DISCLAIMER

All labeling reflected on this website is for informational and promotional purposes only. It is not intended to be used by healthcare professionals or patients for the purpose of prescribing or administering these products. Questions regarding the current content of product labeling should be directed to Akorn's Customer Service department at 800.932.5676.
Atropine Sulfate Ophthalmic Solution, USP 1%

INDICATIONS AND USAGE
Atropine is an anti-muscarinic agent indicated for:
- Cycloplegia (1.1)
- Mydriasis (1.2)
- Penalization of the healthy eye in the treatment of amblyopia (1.3)

DOSE AND ADMINISTRATION

1. INDICATIONS AND USAGE
   Atropine Sulfate Ophthalmic Solution, USP 1% is indicated for:
   - Cycloplegia (1.1)
   - Mydriasis (1.2)
   - Penalization of the healthy eye in the treatment of amblyopia (1.3)

2. DOSAGE AND ADMINISTRATION
   - In individuals from three (3) months of age or greater, 1 drop topically to the cul-de-sac of the conjunctiva, forty minutes prior to the intended maximal dilation time. (2)
   - In individuals 3 years of age or greater, doses may be repeated up to twice daily as needed. (2)

3. DOSAGE FORMS AND STRENGTHS
   Atropine Sulfate Ophthalmic Solution, USP 1% (3)

ADVERSE REACTIONS

6. ADVERSE REACTIONS
   The following adverse reactions have been identified following use of atropine sulfate ophthalmic solution, USP 1%:
   - Elevation in Blood Pressure [See Warnings and Precautions (5.2)]
   - Photophobia and Blurred Vision [See Warnings and Precautions (5.1)]

   The following serious adverse reactions are described below and elsewhere in the labeling:
   - Hypersensitivity or allergic reaction to any ingredient in formulation. (4.1)

CONTRAINdications

4. CONTRAINDICATIONS
   • Hypersensitivity to any Component of this Medication

WARNINGS AND PRECAUTIONS

5. WARNINGS AND PRECAUTIONS
   - Photophobia and blurred vision due to pupil unresponsiveness and cycloplegia may last up to 2 weeks. (5.1)
   - Risk of blood pressure increase from systemic absorption. (5.2)

DRUG INTERACTIONS

6. DRUG INTERACTIONS
   The use of atropine and monoamine oxidase inhibitors (MAOI) is generally not recommended because of the potential to precipitate hypertensive crisis. (7)

USE IN SPECIFIC POPULATIONS

7. USE IN SPECIFIC POPULATIONS
   - Pregnancy
   - Nursing Mothers
   - Pediatric Use
   - Geriatric Use

8. USE IN SPECIFIC POPULATIONS
   - Pregnancy
   - Nursing Mothers
   - Pediatric Use
   - Geriatric Use

9. CONTRAINDICATIONS
   - Hypersensitivity or allergic reaction to any ingredient in formulation. (4.1)

10. OVERDOSAGE
   - Hypersensitivity or allergic reaction to any ingredient in formulation. (4.1)

FULL PRESCRIBING INFORMATION: CONTENTS*

1. INDICATIONS AND USAGE
   1.1 Cycloplegia
   1.2 Mydriasis
   1.3 Penalization of the healthy eye in the treatment of amblyopia

2. DOSAGE AND ADMINISTRATION
   - In individuals from three (3) months of age or greater, 1 drop topically to the cul-de-sac of the conjunctiva, forty minutes prior to the intended maximal dilation time. (2)
   - In individuals 3 years of age or greater, doses may be repeated up to twice daily as needed. (2)

3. DOSAGE FORMS AND STRENGTHS
   Atropine Sulfate Ophthalmic Solution, USP 1%: each mL contains 10 mg of atropine sulfate equivalent to 8.3 mg of atropine.

4. CONTRAINDICATIONS
   4.1 Hypersensitivity to any Component of this Medication

5. WARNINGS AND PRECAUTIONS
   5.1 Photophobia and Blurred Vision
   5.2 Elevation of Blood Pressure

6. ADVERSE REACTIONS
   6.1 Ocular Adverse Reactions
   6.2 Systemic Adverse Reactions

7. DRUG INTERACTIONS
   7.1 Monoamine oxidase inhibitors (MAOI)

8. USE IN SPECIFIC POPULATIONS
   8.1 Pregnancy
   8.3 Nursing Mothers
   8.4 Pediatric Use
   8.5 Geriatric Use

9. CONTRAINDICATIONS
   - Hypersensitivity or allergic reaction to any ingredient in formulation. (4.1)

10. OVERDOSAGE
    - Hypersensitivity or allergic reaction to any ingredient in formulation. (4.1)

*Sections or subsections omitted from the full prescribing information are not listed.

