

## ATROPINE (Ophthalmic)

### Introduction

VA CLASSIFICATION (Primary)<sup>3</sup>OP600

Commonly used brand name(s): Atropair; Atropine Care; Atropine Sulfate S.O.P.; Atropisol; Atrosulf; I-Tropine; Isopto Atropine; Minims Atropine; Ocu-Tropine.

Note: For a listing of dosage forms and brand names by country availability, see Dosage Forms section(s).

### Category

Cycloplegic; mydriatic.

### Indications

Note: Bracketed information in the Indications section refers to uses that are not included in U.S. product labeling.

#### Accepted

Refraction, cycloplegic 4, 5, 6, 7, 22, 34, 65, 72, 93, 98<sup>3</sup>Atropine is indicated for measurement of refractive errors. Atropine is a commonly used 59 cycloplegic for refraction in children up to 6 years of age and in children with convergent strabismus. 59 It is not useful for refraction in adults, because of its long duration of action.

Uveitis (treatment) 3, 4, 5, 6, 7, 22, 34, 65, 72, 93, 98<sup>3</sup>Atropine is indicated for pupil dilation 87, 91 and ciliary muscle relaxation, which are desirable in acute 43, 48 inflammatory conditions of the iris and uveal tract.

[Synechiae, posterior (prophylaxis and treatment)] 65, 72<sup>3</sup>Atropine may be used for pupil dilation to break posterior synechiae and decrease the possibility of serious complications resulting from synechiae. However, a more rapidly acting medication is usually used. 42 Atropine may also be used to prevent formation of posterior synechiae.

[Mydriasis, preoperative and postoperative] 65, 72<sup>3</sup>Atropine may be used for preoperative and postoperative mydriasis.

[Glaucoma, malignant (treatment)] \*<sup>3</sup>Atropine is used in the treatment of malignant (ciliary block) glaucoma, which may occur after inflammation, surgery, trauma, or use of miotics.

\* Not included in Canadian product labeling.

### Pharmacology/Pharmacokinetics

#### Mechanism of action/Effect:

Atropine (a belladonna alkaloid) is an anticholinergic agent that blocks the responses of the sphincter muscle of the iris and the accommodative muscle of the ciliary body to stimulation by acetylcholine. 4 Dilation of the pupil (mydriasis) and paralysis of accommodation (cycloplegia) result. 4

Duration of action:

Long-acting; effects on accommodation may last 6 days; 48 mydriasis may persist for 12 days. 48

Precautions to Consider

Cross-sensitivity and/or related problems

Patients sensitive to any of the other belladonna alkaloids may be sensitive to atropine also. 4, 7, 87

Carcinogenicity/Mutagenicity

Studies have not been done in either animals or humans to evaluate the carcinogenic or mutagenic potential of atropine. 93, 98

Pregnancy/Reproduction

Fertility¾Studies have not been done in either animals or humans to evaluate the potential of atropine impairing fertility. 93, 98

Pregnancy¾Studies have not been done in humans; however, ophthalmic atropine may be systemically absorbed. 93, 98

Studies have not been done in animals. 93, 98

FDA Pregnancy Category C. 93, 98

Breast-feeding

Systemic atropine is distributed into breast milk in very small amounts. Ophthalmic atropine may be systemically absorbed and may possibly cause adverse effects, such as fast pulse, fever, or dry skin, in nursing infants of mothers using ophthalmic atropine.

Pediatrics

Atropine should not be used in children who have previously had a severe systemic reaction to atropine. 48, 65

An increased susceptibility to atropine has been reported in infants 59, 66, 98 and young children 59, 98 and in children with blond hair, 59 blue eyes, 59 Down's syndrome, 59 spastic paralysis, 59 or brain damage 59 ; therefore, atropine should be used with great caution in these patients. 4, 98

The ointment dosage form is generally preferred for use in children, since use of the solution presents a greater chance of systemic absorption.

#### Geriatrics

Geriatric patients are more susceptible to the effects of atropine, 59 thus increasing the potential for systemic side effects. 27, 59

#### Drug interactions and/or related problems

The following drug interactions and/or related problems have been selected on the basis of their potential clinical significance (possible mechanism in parentheses where appropriate) %not necessarily inclusive (>> = major clinical significance):

Note: Combinations containing any of the following medications, depending on the amount present, may also interact with this medication.

