1. NAME OF THE MEDICINAL PRODUCT

ALCON ATROPINE SULFATE EYE DROPS 0.5% or 1%

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

ALCON ATROPINE SULFATE EYE DROPS 0.5%: 1 ml of solution contains 5 mg atropine sulfate.
ALCON ATROPINE SULFATE EYE DROPS 1%: 1 ml of solution contains 10 mg atropine sulfate.
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
Viscous clear, colourless solution

4. CLINICAL PARTICULARS

4.1 Therapeutic Indications

ALCON ATROPINE SULFATE EYE DROPS contains atropine sulfate, a parasympatholytic agent which produces mydriasis and cycloplegia.
ALCON ATROPINE SULFATE EYE DROPS is used for refraction or for the iris dilation desired in acute inflammatory conditions of the iris and uveal tract.

4.2 Posology and method of administration

Posology

Use in adults:

- For uveitis: 1 drop in the eye(s), 3 times daily.
- For refraction: 1 drop in the eye(s), repeated 1 hour before the examination.

Children:

ALCON ATROPINE SULFATE EYE DROPS is contraindicated in children less than 12 years because of the risk of serious systemic side effects (see sections 4.3, 4.4, 4.8 and 4.9). When dosed in older children the lowest strength should be used:

- For uveitis: 1 drop of ALCON ATROPINE SULFATE EYE DROPS 0.5% in the eye(s), 3 times daily.
- For refraction: 1 drop of ALCON ATROPINE SULFATE EYE DROPS 0.5% in the eye(s), twice daily for 1 or 2 days before the examination and 1 hour before the examination.

Use in patients with hepatic or renal impairment

The safety and efficacy of ALCON ATROPINE SULFATE EYE DROPS in patients with hepatic and 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. This is particularly important in children.

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.
- Hypersensitivity to belladonna alkaloids.
- Patients with known or suspected glaucoma or a tendency towards glaucoma.
- Children less than 12 years (see section 4.4).
- Children with Down's syndrome, spastic paralysis or brain damage

4.4 Special Warnings and precautions for use

- For topical ocular use only. Not for internal use.
- Excessive use in children or certain individuals may produce systemic symptoms of atropine poisoning.
- ALCON ATROPINE SULFATE EYE DROPS may cause increased intraocular pressure (see section 4.8). The possibility of undiagnosed glaucoma should be considered in some patients, such as elderly patients. Determine the intraocular pressure and an estimation of the depth of the angle of the anterior chamber prior to initiation of therapy to avoid glaucoma attacks.
- ALCON ATROPINE SULFATE EYE DROPS -induced psychotic reactions and behavioural disturbances may occur in patients with increased susceptibility to anticholinergic drugs (see section 4.8). Use with caution in children and elderly patients, but reactions may occur at any age.
- Patients may experience sensitivity to light and should protect eyes in bright illumination.
- Because of risk of provoking hyperthermia (see section 4.8), use with caution in patients, especially in children, who may be exposed to elevated environmental temperatures or who are febrile.
- This product 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 application of ALCON ATROPINE SULFATE EYE DROPS and wait 15 minutes before reinsertion.
- Paediatric population:
  - Because of the risk of serious systemic side effects, ALCON ATROPINE SULFATE EYE DROPS is contraindicated in children below 12 years and caution is advised in older children. The lowest dose necessary to produce the desired effect should always be used. (See section 4.3, 4.4, 4.8 and 4.9).
  - **Children, especially premature and low birth weight, or patients with Down syndrome, spastic paralysis or brain** damage are particularly susceptible to central nervous system disturbances, cardiopulmonary and gastrointestinal toxicity from systemic absorption of atropine (see section 4.8).
  - Fair-skinned children with blue eyes may exhibit an increased response and/or increased susceptibility to adverse reactions.

