AUSTRALIAN PRODUCT INFORMATION – LOMIDE (LODOXAMIDE TROMETAMOL) EYE DROPS, SOLUTION

1 NAME OF THE MEDICINE

lodoxamide trometamol.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

LOMIDE Eye Drops contain 1.78 mg/mL lodoxamide trometamol (equivalent to 1.0 mg/mL lodoxamide).

Excipients with known effect: benzalkonium chloride as a preservative.

For the full list of excipients, see Section 6.1 LIST OF EXCIPIENTS.

3 PHARMACEUTICAL FORM

Eye Drops, a clear, colourless sterile solution for topical application to the eye.

4 CLINICAL PARTICULARS

4.1 THERAPEUTIC INDICATIONS

Seasonal allergic conjunctivitis and vernal keratoconjunctivitis in adults and children four years of age and older.

Prophylactic use of LOMIDE Eye Drops may help in the management of seasonal allergic conjunctivitis and assist in reducing the allergic symptoms.

4.2 DOSE AND METHOD OF ADMINISTRATION

Adults and children 4 years and older

One drop in each eye four times a day at regular intervals.

Patients who experience regular symptoms associated with seasonal allergic conjunctivitis should be advised to begin treatment with LOMIDE Eye Drops about one week prior to the expected onset of the allergy season(s). Treatment should be continued for the duration of the allergy season.

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

Improvements in signs and symptoms in response to therapy with LOMIDE Eye Drops (decreased discomfort, itching, foreign body sensation, photophobia, acute ocular pain, tearing, discharge, erythema/swelling, conjunctival redness, limbal reaction, epithelial disease, ptosis) are usually evident within a few days, however, longer treatment for up to four weeks is sometimes required. Further, continued treatment may result in ongoing improvement in signs and symptoms for at least 3 months. Once symptomatic improvement has been established, therapy should be continued for as long as needed to sustain improvement.

Patients should be advised to wait 10 minutes after instilling LOMIDE Eye Drops before instilling any other eye drops.

4.3 CONTRAINDICATIONS

Known hypersensitivity to lodoxamide or any excipient.

4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE

LOMIDE Eye Drops are not for injection.

Information for the patient

Patients should be advised that effect of therapy with lodoxamide eye drops is dependent upon administration at regular intervals. The recommended frequency of administration should not be exceeded.

In situations where the condition does not improve within a few days, or unmanageable symptoms occur during treatment, the patient should be advised to consult a doctor or pharmacist.

Patients should also be advised that instillation of eye drops may cause discomfort or transient burning or stinging initially. Should these symptoms persist, the patient should be advised to contact a doctor, optometrist or pharmacist.

Due to the severe nature of the disease, patients should be advised not to wear contact lenses while being treated for vernal keratoconjunctivitis. In the event that a patient does wear soft contact lenses, the lenses should be removed prior to instillation of the drops and should not be re-inserted earlier than 15 minutes after dosing.

Lodoxamide eye drops should not affect a patient's ability to drive or to use machinery.

Contact Lenses

LOMIDE Eye Drops contain benzalkonium chloride which may cause eye irritation and are known to discolour soft contact lenses. Avoid contact with soft contact lenses. Patients must be instructed to remove contact lenses prior to application of LOMIDE Eye Drops and wait at least 15 minutes before reinsertion.

Paediatric Use

The safety and effectiveness of LOMIDE Eye Drops in children below the age of four years have not been established.

Use in the elderly

There are no special precautions to be followed in prescribing LOMIDE Eye Drops for the elderly.

Effects on laboratory tests

No data available.

4.5 INTERACTIONS WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTIONS

No specific drug interaction studies, either with ophthalmic or systemic medications, have been conducted. Limited concomitant medications, however, were permitted during the clinical studies and no interactions were observed. Concomitant medications included: corticosteroids (systemic and ophthalmic), naphazoline, antazoline, ketorolac, ciprofloxacin, gentamicin, sulfacetamide, tetracycline, tobramycin, timolol and dipivefrine.

