SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Timoptol-LA 0.5% w/v gel-forming eye drops, solution

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each millilitre of 0.5% w/v solution contains an amount of timolol maleate equivalent to 5 mg timolol.

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Gel-forming eye drops solution.

Colourless or nearly colourless, slightly opalescent, slightly viscous, sterile eye drop solution.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

A beta-adrenoreceptor blocker used topically in the reduction of elevated intra-ocular pressure in various conditions including the following: patients with ocular hypertension; patients with chronic open-angle glaucoma including aphakic patients; some patients with secondary glaucoma.

4.2 Posology and method of administration

Posology

Recommended therapy is one drop 0.25% solution in each affected eye once a day.

If clinical response is not adequate, dosage may be changed to one drop 0.5% solution in each affected eye once a day.

If needed, Timoptol-LA may be used with other agent(s) for lowering intra-ocular pressure. Other topically applied medication should be administered not less than 10 minutes before Timoptol-LA. The use of two topical beta-adrenergic blocking agents is not recommended (see section 4.4).

Intra-ocular pressure should be reassessed approximately four weeks after starting treatment because response to Timoptol-LA may take a few weeks to stabilise.

Transfer from other agents
When transferring a patient from Timoptol to Timoptol-LA, discontinue Timoptol after a full day of therapy, starting treatment with the same concentration of Timoptol-LA on the following day.

When another topical beta-blocking agent is being used, discontinue its use after a full day of therapy and start treatment with Timoptol-LA the next day with one drop of 0.25% Timoptol-LA in each affected eye once a day. The dosage may be increased to one drop of 0.5% solution in each affected eye once a day if the response is not adequate.

When transferring a patient from a single anti-glaucoma agent other than a topical beta-blocking agent, continue the agent and add one drop of 0.25% Timoptol-LA in each affected eye once a day. On the following day, discontinue the previous agent completely, and continue with Timoptol-LA. If a higher dosage of Timoptol-LA is required, substitute one drop of 0.5% solution in each affected eye once a day (see section 5.1).

Paediatric population
Not currently indicated.

Elderly
There has been wide-experience with the use of timolol maleate in elderly patients. The dosage recommendations given above reflect the clinical data derived from this experience.

Method of administration
Invert the closed container and shake once before each use. It is not necessary to shake the container more than once.

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

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.

4.3 Contraindications

Reactive airway disease including bronchial asthma or a history of bronchial asthma, severe chronic obstructive pulmonary disease; sinus bradycardia, sick sinus syndrome sino-atrial block, second- or third-degree atrioventricular block, not controlled with pace-maker, overt cardiac failure, cardiogenic shock.

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1. Timoptol-LA should not be used in patients wearing contact lenses as it has not been studied in these patients.

4.4 Special warnings and precautions for use

Like other topically applied ophthalmic agents, timolol is absorbed systemically. Due to beta-adrenergic component, timolol, the same types of cardiovascular, pulmonary and other adverse reactions seen with systemic beta-adrenergic blocking agents may occur. 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
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.

Due to its negative effect on conduction time, beta-blockers should only be given with caution to patients with first degree heart block.

Cardiac failure should be adequately controlled before beginning therapy with Timoptol-LA. Patients with a history of severe cardiac disease should be watched for signs of cardiac failure and have their pulse rates monitored.

Vascular disorders
Patients with severe peripheral circulatory disturbance/disorders (i.e. severe forms of Raynaud’s disease or Raynaud’s syndrome) should be treated with caution.

Respiratory disorders
Respiratory reactions, including death due to bronchospasm in patients with asthma have been reported following administration of some ophthalmic beta-blockers.

Timoptol-LA should be used with caution, in patients with mild/moderate chronic obstructive pulmonary disease (COPD) and only if the potential benefit outweighs the potential risk.

Hypoglycaemia/diabetes
Beta-blockers should be administered with caution in patients subject to spontaneous hypoglycaemia or to patients with labile diabetes, as beta-blockers may mask the signs and symptoms of acute hypoglycaemia.

Beta-blockers may also mask the signs of hyperthyroidism.

