIMOPTOL® should not be used during pregnancy.

To reduce the systemic absorption, see section 4.2.

Epidemiological studies have not revealed malformative effects but show a risk for intra uterine growth retardation when beta-blockers are administered by the oral route. In addition, signs and symptoms of beta-blockade (e.g. bradycardia, hypotension, respiratory distress and hypoglycaemia) have been observed in the neonate when beta-blockers have been administered until delivery. If TIMOPTOL® is administered until delivery, the neonate should be carefully monitored during the first days of life.

Breastfeeding

TIMOPTOL® is detectable in human milk. Because of the potential for serious adverse reactions from TIMOPTOL® 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.

4.7 Effects on ability to drive and use machines

Possible side effects such as dizziness, visual disturbances, refractive changes, diplopia, ptosis, frequent episodes of mild and transient blurred vision and fatigue may affect some patients' ability to drive or operate machinery.

4.8 Undesirable effects

Like other topically applied ophthalmic medicines, timolol is absorbed into the systemic circulation. This may cause similar undesirable effects as seen with systemic beta-blocking agents. Incidence of systemic ADRs after topical ophthalmic administration is lower than for systemic administration.

TIMOPTOL® ophthalmic solution is usually well tolerated. The following adverse reactions have been reported with ocular administration of this or other timolol maleate formulations, either in clinical trials or since the medicine has been marketed.

Additional side effects have been reported in clinical experiences with systemic timolol maleate, and may be considered potential effects of ophthalmic timolol maleate. Also listed are adverse reactions seen within the class of ophthalmic beta-blockers and may potentially occur with TIMOPTOL®.

Very Common (≥ 1/10)	**Common** (≥ 1/100 to <1/10)	**Uncommon** (≥ 1/1 000 to <1/100)	**Rare** (≥ 1/10 000 to <1/1 000)	**Not Known**
Blood and lymphatic system disorders *Systemic*				
				non-thrombocytopenic purpura
Immune system disorders *Ocular*				

Very Common (≥ 1/10)	**Common** (≥ 1/100 to <1/10)	**Uncommon** (≥ 1/1 000 to <1/100)	**Rare** (≥ 1/10 000 to <1/1 000)	**Not Known**
			systemic lupus erythematosus	pruritus
Systemic				
			signs and symptoms of allergic reactions including anaphylaxis, angioedema, urticaria, localised and generalised rash	anaphylactic reaction
Psychiatric disorders *Ocular*				
		depression	insomnia, nightmares, memory loss	hallucination
Systemic				
				diminished concentration, increased dreaming
Nervous system disorders *Ocular*				

Very Common (≥ 1/10)	**Common** (≥ 1/100 to <1/10)	**Uncommon** (≥ 1/1 000 to <1/100)	**Rare** (≥ 1/10 000 to <1/1 000)	**Not Known**
	headache	syncope, dizziness	cerebrovascular accident, cerebral ischaemia, paraesthesia, increase in signs and symptoms of myasthenia gravis	
Systemic				
				vertigo, local weakness
Eye disorders *Ocular*				
	signs and symptoms of ocular irritation (including burning, stinging, itching, tearing, redness) conjunctivitis, blepharitis, keratitis, decreased corneal	visual disturbances including refractive changes (due to withdrawal of miotic therapy in some cases)	ptosis, diplopia, choroidal detachment (following filtration surgery, see section 4.4), cases of corneal calcification have been reported very rarely in association with the use of phosphate containing eye drops in some	blurred vision, corneal erosion

Very Common (≥ 1/10)	**Common** (≥ 1/100 to <1/10)	**Uncommon** (≥ 1/1 000 to <1/100)	**Rare** (≥ 1/10 000 to <1/1 000)	**Not Known**
	sensitivity and dry eyes		patients with significantly damaged corneas	
Ear and labyrinth disorders *Ocular*				
			tinnitus	
Cardiac disorders *Ocular*				
		bradycardia	chest pain, palpitation, oedema, arrhythmia, congestive heart failure, heart block, cardiac arrest	cardiac failure, oedema
Systemic				
				atrioventricular block (second- or third-degree), sino-atrial block, pulmonary oedema, worsening of arterial insufficiency, worsening of

Very Common (≥ 1/10)	**Common** (≥ 1/100 to <1/10)	**Uncommon** (≥ 1/1 000 to <1/100)	**Rare** (≥ 1/10 000 to <1/1 000)	**Not Known**
				angina pectoris, vasodilation
Vascular disorders *Ocular*				
			claudication, hypotension, Raynaud's phenomenon, cold hands and feet	
Respiratory, thoracic and mediastinal disorders *Ocular*				
		dyspnoea	bronchospasm (predominantly in patients with pre-existing bronchospastic disease), respiratory failure, cough	
Systemic				
				rales
Gastrointestinal disorders *Ocular*				

Very Common (≥ 1/10)	**Common** (≥ 1/100 to <1/10)	**Uncommon** (≥ 1/1 000 to <1/100)	**Rare** (≥ 1/10 000 to <1/1 000)	**Not Known**
		nausea, dyspepsia	diarrhoea, dry mouth	abdominal pain, dysgeusia, vomiting
Skin and subcutaneous tissue disorders *Ocular*				
			alopecia, psoriasiform rash or exacerbation of psoriasis	skin rash
Systemic				
				sweating, exfoliative dermatitis
Reproductive system and breast disorders *Ocular*				
			Peyronie's disease, decreased libido	sexual dysfunction such as impotence
Systemic				
				micturition difficulties
General disorders and administration site conditions *Ocular*				
		asthenia/fatigue		
Systemic				

Very Common (≥ 1/10)	**Common** (≥ 1/100 to <1/10)	**Uncommon** (≥ 1/1 000 to <1/100)	**Rare** (≥ 1/10 000 to <1/1 000)	**Not Known**
				extremity pain, decreased exercise tolerance
Metabolism and nutrition disorders *Ocular*				
				hypoglycaemia
Systemic				
				hyperglycaemia
Musculoskeletal and connective tissue disorders *Ocular*				
				myalgia
Systemic				
				arthralgia

Respiratory reactions and cardiac reactions, including death due to bronchospasm in cardiac failure have been reported following administration of TIMOPTOL®. The frequency of these events has not been determined.

