PROFESSIONAL INFORMATION LEAFLET FOR GLAUCOPRESS

SCHEDULING STATUS **S3**

1. NAME OF THE MEDICINE

Glaucopress® 20 mg/ml Ophthalmic Solution

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Dorzolamide hydrochloride equivalent to 20 mg dorzolamide base.

Excipient(s) with known effect: Preservative: Benzalkonium Chloride 0,0075 % *m/v*

For full list of excipients, see section 6.1.

3. PHARMACEUTIAL FORM

Ophthalmic solution.

Sterile, clear, colourless or slightly yellowish, slightly viscous solution.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

GLAUCOPRESS is indicated in the treatment of elevated intra-ocular pressure in patients with:

- ocular hypertension
- open angle glaucoma
- pseudoexfoliative glaucoma and other secondary open-angle glaucomas

4.2 Posology and method of administration

Posology:

When used as monotherapy, the dose is one drop of GLAUCOPRESS in the affected eye(s) three times a day.

When used as adjunctive therapy with an ophthalmic ß-adrenergic blocker, the dose is one drop of GLAUCOPRESS in the affected eye(s) twice daily.

When substituting GLAUCOPRESS for another ophthalmic antiglaucoma agent, discontinue the other agent after completing the proper dosing on one day, and start the GLAUCOPRESS the next day.

Benzalkonium chloride may be absorbed by soft contact lenses. Patients wearing soft contact lenses should be instructed to wait at least 15 minutes after instilling GLAUCOPRESS to insert soft contact lenses (see section 4.4).

If more than one topical ophthalmic medication is being used, the medicines should be administered at least ten minutes apart.

4.3 Contraindications

- Hypersensitivity to dorzolamide or any of the ingredients contained in GLAUCOPRESS.
- GLAUCOPRESS has not been evaluated in patients with moderate to severe renal impairment (i.e. creatinine clearance less than 30 ml/minute). Due to renal excretion of dorzolamide and *N*-desethyldorzolamide, topical ocular use of GLAUCOPRESS in patients with severe renal impairment is not recommended.
- GLAUCOPRESS has not been evaluated in patients with hepatic impairment, and GLAUCOPRESS should be used with caution in such patients.
- GLAUCOPRESS has not been evaluated in patients wearing contact lenses. The preservative in GLAUCOPRESS, benzalkonium chloride, may be absorbed by soft contact lenses.

4.4 Special warnings and precautions for use

GLAUCOPRESS is a sulphonamide and topical administration can result in systemic absorption. Thus side-effects pertaining to sulphonamides may be experienced. These include Stevens-Johnson Syndrome, toxic epidermal necrolysis, fulminant hepatic necrosis, agranulocytosis, aplastic anaemia and other blood dyscrasis.
Sensitisation may recur when a sulphonamide is re-administered irrespective of the route of administration.
If signs of serious reactions or hypersensitivity occur, discontinue the use of GLAUCOPRESS and consult your doctor.

There is a potential for an additive effect on the systemic effects of the inhibition of carbonic anhydrase in patients taking an oral carbonic anhydrase inhibitor and GLAUCOPRESS concurrently. Thus concurrent administration of the GLAUCOPRESS and oral carbonic anhydrase inhibitors is not recommended (see section 4.5).

Safety and efficacy of dorzolamide ophthalmic solution in children younger than 16 years of age has not been established.

In patients 65 years of age or older compared with younger patients, safety and efficacy of dorzolamide were similar however the possibility of greater sensitivity of some older patients cannot be ruled out.

In clinical studies, local ocular adverse effects, primarily conjunctivitis and lid reactions, were reported with chronic administration of GLAUCOPRESS ophthalmic solution.
Some of these reactions had the clinical appearance and course of an allergic-type reaction that resolved upon discontinuation of GLAUCOPRESS therapy. If such reactions occur, treatment with GLAUCOPRESS should be discontinued, and the patient evaluated before restarting GLAUCOPRESS is considered.
As the possibility of adverse effects on the corneal 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, such as GLAUCOPRESS, over an extended period in patients with extensive ocular surface disease.

The management of patients with acute angle-closure glaucoma requires therapeutic intervention in addition to ocular hypotensive agents.
Incorrect handling of ophthalmic solutions can result in bacterial contamination of the solution and subsequent ocular infections. Thus avoid allowing the tip of the dispensing container to come in contact with the eye or surrounding areas.
Serious damage to the eye and subsequent loss of vision may result from using contaminated ophthalmic solutions.
GLAUCOPRESS contains mannitol, which may have a mild laxative effect.

4.5 Interaction with other medicines and other forms of interaction
Specific interaction studies with GLAUCOPRESS have not been performed however, in clinical studies dorzolamide was used concomitantly with the following medicines without evidence of adverse interactions: timolol ophthalmic solution, betaxolol ophthalmic solution and systemic medication including ACE-Inhibitors, calcium channel blockers, diuretics, non-steroidal anti-inflammatory drugs (NSAIDs) and hormones (e.g. oestrogen, insulin, thyroxine).
GLAUCOPRESS is a carbonic anhydrase inhibitor and although administered topically, is absorbed systemically.
Acid-base disturbances have been reported with oral carbonic anhydrase inhibitors and have in some cases resulted in interactions (e.g. toxicity associated with high-dose salicylate therapy). Thus the potential for such interactions in patients using GLAUCOPRESS should be considered.

