Approved Professional Information for Medicines for Human Use:

DORZOPT

SCHEDULING STATUS

S3

1. NAME OF THE MEDICINE

DORZOPT 20 mg/mL Eye Drops Solution

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each mL of solution contains:

22,26 mg dorzolamide hydrochloride equivalent to 20 mg dorzolamide base.

Preservative: Benzalkonium chloride, 0,0075 % (m/v).

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Eye Drops, Solution

Slightly opalescent, nearly colorless, slightly viscous solution

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

DORZOPT is indicated in the treatment of elevated intraocular pressure in patients with:

• ocular hypertension

• open-angle glaucoma

• pseudoexfoliative glaucoma and other secondary open angle glaucomas

• and in the short-term treatment of paediatric glaucomas as adjunctive therapy to beta-blockers and for monotherapy.

4.2 Posology and method of administration

Posology

When used as monotherapy, the dose is one drop of DORZOPT in the affected eye(s) 3 times daily.

When used as adjunctive therapy with an ophthalmic beta-blocker, the dose is one drop of DORZOPT in the affected eye(s) 2 times daily.

When substituting DORZOPT for another ophthalmic anti-glaucoma medicine, discontinue the other medicine after proper dosing in one day, and start DORZOPT on the next day. If more than one topical ophthalmic medicine is being used, the medicines should be administered at least 10 minutes apart.

4.3 Contraindications

- Hypersensitivity to the dorzolamide hydrochloride or to any of the excipients listed in section 6.1.
- DORZOPT has not been studied in patients with moderate progressing to severe renal impairment (CrCl < 30 mL/min). Because DORZOPT and its metabolite are excreted predominantly by the kidney, DORZOPT is not recommended in such patients.
- DORZOPT has not been studied in patients wearing contact lenses. DORZOPT contains the preservative, benzalkonium chloride, which may be absorbed by soft contact lenses. Therefore, DORZOPT should not be administered while wearing soft contact lenses.

4.4 Special warnings and precautions for use

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

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

Dorzolamide as in DORZOPT contains a sulphonamide group, which also occurs in sulphonamides and although administered topically, is absorbed systemically. Therefore, the same types of adverse reactions that are attributable to sulphonamides may occur with DORZOPT, including severe reactions such as Stevens-Johnson syndrome and toxic epidermal necrolysis. Sensitisation may occur when a sulphonamide is re-administered irrespective of route of administration. If signs of serious reactions or hypersensitivity occur, discontinue the use of this preparation.

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 as in DORZOPT, urolithiasis has been reported infrequently. Because dorzolamide is 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 DORZOPT. The concomitant administration of DORZOPT and oral carbonic anhydrase inhibitors is not recommended.

If allergic reactions (e.g., conjunctivitis and eye-lid reactions) are observed, discontinuation of treatment should be considered.

Corneal oedemas and irreversible corneal decompensations have been reported in patients with pre-existing chronic corneal defects and/or a history of intra-ocular surgery while using Dorzolamide. DORZOPT should be used with caution in such patients.

Choroidal detachment concomitant with ocular hypotony have been reported after filtration procedures with administration of Dorzolamide.

Use in the Elderly

No overall differences in effectiveness or safety were observed between patients 65 – 75 years old and younger patients, but greater sensitivity of some older individuals to DORZOPT cannot be rules out.

Benzalkonium chloride

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.

Contact Lens Use

DORZOPT contains benzalkonium chloride as preservative. Contact lenses should be removed prior to application and wait at least 15 minutes before reinsertion. Benzalkonium chloride is known to discolour soft contact lenses.

Paediatric population

Dorzolamide has not been studied in patients less than 36 weeks gestational age and less than 1 week of age.

4.5 Interaction with other medicines and other forms of interaction

Specific drug interaction studies have not been performed with dorzolamide as in DORZOPT.

In clinical studies, dorzolamide was used concomitantly with the following medications without evidence of adverse interactions:

timolol ophthalmic solution, betaxolol ophthalmic solution and systemic medications, including ACE-inhibitors, calcium-channel blockers, diuretics, non-steroidal anti-inflammatory drugs including aspirin, and hormones (e.g. oestrogen, insulin, thyroxine).

Association between dorzolamide as in DORZOPT and miotics and adrenergic agonists has not been fully evaluated during glaucoma therapy.

4.6 Fertility, pregnancy and lactation

Pregnancy

Dorzolamide should not be used during pregnancy. There are no or limited amount of data from the use of dorzolamide in pregnant women. In rabbits, dorzolamide produced teratogenic effects at maternotoxic doses.

Breastfeeding

Safety during breastfeeding has not been established.

Fertility

Human data are lacking.

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 dizziness and visual disturbances may affect the ability to drive and use machines.

4.8 Undesirable effects

Tabulated list of adverse reactions.