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

Other beta-blocking agents
The effect on intra-ocular pressure or the known effects of systemic beta-blockade may be potentiated when timolol is given to patients already receiving a systemic beta-blocking agent. The response of these patients should be closely observed. 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 drugs. The reported incidence is small and in most cases the symptoms have cleared when treatment was withdrawn. Discontinuation of the drug should be considered if any such reaction is not otherwise explicable. Cessation of therapy involving beta-blockade should be gradual.

The dispenser of Timoptol-LA contains benzododecinium bromide as a preservative. In a clinical study, the time required to eliminate 50% of the gellan solution from the eye was up to 30 minutes.

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-LA has little or no effect on the pupil. When Timoptol-LA is used to reduce elevated intra-ocular pressure in angle-closure glaucoma it should be used with a miotic and not alone.

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

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.

Transient blurred vision following instillation may occur, generally lasting from 30 seconds to 5 minutes, and in rare cases up to 30 minutes or longer. Blurred vision and potential visual disturbances may impair the ability to perform hazardous tasks such as operating machinery or driving a motor vehicle.

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 (see section 4.2).

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.

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, and may be unresponsive to the usual dose of epinephrine (adrenaline) used to treat anaphylactic reactions.

4.5 Interaction with other medicinal products and other forms of interaction

No specific drug interaction studies have been performed with timolol.

There is a potential for additive effects resulting in hypotension and/or marked bradycardia when ophthalmic beta-blockers solution is administered concomitantly with oral calcium channel blockers, beta-adrenergic blocking agents, antiarrhythmics (including amiodarone), digitalis glycosides, rauwolfia alkaloids, parasympathomimetics, guanethidine.

Although Timoptol-LA alone has little or no effect on pupil size, mydriasis resulting from concomitant use of ophthalmic beta-blockers and epinephrine (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.

The potential exists for hypotension, atrioventricular (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, fluoxetine, paroxetine) and timolol.

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

4.6 Fertility, pregnancy and lactation

Pregnancy
There are no adequate data for the use of timolol in pregnant women. Timoptol-LA should not be used during pregnancy unless clearly necessary. 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-LA is administered until delivery, the neonate should be carefully monitored during the first days of life.

Breast-feeding
Timolol is detectable in human milk. A decision for breastfeeding mothers, either to stop taking Timoptol-LA or stop nursing, should be based on the importance of the drug to the mother.

4.7 Effects on ability to drive and use machines

Transient blurred vision following instillation may occur, generally lasting from 30 seconds to 5 minutes, and in rare cases, up to 30 minutes or longer. Blurred vision and potential visual disturbances, refractive changes, diplopia, ptosis, frequent episodes of mild and transient blurred vision and fatigue may impair the ability to perform hazardous tasks such as operating machinery or driving a motor vehicle.

4.8 Undesirable effects

Like other topically applied ophthalmic drugs, 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. The most frequent drug-related complaint in clinical studies was transient blurred vision (6.0%), lasting from 30 seconds to 5 minutes following instillation.

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

Ocular: burning and stinging, discharge, foreign body sensation, itching.

The following adverse reactions reported with Timoptol, either in clinical trials or since the drug has been marketed, are potential side effects of Timoptol-LA. Additional adverse reactions have been reported in clinical experiences with *systemic* timolol, and may be considered potential effects of ophthalmic timolol. Also listed are adverse reactions seen within the class of ophthalmic beta-blockers and may potentially occur with Timoptol-LA.

Eye disorders
ocular: signs and symptoms of ocular irritation (e.g. burning, stinging, itching, tearing, redness), conjunctivitis, blepharitis, keratitis, dry eyes, decreased corneal sensitivity, and corneal erosion. Visual disturbances, including refractive changes (due to withdrawal of miotic therapy in some cases), diplopia, ptosis, and choroidal detachment following filtration surgery (see section 4.4).

Ear and labyrinth disorders
Ocular: tinnitus.

Cardiac disorder:
ocular: bradycardia, chest pain, arrhythmia, heart block, congestive heart failure, palpitations, cardiac arrest, atrioventricular block, cardiac failure, oedema.
systemic: AV block (second- or third-degree), sino-atrial block, pulmonary oedema, worsening of arterial insufficiency, worsening of angina pectoris, vasodilation.