Anticholinergics or medications with anticholinergic activity, other (See Appendix II )

(if significant systemic absorption of ophthalmic atropine occurs, concurrent use of other anticholinergics or medications with anticholinergic activity may result in potentiated anticholinergic effects 76 )

Antiglaucoma agents, cholinergic, long-acting, ophthalmic 65, 78, 79, 80, 81, 87

(concurrent use with atropine may antagonize the antiglaucoma and miotic actions of ophthalmic long-acting cholinergic antiglaucoma agents, such as demecarium, echothiophate, and isoflurophate; concurrent use with atropine may also antagonize the antiaccommodative convergence effects of these medications when they are used for the treatment of strabismus 87, 91 )

Antimyasthenics or 85

Potassium citrate 84 or

Potassium supplements 83

(if significant systemic absorption of ophthalmic atropine occurs, concurrent use may increase the chance of toxicity and/or side effects of these systemic medications because of the anticholinergic-induced slowing of gastrointestinal motility)

Carbachol or 87, 91

Physostigmine or 87, 91

Pilocarpine 87, 91

(concurrent use with atropine may interfere with the antiglaucoma action of carbachol, physostigmine, 87 or pilocarpine. Also, concurrent use may 87 counteract the mydriatic effect of atropine; 91 this counteraction may be used to therapeutic advantage 87 )

CNS depression-producing medications (See Appendix II )

(if significant systemic absorption of ophthalmic atropine occurs, concurrent use of medications having CNS effects, such as antiemetic agents, phenothiazines, or barbiturates, may result in opisthotonos, convulsions, coma, and extrapyramidal symptoms 82 )

Medical considerations/Contraindications

The medical considerations/contraindications included have been selected on the basis of their potential clinical significance (reasons given in parentheses where appropriate)¼ not necessarily inclusive (>> = major clinical significance).

Except under special circumstances, this medication should not be used when the following medical problem exists

>> Severe systemic reaction to atropine, especially in children, history of 48, 65

Risk-benefit should be considered when the following medical problems exist

Brain damage, in children 59

Down's syndrome (mongolism), in children and adults 59

>> Glaucoma, primary, or predisposition to angle closure 4, 48, 65

Keratoconus

(atropine may produce fixed dilated pupil)

Sensitivity to atropine 4

Spastic paralysis, in children 59

Synechiae between the iris and lens 48

Side/Adverse Effects

Note: An increased susceptibility to atropine has been reported in infants, 4, 48, 59 young children, 4, 48, 59 children with blond hair 59 or blue eyes, 59 adults and children 59 with Down's syndrome, 59 children with brain damage 59 or spastic paralysis, 59 and the elderly. 27, 48, 59 This susceptibility increases the potential for systemic side effects.

Prolonged use of atropine may produce local irritation, 48, 65 resulting in follicular conjunctivitis, 48 vascular congestion, 48 edema, 48 exudate, 48 contact dermatitis, or an eczematoid dermatitis. 48, 98

Severe reactions to atropine may occur and are evidenced by hypotension with progressive respiratory depression. 48 Coma and death have been reported in the very young. 48

The following side/adverse effects have been selected on the basis of their potential clinical significance (possible signs and symptoms in parentheses where appropriate) not necessarily inclusive:

Those indicating need for medical attention

Symptoms of systemic absorption

Clumsiness or unsteadiness 4, 48, 98; confusion or unusual behavior 4, 48; dizziness 65; dryness of skin 4, 48, 57, 60, 98; fever 4, 48, 65, 98; flushing or redness of face 4, 48, 65, 98; hallucinations 4, 48, 98; skin rash 4, 48, 65, 98; slurred speech; swollen stomach in infants 4, 48, 98; tachycardia 65, 98 (fast 4, 48, 65 or irregular 4, 27, 48 heartbeat); unusual drowsiness 4, 48; tiredness or weakness; xerostomia 65 (thirst or dryness of mouth)

Those indicating need for medical attention only if they continue or are bothersome

Blurred vision 4, 48, 65, 98; eye irritation not present before therapy 4, 48, 65; increased sensitivity of eyes to light 4, 48, 65; swelling of the eyelids 48, 56, 65

Overdose

For specific information on the agents used in the management of ophthalmic atropine overdose, see:

- Atropine in Anticholinergics/Antispasmodics (Systemic) monograph;
- Diazepam in Benzodiazepines (Systemic) monograph; and/or
- Physostigmine (Systemic) monograph.

For more information on the management of overdose or unintentional ingestion, contact a Poison Control Center (see Poison Control Center Listing ).