The following adverse reactions have been reported either during clinical trials or during post-marketing experience with dorzolamide:

[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: (cannot be estimated from the available data)]

System Organ Class	**Frequency**		
	Frequent	**Less Frequent**	**Not known**
Nervous system disorders	Headache	Dizziness, paraesthesia	--
Eye disorders	Burning and stinging, superficial punctate keratitis, tearing, conjunctivitis, eyelid inflammation, eye itching, eyelid irritation, blurred vision	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
Cardiac disorders	--	--	palpitations

Respiratory, thoracic and mediastinal disorders	--	Epistaxis	Dyspnoea
Gastrointestinal disorders	Nausea, bitter taste	Throat irritation, dry mouth	--
Skin and subcutaneous tissue disorders	--	Contact dermatitis, Stevens-Johnson syndrome, toxic epidermal necrolysis	--
Renal and urinary disorders	--	Urolithiasis	--
General disorders and administration site conditions	Asthenia/fatigue	Hypersensitivity: signs and symptoms of local reactions (palpebral reactions) and systemic allergic reactions, including angioedema, urticaria and	--

		pruritus, rash, shortness of breath, rarely bronchospasm	
Investigations	Dorzolamide was not associated with clinically meaningful electrolyte disturbances. Paediatric population See section 5.1.		

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. Healthcare professionals are asked to report any suspected adverse reactions to SAHPRA via the "6.04 Adverse Drug Reaction Reporting Form", found online under SAHPRA's publications: https://www.sahpra.org.za/Publications/Index/8

4.9 Overdose

Only limited information is available with regard to human overdose by accidental or deliberate ingestion of dorzolamide hydrochloride.

Symptoms

The following have been reported with oral ingestion: somnolence; topical application: nausea, dizziness, headache, fatigue,

abnormal dreams, and dysphagia.

Treatment

Treatment should be symptomatic and supportive. Electrolyte imbalance, development of an acidotic state, and possible central nervous system effects may occur. Serum electrolyte levels (particularly potassium) and blood pH levels should be monitored.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Category and Class: A.15.4 Ophthalmic preparations, other.

Pharmacotherapeutic group: Antiglaucoma preparations and miotics, Carbonic Anhydrase Inhibitors, dorzolamide

ATC Code: S01EC03

Mechanism of action

Dorzolamide hydrochloride, is a carbonic anhydrase inhibitor formulated for topical ophthalmic use. Carbonic anhydrase (CA) is an enzyme found in many tissues of the body including the eye. It catalyses the reversible reaction involving the hydration of carbon dioxide and the dehydration of carbonic acid. In humans, carbonic anhydrase exists as a number of isoenzymes, the most active being carbonic anhydrase II (CA-II) found primarily in red blood cells (RBCs) but also in other

tissues. Inhibition of carbonic anhydrase in the ciliary processes of the eye decreases aqueous humour secretion, presumably by slowing the formation of bicarbonate ions with subsequent reduction in sodium and fluid transport. The result is a reduction in intraocular pressure (IOP).

5.2 Pharmacokinetic properties

When topically applied, dorzolamide reaches the systemic circulation. Dorzolamide accumulates in red blood cells (RBCs) during chronic dosing as a result of selective binding to CA-II while extremely low concentrations of free dorzolamide in plasma are maintained.

Dorzolamide 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 red blood cells (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 nonlinearly, resulting in a rapid decline of medicine concentration 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 dorzolamide or metabolite in plasma. CA inhibition in red blood cells (RBC's) 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. However, some elderly patients with mild to moderate renal impairment (estimated CrCl 30 to 60 ml/min) had higher metabolite concentrations in red blood cells (RBC's), but no meaningful differences in carbonic anhydrase inhibition and no clinically significant systemic side effects were directly attributable to this finding.

Paediatric population

Safety and IOP-lowering effects of DORZOPT have been evaluated in paediatric patients younger than 6 years of age with glaucoma or elevated intraocular pressure (baseline IOP higher than 22 mm Hg). Use of DORZOPT in this age group is supported by evidence from a 3-month, controlled study.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Benzalkonium Chloride

Hydroxyethyl Cellulose

Mannitol

Sodium Citrate Dihydrate

Sodium Hydroxide solution 1 N

water for injection

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

24 months

After first use: 28 days (4 weeks)

6.4 Special precautions for storage

Store at or below 30 °C

Do not use this medicine after the month and year following EXP on the bottle.

Do not use this medicine more than 28 days after opening.

6.5 Nature and contents of container

DORZOPT is available in a 10 mL LDPE bottle with dropper and seal and packed into a cardboard carton.

Each bottle contains 5 mL of DORZOPT.

The following pack sizes are available: cartons containing 1 or 3's.

Not all pack sizes are marketed.

6.6 Special precautions for disposal <and other handling

No special requirements.

7. HOLDER OF CERTIFICATE OF REGISTRATION

Austell Pharmaceuticals (Pty) Ltd

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8. REGISTRATION NUMBER(S)

55/15.4/0345

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

13 June 2023

10. DATE OF REVISION OF THE TEXT