Vascular disorders
ocular: claudication, hypotension, Raynaud's phenomenon, cold hands and feet.

Respiratory, thoracic and mediastinal disorders
ocular: bronchospasm (predominantly in patients with pre-existing bronchospastic disease), respiratory failure, dyspnoea, cough.
systemic: rales.

General disorders and administration site conditions
ocular: asthenia, fatigue.
systemic: extremity pain, decreased exercise tolerance.

Skin and subcutaneous tissue disorders
ocular: alopecia, skin rash, psoriasiform rash or exacerbation of psoriasis.
systemic: sweating, exfoliative dermatitis.

Immune system disorders

ocular: 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: syncope, cerebrovascular accident, cerebral ischaemia, headache, dizziness, increase in signs and symptoms of myasthenia gravis, paraesthesia.
systemic: vertigo, local weakness.

Gastrointestinal disorders
ocular: nausea, diarrhoea, dyspepsia, dry mouth, dysgeusia, abdominal pain, vomiting.

Reproductive system and breast disorders
ocular: decreased libido, Peyronie's disease, sexual dysfunction such as impotence.
systemic: micturition difficulties.

Metabolism and nutrition disorders
ocular: hypoglycaemia.
systemic: hyperglycaemia.

Musculoskeletal and connective tissue disorders
ocular: myalgia.
systemic: arthralgia.

Blood and lymphatic system disorders
systemic: non-thrombocytopenic purpura.

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the Yellow Card Scheme, website www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

4.9 Overdose

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, cardiac arrest, acute cardiovascular insufficiency and hypotension (see section 4.8).

If overdosage occurs, the following measures should be considered:

1. Symptomatic bradycardia: atropine sulphate, 0.25 to 2 mg intravenously, should be used to induce vagal blockade. If bradycardia persists, intravenous isoprenaline hydrochloride should be administered cautiously. In refractory cases, the use of a cardiac pacemaker may be considered.

2. Hypotension: a sympathomimetic pressor agent such as dopamine, dobutamine or norepinephrine (noradrenaline) should be used. In refractory cases, the use of glucagon has been reported to be useful.

3. Bronchospasm: isoprenaline hydrochloride should be used. 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, which has been reported useful.

5. Heart block (second- or third-degree): isoprenaline hydrochloride or a pacemaker should be used.

Timolol does not dialyse readily.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Ophthalmologicals, antiglaucoma preparations and miotics, betablocking agents, ATC code: S01ED01.

Mechanism of action
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 intra-ocular 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.

Timoptol-LA is an ophthalmic formulation comprising timolol maleate, which reduces intra-ocular pressure, whether or not associated with glaucoma, and a new delivery vehicle. Gellan solution contains a highly purified anionic heteropolysaccharide derived from gellan gum. Aqueous solutions of gellan gum form a clear transparent gel at low polymer concentrations in the presence of cations. When Timoptol-LA contacts the precorneal tear film, it becomes a gel. Gellan gum increases the contact time of the drug with the eye.

Pharmacodynamic effects
Onset of action of timolol maleate is usually rapid, occurring approximately 20 minutes after topical application to the eye.

Maximum reduction of intra-ocular pressure occurs in two to four hours with Timoptol-LA. Significant lowering of intra-ocular pressure has been maintained for 24 hours with both 0.25% and 0.5% Timoptol-LA.

Clinical efficacy and safety

In parallel active treatment controlled, double-masked, multiclinic studies in patients with untreated elevated intra-ocular pressure of greater than 22 mmHg in one or both eyes, 0.25% and 0.5% Timoptol-LA administered once daily had an intra-ocular pressure-lowering effect equivalent to the same concentration of Timoptol administered twice daily (see table below).

For the five independent comparative studies listed in the table below, the entrance criterion was an intra-ocular pressure of greater than 22 mmHg in one or both eyes after a washout period of one week for most antiglaucoma medications and up to three weeks for ophthalmic beta-adrenergic antagonists. The dosage used was one drop of Timoptol-LA in each affected eye once daily versus one drop of Timoptol in each affected eye twice daily.

