SUMMARY OF PRODUCT CHARACTERISTICS

1. Name of the Medicinal Product

Dorzolamide/Timolol 20 mg/ml + 5 mg/ml, Preservative-Free, Single Dose Eye Drops, Solution

2. Qualitative and Quantitative Composition

Each ml contains 20 mg of dorzolamide as dorzolamide hydrochloride and 5 mg of timolol as timolol maleate.

For the full list of excipients, see section 6.1.

3. Pharmaceutical Form

Eye drops, solution.
Single-dose container
Colourless, clear, viscous solution, free from visible particles.

4. Clinical Particulars

4.1 Therapeutic indications

This medicinal product is indicated in the treatment of elevated intra-ocular pressure (IOP) in patients with open-angle glaucoma or pseudo-exfoliative glaucoma when topical beta-blocker monotherapy is not sufficient.

4.2 Posology and method of administration

Posology

The dose is one drop of dorzolamide/timolol in the (conjunctival sac of the) affected eye(s) two times daily.

If another topical ophthalmic agent is being used, dorzolamide/timolol and the other agent should be administered at least ten minutes apart.

Dorzolamide/Timolol is a sterile solution that does not contain a preservative. The solution from one individual single dose container is to be used immediately after opening for administration to the affected eye(s). Since sterility cannot be maintained after the individual single dose container is opened, any remaining contents must be discarded immediately after administration.

Patients should be instructed to avoid allowing the tip of the container to come into contact with the eye or surrounding structures.

Please see section 6.6. for *Usage Instructions*

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.

Paediatric population

The efficacy of dorzolamide/timolol in children aged 0 to 18 years has not been established. No data are available.

The safety of dorzolamide/timolol in children aged 0 to 18 years has not been established. Currently available data on children aged ≥ 2 and < 6 years are described in section 5.1 but no recommendation on a posology can be made.

4.3 Contraindications

This medicinal product is contraindicated in patients with:

- hypersensitivity to one or both active substances or to any of the excipients listed in section 6.1.
- reactive airway disease, including bronchial asthma or a history of bronchial asthma, or severe chronic obstructive pulmonary disease
- sinus bradycardia, sick sinus syndrome, sino-atrial block, second- or third-degree atrioventricular block not controlled with a pace-maker, overt cardiac failure, cardiogenic shock
- severe renal impairment (CrCl < 30 ml/min) or hyperchloraemic acidosis

The above are based on the components and are not unique to the combination.

4.4 Special warnings and precautions for use

Cardiovascular/respiratory reactions

Like other topically-applied ophthalmic agents, the active substances are absorbed systemically. Due to the beta-adrenergic component, timolol, the same types of cardiovascular, pulmonary and other adverse reactions seen with systemic beta-adrenergic blocking agents may occur with topical administration, including worsening of Prinzmetal angina, worsening of severe peripheral and central circulatory disorders, and hypotension.. The 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 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.

Because of the timolol maleate component, cardiac failure should be adequately controlled before beginning therapy with dorzolamide + timolol. 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 their negative effect on conduction time, beta-blockers should only be given with caution to patients with first degree heart block.

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 timolol maleate.

Because of the timolol maleate component, this medicinal product 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.

Hepatic impairment

Dorzolamide/timolol has not been studied in patients with hepatic impairment and therefore should be used with caution in such patients.

Immunology and hypersensitivity

As with other topically-applied ophthalmic agents, this medicinal product may be absorbed systemically. Dorzolamide contains a sulphonamido group, which also occurs in sulfonamides. Therefore, the same types of adverse reactions found with systemic administration of sulphonamides may occur with topical administration, including severe reactions such as Stevens-Johnson syndrome and toxic epidermal necrolysis. If signs of serious reactions or hypersensitivity occur, discontinue use of this preparation.

Local ocular adverse effects, similar to those observed with dorzolamide hydrochloride eye drops, have been seen with dorzolamide/timolol. If such reactions occur, discontinuation of dorzolamide/timolol should be considered.