Other commonly occurring adverse reactions include, blurred vision, photophobia, superficial keratitis and decreased lacrimation. Allergic reactions such as papillary conjunctivitis, contact dermatitis, and lid edema may also occur less commonly.

6.2 Systemic Adverse Reactions

Systemic effects of atropine are related to its anti-muscarinic activity. Systemic adverse events reported include dryness of skin, mouth, and throat from decreased secretions from mucus membranes; restlessness, irritability or delirium from stimulation of the central nervous system; tachycardia; flushed skin of the face and neck.

7. DRUG INTERACTIONS

7.1 Monoamine oxidase inhibitors (MAOI)

The use of atropine and monoamine oxidase inhibitors (MAOI) is generally not recommended because of the potential to precipitate hypertensive crisis.

8. USE IN SPECIFIC POPULATIONS

8.1 Pregnancy
8.3 Nursing Mothers
8.4 Pediatric Use
8.5 Geriatric Use

There are no adequate and well-controlled studies of atropine sulfate in pregnant women. Animal development and reproduction studies have not been conducted with atropine sulfate. Since it is not known whether topically administered atropine sulfate can cause fetal harm, atropine sulfate ophthalmic solution, USP 1% should only be used during pregnancy if the potential benefit justifies the potential risk to the fetus.

8.3 Nursing Mothers

Traces of atropine have been found in human milk following administration of atropine solution for injection. Because some systemic absorption occurs from topical administration, caution should be exercised when Atropine Sulfate Ophthalmic Solution, USP 1% is administered to a nursing woman.

8.4 Pediatric Use

Due to the potential for systemic absorption of atropine sulfate ophthalmic solution, the use of atropine sulfate ophthalmic solution, USP 1% in children under the age of 3 months is not recommended and the use in children under 3 years of age should be limited to no more than one drop per eye per day.

8.5 Geriatric Use

No overall differences in safety and effectiveness have been observed between elderly and younger adult patients.

10. OVERDOSAGE

In the event of accidental ingestion or toxic overdosage with atropine sulfate ophthalmic solution, supportive care may include a short acting barbiturate or diazepam as needed to control marked excitement and convulsions. Large doses for sedation should be avoided because central depressant action may coincide with the depression occurring late in atropine poisoning. Central stimulants are not recommended.
Atropine sulfate was negative in the salmonella/microsome mutagenicity test. Studies to evaluate carcinogenicity and impairment of fertility have not been conducted.

14. CLINICAL STUDIES

Topical administration of atropine sulfate ophthalmic solution, USP 1% results in cycloplegia and mydriasis which has been demonstrated in several controlled clinical studies in adults and pediatric patients. Maximal mydriasis usually occurs in about 40 minutes and maximal cycloplegia is usually achieved in about 60 to 90 minutes after single administration. Full recovery usually occurs in approximately one week, but may last a couple of weeks.

16. HOW SUPPLIED/STORAGE AND HANDLING

Atropine Sulfate Ophthalmic Solution, USP 1% is supplied in a plastic dropper bottle with a red cap in the following sizes:

- NDC 17478-215-02 2 mL fill in 6cc bottle
- NDC 17478-215-05 5 mL fill in 6cc bottle
- NDC 17478-215-15 15 mL fill in 15cc bottle

Storage: Store at 20° to 25°C (68° to 77°F). Keep tightly closed.

17. PATIENT COUNSELING INFORMATION

Advise patients not to touch the dropper tip to any surface as this may contaminate the solution.

Advise patients that drops will sting upon instillation and advise patients that they will experience sensitivity to light and blurred vision which may last for a couple of weeks.

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Manufactured by: Akorn, Inc.
Lake Forest, IL 60045

AS00N Rev. 10/16

Chemical Name: Benzeneacetic acid, α-(hydroxymethyl)-, 8-methyl-8-azabicyclo[3.2.1.]oct-3-yl ester, (−)-(±)-, sulfate (2:1) (salt), monohydrate.

