

PRODUCT MONOGRAPH

Pr **ALOMIDE[®]**

Lodoxamide Ophthalmic Solution

0.1 % w/v (as lodoxamide tromethamine)

Anti-allergy Agent

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Date of Preparation:
March 29, 1995

Date of Revision:
March 22, 2017

Submission Control No: 202728

Novartis version:
March 4, 2024

ALOMIDE is a registered trademark

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ALOMIDE®

Lodoxamide Ophthalmic Solution

PART I: HEALTH PROFESSIONAL INFORMATION

SUMMARY PRODUCT INFORMATION

Route of Administration	Dosage Form / Strength	Nonmedicinal Ingredients
Topical ophthalmic	Ophthalmic solution/ Lodoxamide 0.1% w/v (as lodoxamide tromethamine)	Benzalkonium chloride (as preservative), mannitol, hydroxypropyl methylcellulose, sodium citrate, tyloxapol, citric acid, edetate disodium, sodium hydroxide and/or hydrochloric acid (to adjust pH) and purified water.

INDICATIONS AND CLINICAL USE

ALOMIDE® (lodoxamide ophthalmic solution) is indicated for the treatment of the ocular signs and symptoms associated with:

- Vernal keratoconjunctivitis.
- Giant papillary conjunctivitis.
- Allergic/atopic conjunctivitis.

Pediatrics (< 4 years of age):

The safety and effectiveness of ALOMIDE in pediatric patients < 4 years of age have not been established.

CONTRAINDICATIONS

ALOMIDE is contraindicated in:

- Patients who are hypersensitive to this drug or to any ingredient in the formulation or component of the container. For a complete listing, see the Dosage Forms, Composition and Packaging section of the product monograph.

WARNINGS AND PRECAUTIONS

Ophthalmologic

Instillation of eye drops may initially cause discomfort or transient burning or stinging (see ADVERSE REACTIONS). Should any of these symptoms persist, the patient should be advised to contact the prescribing physician.

ALOMIDE contains the preservative benzalkonium chloride, which may cause eye irritation. Benzalkonium is known to discolour soft contact lenses. As with all ophthalmic medications containing benzalkonium chloride, patients should be advised to remove their contact lenses before instilling ALOMIDE as benzalkonium accumulates in contact lenses and its subsequent release may possibly irritate the cornea. Patients should be advised to wait at least 15 minutes before reinserting the lenses.

Temporary blurred vision or other visual disturbances may affect the ability to drive or use machines. If blurred vision occurs at instillation, the patient must wait until the vision clears before driving or using machinery.

Sexual Function/Reproduction

There is no data available on the effect of lodoxamide on fertility in humans.

Special Populations

Pregnancy: Reproduction studies with lodoxamide tromethamine administered orally to rats and rabbits have not shown any effects of the product on fertility or reproductive performance, or any evidence of embryotoxicity or pre- and post-natal toxicity. However, there are no adequate and well controlled studies in pregnant women. Since animal reproductive studies are not always predictive of human response, ALOMIDE should be used during pregnancy only if clearly needed.

Nursing Women: It is not known whether lodoxamide is excreted in human milk. There is insufficient information on the excretion of lodoxamide in animal milk. A risk to the suckling child cannot be excluded. Caution should be exercised when ALOMIDE is given to a nursing mother.

Pediatrics (< 4 years of age): The safety and effectiveness of ALOMIDE in pediatric patients < 4 years of age have not been established.

ADVERSE REACTIONS

Adverse Drug Reaction Overview

ALOMIDE has been generally well tolerated. In controlled clinical studies, the most common side effect reported was mild and transient discomfort upon instillation (8.7% of patients) expressed as burning, stinging, itching or tearing.

Post-Market Adverse Drug Reactions

Adverse reactions identified in subsequent clinical trials are listed below.

Eye disorders: anterior chamber cell, asthenopia, blepharitis, corneal abrasion, corneal deposits, corneal epithelium defect, corneal erosion, corneal scar, dry eye, eye discharge, eye edema, eye pain, eye pruritus, keratitis, ocular hyperemia, vision blurred, visual impairment;

Gastrointestinal disorders: abdominal discomfort, nausea;

General disorders and administration site conditions: feeling hot;

Immune system disorders: drug hypersensitivity;

Nervous system disorders: dizziness, dysgeusia, headache, somnolence;

Respiratory, thoracic and mediastinal disorders: nasal dryness, sneezing;

Skin and subcutaneous tissue disorders: eyelid exfoliation, rash.