Mean change in intra-ocular pressure (mmHg) from baseline at trough (immediately before the morning dose) for the final week of the double-masked study

Concentration	Timoptol-LA (n)	Timoptol (n)	Week
0.25%	-5.8 (94)	-5.9 (96)	12
0.25%	-6.0 (74)	-5.9 (73)	12
0.50%	-8.3 (110)*	-8.2 (111)*	12
0.50%	-5.6 (189)	-6.3 (94)	24
0.50%	-6.4 (212)	-6.1 (109)	24

*The baseline intra-ocular pressure was elevated in comparison to the other studies due to the higher intra-ocular pressure of patients with pseudoexfoliative glaucoma.

Onset of action of timolol maleate is usually rapid, occurring approximately 20 minutes after topical application to the eye.

Maximum reduction of intra-ocular pressure occurs in two to four hours with Timoptol-LA. Significant lowering of intra-ocular pressure has been maintained for 24 hours with both 0.25% and 0.5% Timoptol-LA.

As compared with 0.5% Timoptol administered twice daily, in three clinical studies 0.5% Timoptol-LA administered once daily reduced mean heart rate less and produced bradycardia less frequently (see section 4.4). At trough (24 hours post-dose Timoptol-LA, 12 hours post-dose Timoptol), the mean reduction in heart rate was 0.8 beats/minute for Timoptol-LA and 3.6 beats/minute for Timoptol; whereas at two hours post-dose, the mean reduction was comparable (3.8 beats/minute for Timoptol-LA and 5 beats/minute for Timoptol).

Unlike miotics, timolol maleate reduces intra-ocular 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-LA, refraction may be necessary after the effects of the miotic have passed.

As with other antiglaucoma drugs, 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 three years, no significant difference in mean intra-ocular pressure was observed after initial stabilisation. This indicates that the intra-ocular pressure-lowering effects of timolol maleate is well maintained.

5.2 Pharmacokinetic properties

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

5.3 Preclinical safety data

No adverse ocular effects were observed in monkeys and rabbits administered Timoptol-LA topically in studies lasting 12 months and one month, respectively. The oral LD_{50} of timolol is 1,190 and 900 mg/kg in female mice and female rats, respectively. The oral LD_{50} of gellan gum is greater than 5,000 mg/kg in rats.

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.

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 were 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, 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.

Gellan gum was devoid of mutagenic potential when evaluated *in vivo* (mouse) in 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 1,000 mcg/plate, which is its limit of solubility) did not induce a twofold or greater increase in revertants relative to the solvent control. It is therefore not detectably mutagenic.

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

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Gellan gum, trometamol, mannitol E421, and water for injections. Benzododecinium bromide is added as preservative.

6.2 Incompatibilities

None known

6.3 Shelf life

The shelf life is 36 months. After opening the shelf life is 28 days.

6.4 Special precautions for storage

OCUMETER PLUS bottles:
Do not store above 25°C. Do not freeze. Keep the bottle in the outer carton in order to protect from light.

Other than OCUMETER PLUS bottles:
Do not store above 25°C. Keep the bottle in the outer carton in order to protect from light.

6.5 Nature and contents of container

'Timoptol'-LA Gel-Forming Eye Drops Solution bottle contains 2.5 ml of solution. Two alternative bottles may be marketed.

White translucent low-density polyethylene bottle with a transparent dropper tip and a white cap

or

OCUMETER Plus ophthalmic dispenser consisting of a translucent high-density polyethylene container with a sealed dropper tip, a flexible fluted side area, which is depressed to dispense the drops, and a two-piece assembly. The two-piece cap mechanism punctures the sealed dropper tip upon initial use, then locks together to provide a single cap during the usage period.

Tamper evidence is provided by a safety strip on the bottle label.

6.6 Special precautions for disposal

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7 MARKETING AUTHORISATION HOLDER

Santen Oy
Niittyhaankatu 20
33720 Tampere
Finland

8 MARKETING AUTHORISATION NUMBER(S)

PL 16058/0022

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 2 April 1996
Date of the latest renewal: 5 March 2010

10 DATE OF REVISION OF THE TEXT

10/12/2019