Treatment of overdose

For accidental ingestion, emesis or gastric lavage with 4% tannic acid solution is recommended. 42

For systemic effects, 0.2 to 1 mg (0.2 mg in children) physostigmine should be administered intravenously, as a dilution containing 1 mg in 5 mL of normal saline. 4, 42, 98 The solution should be injected over a period of not less than 2 minutes. 4, 42, 98 Dosage may be repeated every 5 minutes up to a total dose of 2 mg in children and 6 mg in adults in each 30-minute period. 4, 42, 98

Physostigmine is contraindicated in hypertensive reactions. 4, 42, 98

ECG monitoring 42 is recommended during physostigmine administration. 4, 42, 98

Excitement may be controlled by diazepam or a short-acting barbiturate. 42

It is recommended that 1 mg of atropine be available for immediate injection if the physostigmine causes bradycardia, convulsion, or bronchoconstriction. 4, 42, 98

Supportive therapy may require oxygen and assisted respiration; 42 cool water baths for fever, especially in children; 42 and catheterization for urinary retention. 42 In infants and small children, the body surface should be kept moist. 4, 42, 98

#### Patient Consultation

As an aid to patient consultation, refer to Advice for the Patient, Atropine/Homatropine/Scopolamine (Ophthalmic).

In providing consultation, consider emphasizing the following selected information (>> = major clinical significance):

Before using this medication

>> Conditions affecting use, especially:

Sensitivity to atropine, homatropine, or scopolamine

Breast-feeding<sup>3</sup> Medication passes into the breast milk in very small amounts and may cause side effects, such as fast pulse, fever, or dry skin, in babies of nursing mothers using ophthalmic atropine

Use in children<sup>3</sup> Infants and young children and children with blond hair or blue eyes 59 may be especially sensitive to the effects of atropine; this may increase the chance of side effects during treatment

Use in the elderly<sup>3</sup> Geriatric patients are more susceptible to the effects of atropine, 59 thus increasing the potential for systemic side effects 27

Other medical problems, especially primary glaucoma or predisposition to angle closure

Proper use of this medication

Proper administration technique

Washing hands immediately after application to remove any medication that may be on them; if applying medication to infants or children, washing their hands immediately afterwards 42, 43 also, and not letting any medication get into their mouths; wiping off any medication that may have accidentally gotten on the infant or child, including his or her face 59 and eyelids 42, 43

Preventing contamination: Not touching applicator tip to any surface; keeping container tightly closed

>> Importance of not using more medication than the amount prescribed

>> Proper dosing

Missed dose

If dosing schedule is  $\frac{3}{4}$  Once a day: Applying as soon as possible if remembered same day; if remembered later, skipping missed dose and going back to regular dosing schedule; not doubling doses

More than once a day: Applying as soon as possible; if almost time for next dose, skipping missed dose and going back to regular dosing schedule; not doubling doses

>> Proper storage

Precautions while using this medication

>> Medication causes blurred vision and increased sensitivity of the eyes to light; checking with physician if these effects continue for longer than 14 days after discontinuation of atropine

Side/adverse effects

Signs of potential side effects, especially symptoms of systemic absorption

General Dosing Information

A stronger concentration may be required to produce adequate cycloplegia <sup>59</sup> in eyes with hazel or brown irides than in eyes with blue or light-colored irides. 4, 48, 98

The ointment dosage form is generally preferred for use in children, since use of the solution presents a greater chance of systemic absorption. 65

For ointment dosage form only

If the ointment is used for refraction, it should be applied several hours prior to the examination; otherwise it may impair the transparency of the cornea and alter the regularity of its refraction.

For solution dosage form only

Although some manufacturers recommend a dose of 2 drops of an ophthalmic solution at appropriate intervals, the conjunctival sac will usually hold only 1 drop. 63

To avoid excessive systemic absorption, patient should press finger to the lacrimal sac during, and for 2 or 3 4, 48, 65, 66 minutes following, instillation of the solution. 4, 48, 65, 66, 98

Ophthalmic Dosage Forms

Note: Bracketed uses in the Dosage Forms section refer to categories of use and/or indications that are not included in U.S. product labeling.