Adverse reactions identified via spontaneous reporting are listed below. Frequencies cannot be estimated from the data.

Cardiac disorders: palpitations.

DOSAGE AND ADMINISTRATION

Recommended Dose

The dose for adults and children ≥ 4 years of age is 1 or 2 drops in each eye 4 times a day at regular intervals.

Patients should be advised that the effect of therapy with ALOMIDE is dependent upon its administration at regular intervals, as directed.

Improvements in signs and symptoms in response to therapy with ALOMIDE (decreased discomfort, itching, foreign body sensation, photophobia, acute ocular pain, tearing, discharge, erythema/swelling, bulbar conjunctivae, limbus, epithelial disease, ptosis) are usually evident within a few days, but longer treatment for up to 4 weeks is sometimes required. Once symptomatic improvement has been established, therapy should be continued for as long as needed to sustain improvement.

Missed Dose

If a dose is missed, a single drop should be applied as soon as possible before reverting to the regular routine. Do not use a double dose to make up for the one missed.

Administration

Patients should be instructed to avoid contamination of the dropper tip.

After the cap is removed, if the tamper evident snap collar is loose, instruct patients to remove it before using the product.

OVERDOSAGE

Overdosage in the use of topical ophthalmic preparations is a remote possibility. Discontinue medication when heavy or protracted use is suspected.

In case of accidental ingestion of doses of 1.0 mg to 10.0 mg of lodoxamide, the following side effects may occur: feeling of warmth, flushing, nausea, vomiting, diaphoresis and abdominal cramping. Transient elevations of systolic and diastolic blood pressure have been noted with doses of 3.0 mg and 10.0 mg of oral lodoxamide, but they resolve spontaneously after a short time. Other possible adverse events after an oral overdose are headache, dizziness, fatigue and loose stools.

If accidentally ingested, efforts to decrease further absorption may be appropriate.

For management of a suspected drug overdose, contact your regional Poison Control Centre.

ACTION AND CLINICAL PHARMACOLOGY

Pharmacodynamics

Lodoxamide, a mast cell stabilizer, inhibits the *in vivo* type I immediate hypersensitivity reaction in animals and man. Allergen-induced bronchospasm and reduced pulmonary function in monkeys are prevented with lodoxamide treatment. A cutaneous vascular permeability increase associated with reagin or IgE and antigen mediated reactions in rats, monkeys and humans is inhibited with lodoxamide therapy. A similar vascular reaction in the palpebral conjunctiva of rats has been inhibited with topical ocular administration of lodoxamide. Therefore, it is anticipated that lodoxamide will be useful in the treatment of ocular diseases where type I immediate hypersensitivity plays a major role in the pathogenesis.

In vitro studies have demonstrated the ability of lodoxamide to stabilize mast cells and prevent the antigen specific induced release of histamine. In addition, lodoxamide prevents the release or other mast cell inflammatory mediators (i.e. SRS-A, slow reacting substances of anaphylaxis, also known as the peptido-leukotrienes) and appears to inhibit eosinophil chemotaxis. Lodoxamide inhibits histamine release *in vitro* by preventing the movement of calcium into the mast cell after stimulation.

Lodoxamide has no intrinsic vasoconstrictor, antihistamine, cyclooxygenase inhibition or other anti-inflammatory activity.

Pharmacokinetics

The disposition of ^{14}C -lodoxamide was studied in six healthy adult volunteers receiving a 3 mg (50 μCi) oral dose of lodoxamide. Urinary excretion was the major route of elimination. The elimination half-life of ^{14}C -lodoxamide was 8.5 hours in urine. In a study conducted in 12 healthy adult volunteers, topical administration of ALOMIDE, 1 drop in each eye 4 times per day for 10 days, did not result in any measurable lodoxamide plasma levels at a detection limit of 2.5 ng/mL.

STORAGE AND STABILITY

Store at room temperature (15°C – 25°C). Keep out of the reach and sight of children.