Molecular Formula: C_{17}H_{23}NO_4•H_2SO_4•H_2O

Molecular Weight: 694.83 g/mol

Each mL of Atropine Sulfate Ophthalmic Solution USP, 1% contains: Active: atropine sulfate 10 mg equivalent to 8.3 mg of atropine. Inactives: benzalkonium chloride 0.1 mg (0.01%), dibasic sodium phosphate, edetate disodium, hypromellose (2910), monobasic sodium phosphate, hydrochloric acid and/or sodium hydroxide may be added to adjust pH (3.5 to 6.0), and water for injection USP.

12. CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Atropine is a reversible antagonist of muscarine-like actions of acetyl-choline and is therefore classified as an antimuscarinic agent. Atropine is relatively selective for muscarinic receptors. Its potency at nicotinic receptors is much lower, and actions at non-muscarinic receptors are generally undetectable clinically. Atropine does not distinguish among the M1, M2, and M3 subgroups of muscarinic receptors.

The pupillary constrictor muscle depends on muscarinic cholinoreceptor activation. This activation is blocked by topical atropine resulting in unopposed sympathetic dilator activity and mydriasis. Atropine also weakens the contraction of the ciliary muscle, or cycloplegia. Cycloplegia results in loss of the ability to accommodate such that the eye cannot focus for near vision.

12.2 Pharmacodynamics

The onset of action after administration of atropine sulfate ophthalmic solution, USP 1%, is usually within 40 minutes with maximal effect being reached in about 2 hours. The effect can last for up to 2 weeks in a normal eye.

12.3 Pharmacokinetics

The bioavailability of atropine sulfate ophthalmic solution, USP 1% was assessed in six healthy subjects, 34 to 29 years of age. Subjects received either 0.3 mg atropine sulfate administered as bolus intravenous injection or 0.3 mg administered as 30 μl instilled unilaterally in the cul-de-sac of the eye. Plasma l-hyoscyamine concentrations were determined over selected intervals up to eight hours after dose administration.

The mean bioavailability of topically applied atropine was 63.5 ± 29% (range 19 to 95%) with large inter-individual differences. Mean maximum observed plasma concentration for the ophthalmic solution was 288 ± 73 pg/mL. Maximum concentration was reached in 28 ± 27 min after administration. Terminal half-life of l-hyoscamine was not affected by route of administration and was calculated to be 3 ± 1.2 hours (intravenous) and 2.5 ± 0.8 hours (topical ophthalmic).

In another placebo-controlled study, the systemic exposure to 1-hyoscyamine, and the anti-cholinergic effects of atropine were investigated in eight ocular surgery patients 56 to 68 years of age, following single topical ocular 0.4 mg atropine dose (given as 40 microliters of atropine sulfate ophthalmic solution, USP 1%). The mean (± standard deviation (SD)) C max of 1-hyoscyamine in these patients was 860 ± 402 pg/mL, achieved within 8 minutes of eyedrop instillation.

Following intravenous administration, the mean (± SD) elimination half-life (t1/2) of atropine was reported to be longer in pediatric subjects under 2 years (6.9 ± 3.3 hours) and in geriatric patients 65 to 75 years (10.0 ± 7.3 hours), compared to in children over 2 years (2.5 ± 1.2 hours) and in adults 16 to 58 years (3.0 ± 0.9 hours). (See 8.4 Pediatric Use).

Atropine is destroyed by enzymatic hydrolysis, particularly in the liver; from 13 to 50% is excreted unchanged in the urine. Traces are found in various secretions, including milk. The major metabolites of atropine are noratropine, atropin-n-oxide, tropine, and tropic acid. Atropine readily crosses the placental barrier and enters the fetal circulation, but is not found in amniotic fluid. Atropine binds poorly (about 44%) to plasma protein, mainly to alpha-1 acid glycoprotein; age has no effect on the serum protein binding of atropine. Atropine binding to alpha-1 acid glycoprotein was concentration dependent (2 to 20 mcg/mL) and nonlinear in vitro and in vivo. There is no gender effect on the pharmacokinetics of atropine administered by injection.

13. NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Atropine sulfate was negative in the salmonella/microsome mutagenicity test. Studies to...