## ATROPINE SULFATE OPHTHALMIC OINTMENT USP

Usual adult and adolescent dose

Uveitis<sup>3/4</sup>Topical, to the conjunctiva, 0.3 to 0.5 cm of a 1% ointment one or two times a day. 7, 22, 48, 93

Usual pediatric dose 53

Cycloplegic refraction<sup>3/4</sup>Topical, to the conjunctiva, 0.3 cm of the following concentrations three times a day for one to three days prior to refraction: 59

Children up to 2 years of age with blue irides<sup>3/4</sup> 0.5%. 59

Children up to 2 years of age with dark irides<sup>3/4</sup> 1%. 59

Children 2 years of age and over<sup>3/4</sup> 1%. 59

Uveitis

[Postoperative mydriasis]<sup>3/4</sup>Topical, to the conjunctiva, 0.3 to 0.5 cm of a 0.5 or 1% ointment one to three times a day. 59

Strength(s) usually available

U.S.<sup>3/4</sup>0.5% (Rx)[Atropine Sulfate S.O.P. (chlorobutanol 0.5%)]

1% (Rx)[Atropair] [Atropine Sulfate S.O.P. (chlorobutanol 0.5%)] [Ocu-Tropine 99] [Generic] (may contain chlorobutanol) 94

Canada<sup>3/4</sup>1% (Rx) [Generic] (may contain methylparaben, propylparaben) 24, 65

Packaging and storage:

Store below 40 °C (104 °F), preferably between 15 and 30 °C (59 and 86 °F), in a tight container, unless otherwise specified by manufacturer. Protect from freezing.

Auxiliary labeling:

- For the eye.
- Keep container tightly closed.

## ATROPINE SULFATE OPHTHALMIC SOLUTION USP



#### Usual adult and adolescent dose

Uveitis¾Topical, to the conjunctiva, 1 drop of a 1% solution one or two times a day. 4, 42, 59 In some cases, up to four doses a day may be required. 59, 98

[To break posterior synechiae]¾Topical, to the conjunctiva, 1 drop of a 1 to 3% solution 87, 91 alternated with 1 drop of a 2.5 or 10% phenylephrine solution every ten minutes 87, 91 for three applications of each. 59 Extreme caution should be used if 10% phenylephrine is administered. 61

[Mydriasis]¾Preoperative: Topical, to the conjunctiva, 1 drop of a 1% solution supplemented with 1 drop of a 2.5 or 10% phenylephrine solution, prior to surgery. 59 Extreme caution should be used if 10% phenylephrine is administered. 61

Postoperative: Topical, to the conjunctiva, 1 drop of a 1 to 3% solution 87, 91 one to three times a day. 59

[Malignant (ciliary block) glaucoma] \*¾Initial: Topical, to the conjunctiva, 1 drop of a 1 to 3% solution 87, 91 administered concurrently with 1 drop of a 2.5 or 10% phenylephrine solution, three or four times a day. 59 Extreme caution should be used if 10% phenylephrine is administered. 61

Maintenance: Topical, to the conjunctiva, 1 drop of a 1 to 3% solution 87, 91 once every other day or once a day. 59

#### Usual pediatric dose

Cycloplegic refraction¾Topical, to the conjunctiva, 1 drop of the following concentrations two times a day for one to three days prior to refraction: 4, 48, 59, 98

Infants up to 1 year of age¾ 0.125%. 59

Children 1 to 5 years of age¾ 0.25%. 59

Children 5 years of age and over with blue irides¾ 0.25% 59.

Children 5 years of age and over with dark irides¾ 0.5 or 1%. 59

Uveitis¾Topical, to the conjunctiva, 1 drop of a 0.125 to 1% solution one to three times a day. 4, 48, 59, 98

[Postoperative mydriasis]¾Topical, to the conjunctiva, 1 drop of a 0.5% solution one to three times a day or as determined by physician. 59

Strength(s) usually available

U.S.¾0.5% (Rx)[Atropisol 97] [Isopto Atropine (benzalkonium chloride 0.01%)]

1% (Rx)[Atropair] [Atropine Care 92] [Atropisol] [Atrosulf 104] [Isopto Atropine 33 (benzalkonium chloride 0.01%)] [I-Tropine 2] [Ocu-Tropine 100] [Generic] (may contain chlorobutanol) 95, 96

2% (Rx)[Atropisol] [Generic]

Canada¾1% (Rx)[Atropisol (benzalkonium chloride)] [Isopto Atropine 103 (benzalkonium chloride)] [Minims Atropine 23] [Generic] (may contain benzalkonium chloride) 24

Note: The 0.125 and 0.25% strengths are no longer commercially available; compounding required for prescriptions.

Packaging and storage:

Store below 40 °C (104 °F), preferably between 15 and 30 °C (59 and 86 °F), unless otherwise specified by manufacturer. Store in a tight container. Protect from freezing.

Auxiliary labeling:

- For the eye.
- Keep container tightly closed.