DOSAGE FORMS, COMPOSITION AND PACKAGING

ALOMIDE is a sterile, isotonic solution containing:

Medicinal ingredient: lodoxamide 0.1% w/v (as 0.178% w/v lodoxamide tromethamine)

Preservative : benzalkonium chloride 0.007% w/v

Non-medicinal ingredients: mannitol, hydroxypropyl methylcellulose, sodium citrate, tyloxapol, citric acid, edetate disodium, sodium hydroxide and/or hydrochloric acid (to adjust pH) and purified water.

ALOMIDE is supplied in natural plastic ophthalmic dispensers containing 10 mL.

Tamper evidence is provided by a closure with an extended skirt that locks to the bottle finish on application and breaks away from the closure on opening.

PART II: SCIENTIFIC INFORMATION

PHARMACEUTICAL INFORMATION

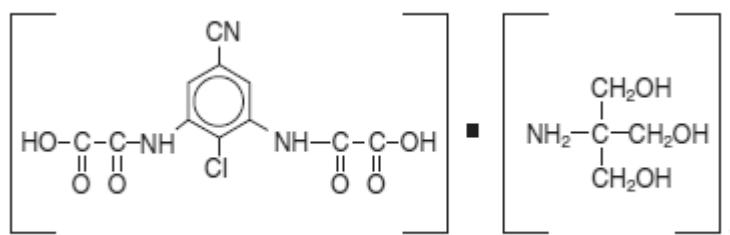
Drug Substance

Proper name: lodoxamide tromethamine

Chemical name: N, N'-(2-chloro-5-cyano-m-phenylene) dioxamic acid tromethamine salt.

Molecular formula and molecular mass: $C_{19}H_{28}ClN_5O_{12}$; 553.91

Structural formula:



Physicochemical properties: White to off-white powder or crystals

CLINICAL TRIALS

In a multi-centre double-masked study (9 centres), 0.1% lodoxamide was more effective than 2% sodium cromoglycate in the treatment of the signs and symptoms of conjunctivitis of an allergic nature (vernal, giant papillary, atopic/allergic types). Ocular signs and symptoms were generally controlled in 14 to 21 days of therapy (q.i.d. dosing), and improvement continued with further therapy. Based upon physician and patient judgments, a therapeutic effect was observed within seven days of the initiation of treatment. In a similar single centre study, 0.1% lodoxamide was judged more effective than 2% sodium cromoglycate, but the difference was not statistically significant.

TOXICOLOGY

Acute Toxicity

Species/Route	LD ₅₀ (mg/kg)	Signs of Toxicity
Mouse, i.p.	4,000 – 5,000	Depression, laboured breathing, partially closed eyes
Mouse, i.p.	3634	Depression, prostration, coma
Mouse, p.o.	> 5,000	None
Rat, p.o.	> 4,000	None
Rat, p.o.	> 5,000	None
Rat, i.p.	5,019	Altered gait, thirstiness, prostration, coma
Rat, i.p.	> 5,000	Slight amount of blood tinged abdominal fluid

Chronic Toxicity

Species/Route Duration	Daily Dose (mg/kg)	Signs of Toxicity
Mouse, p.o. 14 days	0, 500, 1600, 5000	None
Dog, p.o. One month	10, 30, 100	None
Mouse, p.o. 3 months	0, 500, 1600, 5000	None
Rat, p.o. 1, 3 months	10, 30, 100	Decreases in erythrocyte parameters in females
Rat, p.o. 1 year	10, 30, 100	Dose related decrease in body weights in males; small renal calculi (relationship questionable)
Monkey, p.o. 1 year	10, 30, 100	No overt effects
Rat, p.o. 2 year (carcinogenicity)	10, 30, 100	Comparable to controls

Mutagenicity

Test System	Result
Ames (<i>Salmonella</i>) (3 strains) with and without activation	Negative up to 2,000 µg/plate
Ames (<i>Salmonella</i>) (2 additional strains) with and without metabolic activation	Negative 250-2000 µg/plate