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. Such patients may be unresponsive to the usual doses of adrenaline (epinephrine) used to treat anaphylactic reactions.

Concomitant therapy

The following concomitant medication is not recommended:

- dorzolamide and oral carbonic anhydrase inhibitors
- topical beta-adrenergic 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).

Withdrawal of therapy

As with systemic beta-blockers, if discontinuation of ophthalmic timolol is needed in patients with coronary heart disease, therapy should be withdrawn gradually.

Additional effects of beta-blockade

Hypoglycaemia/diabetes
Therapy with 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.

Therapy with beta-blockers may also mask the signs of hyperthyroidism. Abrupt withdrawal of beta-blocker therapy may precipitate a worsening of symptoms.

Therapy with beta-blockers may aggravate symptoms of myasthenia gravis.

Additional effects of carbonic anhydrase inhibition

Therapy with oral carbonic anhydrase inhibitors has been associated with urolithiasis as a result of

acid-base disturbances, especially in patients with a prior history of renal calculi. Although no acid-base disturbances have been observed with dorzolamide/timolol, urolithiasis has been reported infrequently. Because dorzolamide/timolol contains a topical carbonic anhydrase inhibitor that is absorbed systemically, patients with a prior history of renal calculi may be at increased risk of urolithiasis while using dorzolamide/timolol.

Other

The management of patients with acute angle-closure glaucoma requires therapeutic interventions in addition to ocular hypotensive agents. Dorzolamide/timolol has not been studied in patients with acute angle-closure glaucoma.

Corneal diseases
Corneal oedema and irreversible corneal decompensation have been reported in patients with pre-existing chronic corneal defects and/or a history of intra-ocular surgery while using dorzolamide. There is an increased potential for developing corneal oedema in patients with low endothelial cell counts. Topical dorzolamide should be used with caution in such patients.

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

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

As with the use of other antiglaucoma drugs, diminished responsiveness to ophthalmic timolol maleate after prolonged therapy has been reported in some patients. However, in clinical studies in which 164 patients have been followed for at least three years, no significant difference in mean intra-ocular pressure has been observed after initial stabilisation.

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

Contact lens use

Dorzolamide/timolol eye drops have not been studied in patients wearing contact lenses.

Paediatric population

See section 5.1.

4.5 Interaction with other medicinal products and other forms of interaction

Specific interaction studies have not been performed with dorzolamide/timolol.
No specific drug interaction studies have been performed with timolol.

In clinical studies, dorzolamide/timolol was used concomitantly with the following systemic agents without evidence of adverse interactions: ACE-inhibitors, calcium channel blockers, diuretics, non-steroidal anti-inflammatory drugs including aspirin, and hormones (e.g. oestrogen, insulin, thyroxine).

However, there is a potential for additive effects resulting in hypotension and/or marked bradycardia when an ophthalmic beta-blocker solution is administered concomitantly with oral calcium channel blockers, catecholamine-depleting drugs or beta-adrenergic blocking agents, antiarrhythmics (including amiodarone), digitalis glycosides, parasympathomimetics and guanethidine, narcotics, and

monoamine oxidase (MAO) inhibitors.

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.

The dorzolamide component of this medicinal product is a carbonic anhydrase inhibitor and although administered topically, is absorbed systemically. In clinical studies, dorzolamide hydrochloride ophthalmic solution was not associated with acid-base disturbances. However, these disturbances have been reported with oral carbonic anhydrase inhibitors and have in some instances, resulted in interactions (e.g., toxicity associated with high-dose salicylate therapy). Therefore, the potential for such interactions should be considered in patients receiving dorzolamide/timolol.

Although dorzolamide/timolol alone has little or no effect on pupil size, mydriasis resulting from concomitant use of ophthalmic beta-blocker and adrenaline (epinephrine) has been reported occasionally.

Beta-blockers may increase the hypoglycaemic effect of antidiabetic agents.