When GLAUCOPRESS is used in conjunction with beta adrenergic blocking agents, the intraocular pressure lowering effect may be additive.

Concomitant administration with oral carbonic anhydrase inhibitors is not recommended due to the potential for an additive effect on the known systemic effects of carbonic anhydrase inhibition.

4.6 Fertility, pregnancy and lactation

Pregnancy:

There are no adequate and controlled studies in pregnant women, and GLAUCOPRESS is not recommended during pregnancy.

In rabbits given maternotoxic doses associated with metabolic acidosis greater than or equal to 2,5 mg/kg/day, malformation of the vertebral bodies were observed.

Lactation:

It is unknown whether dorzolamide is excreted into human milk. Due to the potential for serious adverse reactions to dorzolamide in breastfed infants, a decision should be made whether to discontinue breastfeeding the infant or the medicine, taking into account the importance of GLAUCOPRESS to the women.

4.7 Effects on ability to drive and use machines:

GLAUCOPRESS may cause vision to be temporarily blurred or unstable just after instillation. Patients should be advised to not drive, use machinery or do any activity that requires clear vision, until they are sure that they can perform such activities safely.

4.8 Undesirable effects

Eye disorders:

Frequent:

Burning and stinging, blurred vision, eye itching, tearing, conjunctivitis, eyelid inflammation, eyelid irritation.

Less frequent:

Iridocyclitis, photophobia.

Frequency unknown:

Transient myopia, superficial punctuate keratitis, eye pain and redness.

General disorders and administrative site conditions:

Frequent:

Asthenia/fatigue.

Nervous system disorders:

Frequent:

Headache.

Frequency unknown:

Dizziness, paraesthesia.

Respiratory, thoracic and mediastinal disorders:

Less frequent:

Epistaxis.

Frequency unknown:

Bronchospasm.

Gastro-intestinal disorders:

Frequent:

Bitter taste, nausea.

Hepato-biliary disorders:

Less frequent:

Fulminant hepatic necrosis.

Blood and the lymphatic system disorders:

Less frequent:

Agranulocytosis, aplastic anaemia

Skin and subcutaneous tissue disorders:

Less frequent:

Rash, Stevens-Johnson syndrome, toxic epidermal necrolysis.

Frequency unknown:

Urticaria, pruritus.

Immune system disorder:

Frequency unknown:

Angioedema.

Renal and urinary disorders:

Less frequent:

Urolithiasis.

4.9 Overdose

Limited data is available in regard to overdosage in humans.

Overdosage of GLAUCOPRESS can be expected to result in electrolyte imbalances, systemic acidosis and possible central nervous system effects.

Serum electrolyte levels (particularly potassium) and blood pH levels should be monitored.

Treatment is supportive and symptomatic.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacological classification: A.15.4 Ophthalmic Preparations, other.

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).

Topically applied beta-adrenergic blocking agents also reduce IOP by decreasing aqueous humour secretion but by a different mechanism of action. When dorzolamide is added to a topical beta-blocker, there is an additional reduction in IOP. This is consistent with the reported additive effects of beta-blockers and oral carbonic anhydrase inhibitors.

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 low concentrations of free dorzolamide in the plasma is maintained. Dorzolamide forms a single N-desethyl metabolite that inhibits CA-II less potently than dorzolamide 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.

5.2 Pharmacokinetic properties

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 red blood cells (RBCs) nonlinearly, resulting in a rapid decline of agent concentration initially, followed by a slower elimination phase with a half-life of about 4 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 is virtually no free dorzolamide or metabolite in plasma. CA inhibition in red blood cells (RBCs) is 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 – 60 ml/min) had higher metabolite concentrations in red blood cells (RBCs), but no meaningful differences in carbonic anhydrase inhibition and no clinically significant systemic side effects were directly attributable to this finding.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium citrate
Hydroxyethylcellulose
Mannitol
Sodium hydroxide
Purified water
Benzalkonium Chloride

6.2 Incompatibilities

Not applicable

6.3 Shelf life

Unopened: 3 years
Discard the product after 30 days of being opened.

6.4 Special precautions for storage

Store at or below 30 °C. Protect from light.
Keep well closed. For external use only.
KEEP OUT OF REACH OF CHILDREN.

6.5 Nature and contents of container

Sterile Opaque, white, low density polyethylene, 5 ml dropper bottle, with white low density polyethylene capillary plugs and blue polypropylene cap in cardboard carton.

6.6 Special precautions for disposal and other handling

No special requirements.
An unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. HOLDER OF THE CERTIFICATE OF REGISTRATION

Gen-Eye (Pty) Ltd[1]

Royal Palm Business Estate

Unit 7, 646 Washington Street

Halfway House, Midrand, 1685, Gauteng, South Africa

8. REGISTRATION NUMBER

45/15.4/1035

9. DATE OF FIRST AUTHORISATION

27 November 2014

10. DATE OF REVISION OF THE TEXT

12 July 2021

® GLAUCOPRESS is a registered trademark of Gen-Eye (Pty) Ltd

[1] Company Registration number: 2009/009360/07

Namibia:
Registration number: 15/15.4/0165
Scheduling status: NS2