- Parents should be warned not to get this preparation in their children's mouth or cheeks and to wash their hands or cheeks following administration.
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4.5 Interaction with other medicinal products and other forms of interaction
The effects of ALCON ATROPINE SULFATE EYE DROPS may be enhanced by concomitant use of other drugs having antimuscarinic properties, such as amantadine, some antihistamines, phenothiazine antipsychotics, and tricyclic antidepressants.

4.6 Fertility, Pregnancy and lactation
Pregnancy
There are no or limited amount of data from the use of ALCON ATROPINE SULFATE EYE DROPS in pregnant women. Animal studies are insufficient with respect to reproductive toxicity (See Section 5.3). There are documented systemic effects stemming from ophthalmic atropine use.
ALCON ATROPINE SULFATE EYE DROPS is not recommended during pregnancy and in women of childbearing potential not using contraception.

Breast-feeding
It is unknown whether atropine is excreted in human milk after ocular administration. Traces of atropine have been found in human milk following administration of atropine. In addition, atropine and antimuscarinic agents have been shown to adversely affect lactation in preclinical and in clinical studies. A risk to the suckling child cannot be excluded.
ALCON ATROPINE SULFATE EYE DROPS should not be used during breast-feeding.

Fertility
Studies have not been performed to evaluate the effects of topical ocular administration of atropine on fertility.

4.7. Effects on ability to drive and use machines
Atropine may cause drowsiness, blurred vision and sensitivity to light. Patients receiving ALCON ATROPINE SULFATE EYE DROPS should be advised not to drive or engage in other hazardous activities unless vision is clear.

4.8 Undesirable Effects
The following adverse reactions have been identified from post- marketing surveillance following administration of ALCON ATROPINE SULFATE EYE DROPS. Frequency cannot be estimated from the available data. Within each System Organ Class, adverse reactions are presented in order of decreasing seriousness.

System Organ Classification	Adverse reactions
Immune system disorders	hypersensitivity
Psychiatric disorders	hallucination, confusional state, disorientation
Nervous system disorders	dizziness, headache
Eye disorders	eyelid oedema, photophobia, vision blurred, drug effect prolonged (mydriasis)
Cardiac disorders	tachycardia, bradycardia
Gastrointestinal disorders	intestinal obstruction, abdominal distension, vomiting
Skin and subcutaneous tissue disorders	erythema, rash
General disorders and administration site conditions	pyrexia

Description of selected adverse reactions
This drug produces reactions similar to those of other anticholinergic drugs. The central nervous system manifestations such as ataxia, incoherent speech, restlessness, hallucinations, hyperactivity, seizures, disorientation as to time and place, and failure to recognize people are possible. Other toxic manifestations of anticholinergic drugs are skin rash, abdominal distension in infants, unusual drowsiness, tachycardia, hyperpyrexia, vasodilation, urinary retention, diminished gastrointestinal motility, and decreased secretion in salivary and sweat glands, pharynx, bronchi and nasal passages. Severe reactions are manifested by hypotension with rapid progressive respiratory depression.

Symptoms of toxicity are usually transient (lasting a few hours), but may last up to 24 hours.

Mydriatics may increase intraocular pressure and provoke glaucoma attacks in patients predisposed to acute angle closure in particular geriatric patients (see section 4.4).

Prolonged use of mydriatics may produce local irritation characterized by conjunctivitis (follicular), ocular hyperaemia, eye oedema, eye discharge, and eczema.

Paediatric population
Use of ALCON ATROPINE SULFATE EYE DROPS has been associated with psychotic reactions and behaviour changes in paediatric patients. Central nervous system reactions manifest similar to those listed above.
ALCON ATROPINE SULFATE EYE DROPS can cause hyperpyrexia in children (see section 4.4).

Increased risk for systemic toxicity has been observed in premature and small infants, young children, or children with Down syndrome, spastic paralysis or brain damage with this class of drug (see section 4.4). Intestinal obstruction, abdominal distension and bradycardia were reported in premature or low birth weight infants.