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

4.6 Fertility, pregnancy and lactation

Pregnancy

Dorzolamide/timolol should not be used during pregnancy.

Dorzolamide
No adequate clinical data in exposed pregnancies are available. In rabbits, dorzolamide produced teratogenic effects at maternotoxic doses (see section 5.3).

Timolol
There are no adequate data for the use of timolol in pregnant women. Timolol 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 dorzolamide/timolol is administered until delivery, the neonate should be carefully monitored during the first days of life (see section 5.3).

Breast-feeding

It is not known whether dorzolamide is excreted in human milk. In lactating rats receiving dorzolamide, decreases in the body weight gain of offspring were observed. Beta-blockers are excreted in breast milk. However, at therapeutic doses of timolol in eye drops it is not likely that sufficient amounts would be present in breast milk to produce clinical symptoms of beta-blockade in the infant.

To reduce the systemic absorption, see section 4.2.

If treatment with dorzolamide/timolol is required, breast feeding is not recommended.

4.7 Effects on ability to drive and use machines

No studies on the effects on the ability to drive and use machines have been performed. Possible side effects such as blurred vision may affect some patients' ability to drive and/or operate machinery.

4.8 Undesirable effects

Summary of the safety profile
In clinical studies for dorzolamide/timolol the observed adverse reactions have been consistent with those that were reported previously with dorzolamide hydrochloride and/or timolol maleate. In general, common adverse experiences were mild and did not cause discontinuation. Like other topically applied ophthalmic drugs, timolol is absorbed into the systemic circulation. This may cause similar undesirable effects to those seen with systemic beta-blocking agents. The incidence of systemic ADRs after topical ophthalmic administration is lower than for systemic administration. Listed adverse reactions include reactions seen within the class of ophthalmic beta-blockers.

During clinical studies, 1,035 patients were treated with dorzolamide/timolol. Approximately 2.4% of all patients discontinued therapy with dorzolamide/timolol because of local ocular adverse reactions, approximately 1.2% of all patients discontinued because of local adverse reactions suggestive of allergy or hypersensitivity (such as lid inflammation and conjunctivitis).

Dorzolamide/timolol **(**preservative-free) has been shown to have a similar safety profile to dorzolamide/timolol (preservative containing formulation) in a repeat dose double-masked, comparative study.

The following adverse reactions have been reported with dorzolamide/timolol or one of its components either during clinical trials or during post-marketing experience.

Tabulated list of adverse reactions:
The frequencies of adverse events are ranked according to the following: very common: (≥1/10), common: (≥1/100 to <1/10), uncommon: (≥1/1000 to <1/100), rare: (≥1/10,000 to <1/1000), very rare (<1/10,000); not known (cannot be estimated from the available data)

System Organ Class (MedDRA)	Formulation	Adverse Drug Reaction Frequency				
		Very common	Common	Uncommon	Rare	Not known
Immune system disorders	Dorzolamide/Timolol				signs and symptoms of systemic allergic reactions, including angioedema, urticaria, pruritus, rash, anaphylaxis, rarely bronchospasm	

System Organ Class (MedDRA)	Formulation	Adverse Drug Reaction Frequency				
		Very common	Common	Uncommon	Rare	Not known
	Timolol maleate eye drops, solution					systemic allergic reactions including angioedema, urticaria, localised and generalised rash, pruritus, anaphylactic reaction
Metabolism and nutrition disorders	Timolol maleate eye drops, solution					hypoglycaemia
Psychiatric disorders	Timolol maleate eye drops, solution			depression*	insomnia*, nightmares*, memory loss	hallucination
Nervous system disorders	Dorzolamide hydrochloride eye drops, solution		headache*		dizziness*, paraesthesia*	
	Timolol maleate eye drops, solution		headache*	dizziness*, syncope*	paraesthesia*, increases in signs and symptoms of myasthenia gravis, decreased libido*, cerebrovascular accident*, cerebral ischaemia	
Eye disorders	Dorzolamide / timolol	Burning and stinging	Conjunctival injection, blurred vision, corneal erosion, ocular itching, tearing			Foreign body sensation in eye
	Dorzolamide hydrochloride eye drops, solution		Eyelid inflammation*, eyelid irritation*	Iridocyclitis*	Irritation including redness*, pain*, eyelid crusting*, transient myopia (which resolved upon discontinuation of therapy), corneal oedema*, ocular hypotony*, choroidal detachment (following filtration surgery)*	Foreign body sensation in eye