Reproduction and Teratology

Species/Route	Dosage (mg/kg/day)	Findings
Rat, p.o. Segment 1	30 – Male 10, 30 – Female	No adverse effects
Rat, p.o. Segment 1	10, 30, 100	Possible decrease in proportion of litter surviving
Rat, p.o. Segment 2	10, 30	No adverse effects
Rat, p.o. Segment 2	10, 30, 100	Not teratogenic
Rat, p.o. Segment 3	10, 30	No adverse effects
Rat, p.o. Segment 3	10, 30, 100	No adverse effects
Rabbit, p.o. Segment 2	10, 30, 100	No adverse effects
Rabbit, p.o. Segment 2	10, 30	No adverse effects

Ocular Studies

Species	Dosage (mg/kg)	Signs of Toxicity
Rabbit Ocular irritation 14 days	0.1%, 1% Both eyes BID	Reddening of eyelids; comparable to control
Rabbit Ocular irritation Every 30 minutes for 12 doses (1 day)	0.25%, 0.5%, 1% Right eye	Minimal to moderate conjunctival congestion and discharge; minimal fluorescein staining; comparable to controls
Rabbit Ocular irritation 1, 3 months	With HPMC – 0.25%, 0.5%, 1%; Without HMPC – 0.5% Right eye QID	Minimal to moderate conjunctival congestion and discharge; sporadic and transient instances of superficial corneal epithelium; irregularities (not dose related) in product and vehicle with HMPC
Monkey Ocular irritation 3 months	0.25%, 0.5%, 1% Right eye QID	None

HPMC = hydroxypropyl methylcellulose

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4. Santos CI, Huang AJ, Abelson MB, Foster S, Friedlander M, McCulley JP. Efficacy of lodoxamide 0.1% ophthalmic solution in resolving corneal epitheliopathy associated with vernal keratoconjunctivitis. Am J Ophthalmol 1994; 117:488-497.

PART III: CONSUMER INFORMATION

ALOMIDE® Lodoxamide Ophthalmic Solution

This leaflet is part III of a three-part "Product Monograph" published when ALOMIDE® was approved for sale in Canada and is designed specifically for Consumers. This leaflet is a summary and will not tell you everything about ALOMIDE. Contact your doctor or pharmacist if you have any questions about the drug.

ABOUT THIS MEDICATION

What the medication is used for:

ALOMIDE is used to treat the signs and symptoms of an eye allergy, such as itching, discomfort and tearing.

What it does:

ALOMIDE contains the active ingredient lodoxamide, which acts by blocking the allergic response.

When it should not be used:

- If you are allergic (*hypersensitive*) to lodoxamide or any other of the ingredients of ALOMIDE (see What the important nonmedicinal ingredients are).

ALOMIDE should not be used in children under the age of 4 years.

What the medicinal ingredient is:

Lodoxamide tromethamine

What the nonmedicinal ingredients are:

Preservative: benzalkonium chloride

Others: citric acid, edetate disodium, hydroxypropyl methylcellulose, mannitol, sodium citrate, tyloxapol, sodium hydroxide and/or hydrochloric acid (to adjust pH), and purified water

What dosage forms it comes in:

ALOMIDE is an eye drop solution that comes in a 10 mL plastic dispenser bottle.

WARNINGS AND PRECAUTIONS

While taking ALOMIDE

You may experience eye discomfort, such as temporary burning or stinging, after applying ALOMIDE. If these symptoms continue, talk to your doctor.

Contact lens wearers

ALOMIDE contains the preservative benzalkonium chloride, which may cause eye irritation. It can also discolour soft contact lenses. Remove your contact lenses before applying ALOMIDE and wait at least 15 minutes before putting them back in.

Driving and using machines

You may find that your vision is blurred for a time just after you use ALOMIDE. Do not drive or use machines until your vision

clears.

Pregnancy or breastfeeding

If you are pregnant, might be pregnant, are breastfeeding or planning to breast-feed, talk to your doctor before using ALOMIDE.

INTERACTIONS WITH THIS MEDICATION

Tell your doctor or pharmacist about all the medications you are taking, recently took or planning to take, including those without a prescription.

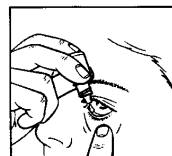
PROPER USE OF THIS MEDICATION

Usual dose:

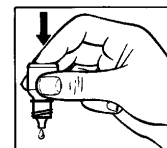
1 or 2 drops in each eye 4 times a day at regular intervals. It is important that you use ALOMIDE regularly. Always follow your doctor's instructions for how to use ALOMIDE.