Aphakic cystoid macular oedema, nasal congestion, anorexia, CNS effects (e.g. behavioural changes including confusion, hallucinations, anxiety, disorientation, nervousness, somnolence, and other psychic disturbances), hypertension, retroperitoneal fibrosis and pseudo pemphigoid have been reported, although a causal relationship to TIMOPTOL® has not been established.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Health care providers are asked to report any suspected adverse reactions to SAHPRA via the "**6.04**

Adverse Drug Reactions Reporting Form", found online under SAHPRA's publications: https://www.sahpra.org.za/Publications/Index/8

Alternatively report to the following e-mail address: ZADrugsafety@mundipharma.co.za.

4.9 Overdose

The most common signs and symptoms to be expected with overdosage with administration of a systemic beta-adrenergic receptor blocking agent are symptomatic bradycardia, hypotension, bronchospasm and acute cardiac failure.

In addition, 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, hypotension, bronchospasm, acute cardiac insufficiency and cardiac arrest (see section 4.8).

The following therapeutic measures should be considered:

1. Symptomatic bradycardia: Use 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.
2. 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.
3. Bronchospasm: Use isoproterenol hydrochloride. Additional therapy with aminophylline may be considered.
4. 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.

5. Heart block (second- or third-degree): Use isoproterenol hydrochloride or a transvenous cardiac pacemaker.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

A.15.4 Ophthalmic Preparations, other.

ATC code: S01ED01.

Mechanism of action

Timolol maleate ophthalmic solution reduces elevated and normal intraocular pressure whether or not associated with glaucoma.

Timolol maleate is a non-selective beta-adrenergic receptor blocking agent that does not have significant intrinsic sympathomimetic, direct myocardial depressant or local anaesthetic (membrane stabilising) activity.

The precise mechanism of action of timolol maleate 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. Timolol maleate reduces intraocular pressure with little or no effect on accommodation or pupil size.

5.2 Pharmacokinetic properties

Onset of action of timolol maleate is usually rapid, occurring approximately 20 minutes after topical application to the eye. Maximum reduction of intraocular pressure occurs in 1 to 2 hours. Significant lowering of intraocular pressure has been maintained for as long as 24 hours with timolol maleate ophthalmic solution.

5.3 Preclinical safety data

No adverse ocular effects were observed in rabbits and dogs administered timolol maleate topically in studies lasting one and two years, respectively. The oral LD_{50} of the medicine is 1,190 and 900 mg/kg in female mice and female rats, respectively.

Carcinogenesis, mutagenesis, impairment of fertility

In a two-year oral study of timolol maleate in rats there was a statistically significant ($p \leq 0,05$) increase in the incidence of adrenal phaeochromocytomas in male rats administered 300 mg/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 ($p \leq 0,05$) increases in the incidence of benign and malignant pulmonary tumours, benign uterine polyps and mammary adenocarcinoma in female mice at

500 mg/kg/day (500 times the maximum recommended human dose), but not at 5 or 50 mg/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 500 mg/kg/day. The increased occurrence of mammary adenocarcinoma was associated with elevations in serum prolactin which occurred in female mice administered timolol at 500 mg/kg/day, but not at doses of 5 or 50 mg/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 60 mg of timolol maleate, the maximum recommended human oral dosage, there were no clinically meaningful changes in serum prolactin.

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, 5,000 or 10,000 mcg/plate, were associated with statistically significant

($p \leq 0,05$) elevations 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. 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.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

The other ingredients are: sodium hydroxide, sodium phosphate dibasic anhydrous, sodium phosphate monobasic and water for injection. Benzalkonium chloride is added as preservative.

6.2 Incompatibilities

None known

6.3 Shelf life

24 months.

6.4 Special precautions for storage

Store TIMOPTOL® at or below 25 ºC. Protect from light.

DO NOT USE MORE THAN 30 DAYS AFTER OPENING.

6.5 Nature and contents of container

TIMOPTOL® Ophthalmic Solution is supplied in Ocumeter™ containers containing 5 ml solution.

TIMOPTOL® Ophthalmic Solution is a colourless to light yellow, clear aqueous solution.

The label on the cap of TIMOPTOL® 0,5 % is lilac.

7. HOLDER OF CERTIFICATE OF REGISTRATION

Mundipharma (Pty) Ltd,

Block D, Grosvenor Square

Park Lane, Century City

Cape Town, 7441

South Africa

8. REGISTRATION NUMBER(S)

South Africa S3

TIMOPTOL® 0,5 %: K/15.4/340

Botswana S2

TIMOPTOL® 0,5 %: B9315915

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

5 December 1978

10. DATE OF REVISION OF THE TEXT

6 December 2022