System Organ Class (MedDRA)	Formulation	Adverse Drug Reaction Frequency				
		Very common	Common	Uncommon	Rare	Not known
	Timolol maleate eye drops, solution		Signs and symptoms of ocular irritation (e.g. burning, stinging, itching, tearing, redness)*, blepharitis*, keratitis*, decreased corneal sensitivity, and dry eyes*	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)*	Blurred vision, corneal erosion
Ear and labyrinth disorders	Timolol maleate eye drops, solution				Tinnitus*	
Cardiac disorders	Timolol maleate eye drops, solution			Bradycardia*	chest pain*, palpitations*, oedema*, arrhythmia*, congestive heart failure*, atrioventricular block*, cardiac arrest*	Cardiac failure
	Dorzolamide hydrochloride eye drops, solution					palpitations
Vascular disorders	Timolol maleate eye drops, solution				hypotension*, claudication, Raynaud's phenomenon*, cold hands and feet*	
Respiratory, thoracic and mediastinal disorders	Dorzolamide / timolol		Sinusitis		respiratory failure, rhinitis	Dyspnoea
	Dorzolamide hydrochloride eye drops, solution				Epistaxis*	Dyspnoea
	Timolol maleate eye drops, solution			Dyspnoea*	Bronchospasm (predominantly in patients with pre-existing bronchospastic disease)*, cough*	
Gastrointestinal disorders	Dorzolamide / timolol	taste perversion				
	Dorzolamide hydrochloride eye drops, solution		Nausea*		Throat irritation, dry mouth*	

System Organ Class (MedDRA)	Formulation	Adverse Drug Reaction Frequency				
		Very common	Common	Uncommon	Rare	Not known
	Timolol maleate eye drops, solution			Nausea*, dyspepsia*	Diarrhoea, dry mouth*	Dysgeusia, abdominal pain, vomiting
Skin and subcutaneous tissue disorders	Dorzolamide / timolol				Contact dermatitis, Stevens-Johnson syndrome, toxic epidermal necrolysis	
	Dorzolamide hydrochloride eye drops, solution				Rash*	
	Timolol maleate eye drops, solution				Alopecia*, psoriasiform rash or exacerbation of psoriasis*	Skin rash
Musculoskeletal and connective tissue disorders	Timolol maleate eye drops, solution				systemic lupus erythematosus	Myalgia
Renal and urinary disorders	Dorzolamide / timolol			Urolithiasis		
Reproductive system and breast disorders	Timolol maleate eye drops, solution				Peyronie's disease*	Sexual dysfunction, decreased libido
General disorders and administration site conditions	Dorzolamide hydrochloride eye drops, solution		Asthenia/ fatigue*			
	Timolol maleate eye drops, solution			Asthenia/ fatigue*		

*These adverse reactions were also observed with dorzolamide/timolol during post-marketing experience.

Laboratory findings

Dorzolamide/timolol was not associated with clinically meaningful electrolyte disturbances in clinical studies.

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 at: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

4.9 Overdose

No data are available in humans in regard to overdosage by accidental or deliberate ingestion of dorzolamide/timolol.

There have been reports of inadvertent overdosage with timolol maleate ophthalmic solution 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. The most common signs and symptoms to be expected with overdosage of dorzolamide are electrolyte imbalance, development of an acidotic state, and possibly central nervous system effects.