Your eye allergy symptoms should start to get better within a few days, but you may need to use ALOMIDE for as long as 4 weeks.

How to use:



1



2

- Get the ALOMIDE bottle and a mirror.
- Wash your hands.
- Twist off the bottle cap.
- After cap is removed: if security snap collar is loose, remove before using product.
- Hold the bottle, pointing down, between your thumb and fingers.
- Tilt your head back and look at the ceiling.
- Pull down your lower eyelid with a clean finger to form a 'pocket' between the eyelid and your eye. The drop will go in here (picture 1).
- Bring the bottle tip close to the eye. Do this in front of a mirror if it helps.
- Do not touch your eye or eyelid, surrounding areas or other surfaces with the dropper. It could infect the liquid left in the dispenser bottle. Gently press on the base of the bottle to release one drop of ALOMIDE at a time.
- Do not squeeze the bottle: it is designed so that a gentle press on the bottom is all that it needs (picture 2). You may practice gently pressing on the bottom once or twice over the sink.
- If a drop misses your eye, try again.
- Repeat the steps for your other eye.
- Close the bottle cap firmly immediately after use.

Overdose:

Rinse your eye with warm water if you use more ALOMIDE than

prescribed. Do not put any more drops in until it is time for your next regular dose.

If you accidentally ingest ALOMIDE, you may experience the following side effects:

- feeling warm
- flushing
- nausea
- vomiting
- sweating
- abdominal cramping
- headache
- dizziness
- fatigue
- loose stools
- a temporary rise in blood pressure

In case of drug overdose, contact a health care practitioner, hospital emergency department or regional Poison Control Centre immediately, even if there are no symptoms.

Missed Dose:

If you forget to use ALOMIDE, use a single dose as soon as you remember. If it is almost time for your next dose, skip the missed dose and continue with your regular routine. Do not use a double dose to make up for a missed dose.

SIDE EFFECTS AND WHAT TO DO ABOUT THEM

The most common side effect is mild eye discomfort. This discomfort happens right after using ALOMIDE. The symptoms are burning, stinging, itching or tearing.

Other side effects in the eye may include:

- blurred vision
- dry eyes
- eye redness
- eye pain
- tired eyes
- white deposits on the eye surface
- eye discharge
- eye irritation
- itchy eyes
- eye scales
- damage and scarring of the cornea
- eye and eyelid inflammation
- visual impairment

Other side effects in the rest of the body include:

- dizziness
- headache
- nausea
- feeling hot
- allergy
- drowsiness
- bad taste in the mouth
- dry nose

- sneezing
- abdominal discomfort
- rash
- feeling like your heart is beating too hard or fast

This is not a complete list of side effects. For any unexpected effects while taking ALOMIDE, contact your doctor or pharmacist.

HOW TO STORE IT

Store at room temperature (15°C-25°C). Keep out of the reach and sight of children.

Reporting Side Effects

You can help improve the safe use of health products for Canadians by reporting serious and unexpected side effects to Health Canada. Your report may help to identify new side effects and change the product safety information.

3 ways to report:

- Online at [MedEffect \(http://hc-sc.gc.ca/dhp-mps/medeff/index-eng.php\)](http://hc-sc.gc.ca/dhp-mps/medeff/index-eng.php);
 - By calling 1-866-234-2345 (toll-free);
 - By completing a Consumer Side Effect Reporting Form and sending it by:
 - Fax to 1-866-678-6789 (toll-free), or
 - Mail to: Canada Vigilance Program
Health Canada, Postal Locator
1912C
Ottawa, ON
K1A 0K9
- Postage paid labels and the Consumer Side Effect Reporting Form are available at [MedEffect](http://www.medeffect.gc.ca).

NOTE: Contact your health professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.

MORE INFORMATION

This document plus the full product monograph, prepared for health professionals can be found at:
www.novartis.ca
or by contacting the sponsor, Novartis Pharmaceuticals Canada Inc., at:
1-800-363-8883

This leaflet was prepared by Novartis Pharmaceuticals Canada Inc.

Last revised: March 22, 2017

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Novartis Version: March 4, 2024