1. NAME OF THE MEDICINAL PRODUCT

ISOPTO® CARPINE

2% sterile ophthalmic solution

ISOPTO® CARPINE

4% sterile ophthalmic solution

(pilocarpine hydrochloride)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

ISOPTO® CARPINE 2 % ophthalmic solution: 1 ml of solution contains 20 mg pilocarpine hydrochloride.

ISOPTO® CARPINE 4 % ophthalmic solution: 1 ml of solution contains 40 mg pilocarpine hydrochloride.

Preservative: 1 ml of solution contains 0.1 mg benzalkonium chloride.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Sterile ophthalmic solution.

Practically clear, colourless to pale yellow solution.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

ISOPTO CARPINE ophthalmic solution contains pilocarpine hydrochloride, a miotic (parasympathomimetic).

ISOPTO CARPINE ophthalmic solution is used to control intraocular pressure in chronic simple glaucoma. In acute glaucoma it may be used alone prior to emergency surgery, or in combination with other miotics or carbonic anhydrase inhibitors. Patients can be maintained on ISOPTO CARPINE ophthalmic solution as long as intraocular tension is controlled and there is no visual deterioration as indicated by changes in the visual field.

4.2 Posology and method of administration

Posology

2 drops topically in the eye(s) 3 times daily or as directed by a physician.

Use in children

The safety and efficacy of ISOPTO CARPINE ophthalmic solution in children have not been established.

Use in patients with hepatic or renal impairment

The safety and efficacy of ISOPTO CARPINE ophthalmic solution in patients with hepatic or renal impairment have not been established.

Method of administration

For ocular use.

After cap is removed, if tamper evident snap collar is loose, remove before using product.

To prevent contamination of the dropper tip and solution care must be taken not to touch the eyelids, surrounding areas or other surfaces with the dropper tip. Keep the bottle tightly closed when not in use.

Nasolacrimal occlusion or gently closing the eyelid after administration is recommended. This may reduce the systemic absorption of medicinal products administered via the ocular route and result in a decrease in systemic adverse reactions.

If more than one topical ophthalmic product is being used, the products must be administered at least 5 minutes apart. Eye ointments should be administered last.

4.3 Contraindications

- Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.
- Miotics are contraindicated in conditions where pupillary constriction is undesirable such as acute iritis or anterior uveitis.

4.4 Special warnings and precautions for use

- Retinal detachment has been reported when miotics are used in susceptible individuals, such as young patients with myopia or patients with history of retinal detachment. Fundus examination is advised prior to initiation of treatment with ISOPTO® CARPINE ophthalmic solution.
- Miotics should be avoided in acute inflammatory diseases of the anterior chamber.
- A paradoxical rise in intraocular pressure may be observed in patients with severely compromised trabecular outflow.
- Caution is advised in the presence of corneal or conjunctival damage to avoid excessive penetration which can produce systemic toxicity.
- ISOPTO CARPINE ophthalmic solution should be used with caution in patients with acute cardiac failure, bronchial asthma, peptic ulcer, hyperthyroidism, gastro-intestinal spasm, Parkinson's disease, urinary tract obstruction, recent myocardial infarction, hypertension and hypotension due to the risk of exacerbating these conditions.
- Contact dermatitis may develop after prolonged use.
- ISOPTO CARPINE ophthalmic solution contains benzalkonium chloride which may cause eye irritation and is known to discolour soft contact lenses. Avoid contact with soft contact lenses. Patients must be instructed to remove contact lenses prior to the application of ISOPTO CARPINE and wait at least 15

minute before reinsertion.

For more information, please consult the doctor or pharmacist.

4.5 Interaction with other medicinal products and other forms of interaction
No interaction studies have been performed.

4.6 Fertility, pregnancy and lactation
Pregnancy
There are no or limited amount of data from the use of ISOPTO CARPINE ophthalmic solution in pregnant women. Animal studies have, however, showed harmful effects of systemic pilocarpine exposure with respect to reproductive toxicity in rats.

ISOPTO CARPINE ophthalmic solution is not recommended during pregnancy.

Breast-feeding
It is unknown whether pilocarpine is excreted in human milk. However, excretion in breast milk should be expected. There is also no information on the safety of pilocarpine ophthalmic formulations used during breast-feeding. However, a risk to the suckling child cannot be excluded.

A decision must be made whether to discontinue breast-feeding or to discontinue / abstain from ISOPTO CARPINE ophthalmic solution therapy taking into account the benefit of breast-feeding for the child and the benefit of therapy for the woman.