Only limited information is available with regard to human overdosage by accidental or deliberate ingestion of dorzolamide hydrochloride. With oral ingestion, somnolence has been reported. With topical application the following have been reported: nausea, dizziness, headache, fatigue, abnormal dreams, and dysphagia.

Treatment should be symptomatic and supportive. Serum electrolyte levels (particularly potassium) and blood pH levels should be monitored. Studies have shown that timolol does not dialyse readily.

5. pharmacological properties

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: S01E D51
(Antiglaucoma preparations and miotics - Beta-Blocking Agents)

Mechanism of action

Dorzolamide/timolol is comprised of two components: dorzolamide hydrochloride and timolol maleate. Each of these two components decreases elevated intra-ocular pressure by reducing aqueous humor secretion, but does so by a different mechanism of action.

Dorzolamide hydrochloride is a potent inhibitor of human carbonic anhydrase II. Inhibition of carbonic anhydrase in the ciliary processes of the eye decreases aqueous humor secretion, presumably by slowing the formation of bicarbonate ions with subsequent reduction in sodium and fluid transport. Timolol maleate is a non-selective beta-adrenergic receptor blocking agent. The precise mechanism of action of timolol maleate in lowering intra-ocular pressure is not clearly established at this time, although 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. The combined effect of these two agents results in additional intra-ocular pressure reduction compared to either component administered alone.

Following topical administration, dorzolamide/timolol reduces elevated intra-ocular pressure, whether or not associated with glaucoma. Elevated intra-ocular pressure is a major risk factor in the pathogenesis of optic nerve damage and glaucomatous visual field loss. Dorzolamide/timolol reduces intra-ocular pressure without the common side effects of miotics such as night blindness, accommodative spasm and pupillary constriction.

Pharmacodynamic effects

Clinical effects
Clinical studies of up to 15 months duration were conducted to compare the IOP-lowering effect of dorzolamide/timolol b.i.d. (dosed morning and bedtime) to individually- and concomitantly-administered 0.5% timolol and 2.0% dorzolamide in patients with glaucoma or ocular hypertension for whom concomitant therapy was considered appropriate in the trials. This included both untreated patients and patients inadequately controlled with timolol monotherapy. The majority of patients were treated with topical beta-blocker monotherapy prior to study enrollment. In an analysis of the combined studies, the IOP-lowering effect of dorzolamide/timolol b.i.d. was greater than that of monotherapy with either 2% dorzolamide t.i.d. or 0.5% timolol b.i.d. The IOP-lowering effect of dorzolamide/timolol b.i.d. was equivalent to that of concomitant therapy with dorzolamide b.i.d. and timolol b.i.d. The IOP-lowering effect of dorzolamide/timolol b.i.d. was demonstrated when

measured at various time points throughout the day and this effect was maintained during long-term administration.

Paediatric population
A three month controlled study, with the primary objective of documenting the safety of 2% dorzolamide hydrochloride ophthalmic solution in children under the age of 6 years has been conducted. In this study, 30 patients under six and greater than or equal to two years of age whose IOP was not adequately controlled with monotherapy by dorzolamide or timolol received dorzolamide/timolol in an open label phase. Efficacy in those patients has not been established. In this small group of patients, twice daily administration of dorzolamide/timolol was generally well tolerated with 19 patients completing the treatment period and 11 patients discontinuing for surgery, a change in medication, or other reasons.

5.2 Pharmacokinetic properties

Dorzolamide hydrochloride

Unlike oral carbonic anhydrase inhibitors, topical administration of dorzolamide hydrochloride allows for the substance to exert its effects directly in the eye at substantially lower doses and therefore with less systemic exposure. In clinical trials, this resulted in a reduction in IOP without the acid-base disturbances or alterations in electrolytes characteristic of oral carbonic anhydrase inhibitors.