4.9 Overdose
A topical overdose of ALCON ATROPINE SULFATE EYE DROPS may be flushed from the eye(s) with lukewarm water.
Systemic toxicity may occur following topical use, particularly in children. It is manifested by flushing and dryness of the skin (a rash may be present in children), blurred vision, a rapid and irregular pulse, fever, abdominal distension in infants, convulsions and hallucinations and the loss of neuromuscular coordination. Severe intoxication is characterized by central nervous system depression, coma, circulatory and respiratory failure, and death.

Treatment is symptomatic and supportive. In infants and small children the body surface must be kept moist.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties
Pharmacotherapeutic group: mydriatics and cycloplegics; anticholinergics, ATC code: S01FA01
Atropine is an anticholinergic alkaloid that acts centrally and peripherally at the same time. In ophthalmology it is used as a cycloplegic and a mydriatic. It blocks the responses of the sphincter of the iris and the ciliary muscle to cholinergic stimulation, producing pupillary dilation (mydriasis) and paralysis of accommodation (cycloplegia).

Pharmacodynamics
It produces peak mydriasis within 40 minutes. The effect of atropine can last up to 2 weeks.

Pediatric population
See Sections 4.2 and 4.3

5.2 Pharmacokinetic properties
Absorption
Nonclinical data on absorption into ocular tissues with topical ocular administration are not available. The active enantiomer of atropine, l-hyoscyamine is absorbed systemically after topical ocular administration in man. The bioavailability (F) and time to maximum concentration (Tmax) after topical ocular administration were variable.

Distribution
Atropine is rapidly distributed throughout the body after intravenous administration which resulted in a volume of distribution greater than total body water. A biphasic disposition showed a distinctive distributional and elimination phases. Distributional properties differ between the two enantiomers, l-hyoscyamide and d-hyoscyamide. The observed plasma protein binding of atropine was low and variable (14-44%) from both in vitro and in vivo studies.

Biotransformation
Atropine is metabolized in the liver to two major metabolites, noratropine and N-atropine oxide along with the minor metabolites, tropine and tropic acid. The inactive enantiomer appears not to be metabolized.

Elimination
The elimination of atropine is similar after intravenous or topical ocular administration with half-life range of 1.5-3.6 hours after ocular administration. Clearance values varied; however, the ocular route did not impact atropine's elimination. Up to 50% of atropine racemate is excreted unchanged in urine as the inactive enantiomer.

Linear/Non Linear Pharmacokinetics
The linearity of atropine's ocular pharmacokinetics has not been studied. Systemic pharmacokinetics of atropine was linear after intravenous administration from a dose of 1.4 mg to a dose of 2.2 mg.

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 in adults.
A low (5%) incidence of skeletal anomalies was observed when atropine was administered subcutaneously to pregnant mice at 50 mg/kg. Teratogenicity was not observed when atropine was given to pregnant rats or dogs.

6. PHARMACEUTICAL PARTICULARS
6.1 List of Excipients
Benzalkonium chloride, boric acid, Hydroxypropyl Methylcellulose (3550 mPa.s) 0.5%, sodium hydroxide and/or hydrochloric acid (to adjust pH) and purified water.

6.2 Incompatibilities
Not applicable

6.3 Special precautions for storage
Store at 8 ° to 30 °C.
Discard 4 weeks after first opening.
Keep out of sight and reach of children.

6.4 Nature and contents of container
ALCON ATROPINE SULFATE 1%: 5 ml plastic DROPTAINER™ dispenser.
Not all presentations may be available locally.

6.5 Instruction for Use and Handling and Disposal
No special requirements.
Any unused product or waste material should be disposed of in accordance with local requirements.

7. PRODUCT OWNER
ALCON PHARMACEUTICALS LTD
FRIBOURG, SWITZERLAND

(Information issued: Dec 2024.SIN)

Alcon