Fertility
Studies have not been performed to evaluate the effect of topical ocular administration of ISOPTO CARPINE ophthalmic solution on fertility.

4.7 Effects on ability to drive and use machines
ISOPTO CARPINE ophthalmic solution has a major influence on the ability to drive and use machines.

Miosis may cause blurred vision and difficulty in dark adaptation. Patients should be advised to exercise caution while driving at night or while performing hazardous tasks in poor light.

4.8 Undesirable effects
The following adverse reactions are classified according to the subsequent convention: 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), very rare (<1 / 10,000) or not known (cannot be estimated from the available data). Within each frequency-grouping, adverse reactions are presented in order of decreasing seriousness. The adverse reactions were obtained from clinical trials and post-marketing surveillance.

System organ class	Adverse reactions
Immune system disorders	*Not known* : hypersensitivity
Nervous system disorders	*Very common* : headache *Common* : dizziness
Eye disorders	*Very common* : vision blurred *Common* : visual acuity reduced (caused by ciliary muscle spasm), eye pain, photopsia, vitreous floaters, eye irritation, ocular hyperaemia *Uncommon* : retinal tear, vitreous haemorrhage, eyelid oedema, miosis, vitreous detachment, glare, foreign body sensation in eyes *Not known* : intraocular pressure increased, corneal oedema
Gastrointestinal disorders	*Common* : nausea *Not known* : vomiting

4.9 Overdose
An ocular overdose of ISOPTO® CARPINE ophthalmic solution may be flushed from the eye(s) with lukewarm water.

In case of overdose, symptoms of toxicity may include: headache, salivation, sweating, syncope, bradycardia, hypotension, abdominal cramps, vomiting, asthma and diarrhoea.
Treatment of overdose is supportive. In cases of severe systemic toxicity therapy with anticholinergics may be necessary.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: cholinergic agonist (miotic)
ATC code: S01 EB 01

Pilocarpine hydrochloride is a direct acting cholinergic parasympathomimetic agent with a dominant action at muscarinic sites both peripherally and centrally. Like other choline esters, pilocarpine affects the cardiovascular system, exocrine glands, and smooth muscle. Although the precise mechanism by which pilocarpine reduces IOP has not been established, the most widely accepted explanation involves direct stimulation of the longitudinal muscle of the ciliary body, which in turn causes the scleral spur to widen the trabecular spaces and increase aqueous outflow.

5.2 Pharmacokinetic properties
Onset of miosis after topical administration of a 1% solution of pilocarpine hydrochloride or nitrate to the conjunctival sac occurs within 10-30 minutes, with maximal effect within 30 minutes. Miosis usually persists for 4-8 hours, rarely, up to 20 hours. Reduction of intraocular pressure is evident within 60 minutes, peaks within 75 minutes and, depending on the concentration of pilocarpine used, persists for 4-14 hours. Spasms of accommodation commence in about 15 minutes and persist for 2-3 hours.
Pilocarpine has a low ocular bioavailability when topically applied and this has been attributed to extensive pre-corneal drug loss in conjunction with the resistance to normal corneal penetration. Further, pilocarpine appears to bind to the eye pigments from which it is gradually released.
Inactivation of pilocarpine in the eye is thought to occur by a hydrolyzing enzyme. The amount of this enzyme is not changed by the prolonged use of pilocarpine by glaucoma patients, nor is it changed in patients poorly controlled by glaucoma therapy.

5.3 Preclinical safety data
Effects in non-clinical studies were observed only at exposures considered sufficiently in excess of the maximum human exposure indicating little relevance to clinical use.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

ISOPTO® CARPINE 2 %, 4 % ophthalmic solution: Benzalkonium chloride, boric acid, sodium citrate, hypromellose, hydrochloric acid and / or sodium hydroxide (to adjust pH), purified water.

6.2 Incompatibilities
Not applicable.

6.3 Special precautions for storage
Store at room temperature (8°C to 30°C).
Do not use this medicine after the expiry date which is stated on the packaging.
Discard 4 weeks after first opening.
Keep this medicine out of the sight and reach of children.

6.4 Nature and contents of container
ISOPTO CARPINE 2 %, 4 % ophthalmic solution: DROPTAINER dispenser containing 15 ml.

6.5 Special precautions for disposal
No special requirements.

6.6 Manufacturer
See folding box

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Novartis Pharma AG, Basel, Switzerland