When topically applied, dorzolamide reaches the systemic circulation. To assess the potential for systemic carbonic anhydrase inhibition following topical administration, parent substance and metabolite concentrations in red blood cells (RBCs) and plasma and carbonic anhydrase inhibition in RBCs were measured. Dorzolamide accumulates in RBCs during chronic dosing as a result of selective binding to CA-II while extremely low concentrations of free substance in plasma are maintained. The parent substance forms a single N-desethyl metabolite that inhibits CA-II less potently than the parent substance but also inhibits a less active isoenzyme (CA-I). The metabolite also accumulates in RBCs where it binds primarily to CA-I. Dorzolamide binds moderately to plasma proteins (approximately 33%). Dorzolamide is primarily excreted unchanged in the urine; the metabolite is also excreted in urine. After dosing ends, dorzolamide washes out of RBCs non-linearly, resulting in a rapid decline of substanceconcentration initially, followed by a slower elimination phase with a half-life of about four months.

When dorzolamide was given orally to simulate the maximum systemic exposure after long term topical ocular administration, steady state was reached within 13 weeks. At steady state, there was virtually no free substance or metabolite in plasma; CA inhibition in RBCs was less than that anticipated to be necessary for a pharmacological effect on renal function or respiration. Similar pharmacokinetic results were observed after chronic, topical administration of dorzolamide hydrochloride. However, some elderly patients with renal impairment (estimated CrCl 30-60 ml/min) had higher metabolite concentrations in RBCs, but no meaningful differences in carbonic anhydrase inhibition and no clinically significant systemic side effects were directly attributable to this finding.

Timolol maleate

In a study of plasma substance concentration in six subjects, the systemic exposure to timolol was determined following twice daily topical administration of timolol maleate ophthalmic solution 0.5%. The mean peak plasma concentration following morning dosing was 0.46 ng/ml and following afternoon dosing was 0.35 ng/ml.

5.3 Preclinical safety data

The ocular and systemic safety profile of the individual components is well established.

Dorzolamide
In rabbits given maternotoxic doses of dorzolamide associated with metabolic acidosis, malformations

of the vertebral bodies were observed.

Timolol
Animal studies have not shown a teratogenic effect.
Furthermore, no adverse ocular effects were seen in animals treated topically with dorzolamide hydrochloride and timolol maleate ophthalmic solution or with concomitantly-administered dorzolamide hydrochloride and timolol maleate. In vitro and in vivo studies with each of the components did not reveal a mutagenic potential. Therefore, no significant risk for human safety is expected with therapeutic doses of dorzolamide/timolol.

6. Pharmaceutical Particulars

6.1 List of excipients

Hydroxyethyl cellulose,
Mannitol
Sodium citrate dihydrate
Sodium hydroxide (to adjust pH)
Water for injections

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

2 years
After first opening of the pouch: 15 days. Discard any unused single dose containers after that time.
Discard the opened single dose container immediately after first use.

6.4 Special precautions for storage

Store below 25°C.
Store in the original package in order to protect from light
Do not refrigerate or freeze.

6.5 Nature and contents of container

0.5 ml low density polyethylene single dose containers containing 0.2 ml of solution. Five or 15 single-dose containers are packed in a foil pouch.
Pack sizes: 5, 20, 30, 60 and 120 single dose containers
Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

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.

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

Usage instructions

1. Open the pouch which contains individual single dose containers.
2. First wash your hands then break off one single dose container from the strip and twist open the top.
3. Tilt your head back and pull your lower eyelid down slightly to form a pocket between your eyelid and eye.
4. Instill one drop in the affected eye(s) as directed by your physician. Each single dose container contains enough solution for both eyes.
5. After instillation, discard the used single dose container even if there is solution remaining.
6. Store the remaining single dose containers in the pouch; the remaining single dose containers must be used within 15 days after opening of the pouch.

7. Marketing Authorisation Holder

Teva UK Limited,
Ridings Point, Whistler Drive,
Castleford, WF10 5HX,
United Kingdom.

8. Marketing Authorisation Number

PL 00289/1239

9. Date of First Authorisation/Renewal of Authorisation

02/12/2010

10. Date of Revision of the Text

05/07/2022