Patients should be advised to wait 10 minutes after instilling LOMIDE Eye Drops before instilling any other eye drops.

4.6 FERTILITY, PREGNANCY AND LACTATION

Effects on fertility

No evidence of impairment of reproductive function was shown in laboratory animal studies.

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

Use in pregnancy – Pregnancy Category B1

Drugs which have been taken by only a limited number of pregnant women and women of childbearing age, without an increase in the frequency of malformation or other direct or indirect harmful effects on the human foetus having been observed. Studies in animals have not shown evidence of an increased occurrence of foetal damage.

Reproduction studies with lodoxamide trometamol administered orally to rats and rabbits in doses of 100 mg/kg/day produced no evidence of developmental toxicity. There are no or a limited amount of data from the use of LOMIDE Eye Drops in pregnant women. Animal studies do not indicate direct or indirect harmful effects with respect to reproductive toxicity. Because animal reproductive studies are not always predictive of human response, lodoxamide eye drops should only be used in pregnancy if clearly needed.

Use in lactation

It is not known whether lodoxamide is excreted in human milk. There is insufficient information on the excretion of lodoxamide from LOMIDE Eye Drops in animal milk. A risk to the breastfed child cannot be excluded. A decision must be made whether to discontinue breastfeeding or to discontinue/abstain from LOMIDE Eye Drops therapy taking into account the benefit of breastfeeding for the child and the benefit of therapy for the woman.

4.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

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.

4.8 ADVERSE EFFECTS (UNDESIRABLE EFFECTS)

LOMIDE Eye Drops were well tolerated in clinical studies with no significant changes in visual acuity, colour vision, intraocular pressure or signs of local toxicity or irritation. No serious adverse events were reported with the use of LOMIDE Eye Drops in these studies. Side effects were mild and self

limiting, resolving within minutes without further intervention. The incidence of side effects was similar to other topical medications such as sodium cromoglycate and only slightly greater than when the vehicle was used alone.

During clinical studies, the most frequently reported ocular adverse experiences were transient burning, stinging or discomfort upon instillation, which occurred in 13% of patients. Other ocular events occurring in 1 to 3.5% of the patients included ocular pruritus (3.5%), blurred vision (1.8%), lid margin crusting (1.6%), dry eye (1.3%), tearing (1.2%) and hyperaemia (1.2%). Events that occurred in less than 1% of the patients included foreign body sensation, ocular pain, discharge, ocular oedema, ocular fatigue, ocular warming sensation, lid oedema, chemosis, anterior chamber cells, epitheliopathy, keratopathy/keratitis, blepharitis, sticky sensation, corneal erosion, dim vision, corneal abrasion and allergy.

Non-ocular events are rare and reported at incidences less than 0.5%. These included a temporary warm sensation, headache, nausea, stomach discomfort, dizziness, somnolence, dry nose, sneezing and rash.

Post Marketing Experience

The following adverse reactions are classified according to the following 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 have been observed during clinical trials and post-marketing experience for lodoxamide eye drops.

System Organ Classification	**MedDRA Preferred Term**
Immune system disorders	*Rare:* drug hypersensitivity
Nervous system disorders	*Uncommon:* dizziness, headache *Rare:* somnolence, dysgeusia
Eye disorders	*Very common:* ocular discomfort *Common:* vision blurred, dry eye, eye pruritus, lacrimation increased, ocular hyperaemia *Uncommon:* eye pain, eye oedema, asthenopia, corneal deposits, conjunctival oedema, abnormal sensation in eye, foreign body sensation in eyes, eye discharge, eye irritation *Rare:* corneal erosion, corneal scar, corneal abrasion, anterior chamber cell, corneal epithelium defect, keratitis, blepharitis, visual

	impairment, eyelid oedema, conjunctival disorder
Respiratory, thoracic and mediastinal disorders	*Rare:* nasal dryness, sneezing
Gastrointestinal disorders	*Uncommon:* nausea *Rare:* abdominal discomfort
Skin and subcutaneous tissue disorders	*Uncommon:* eyelid exfoliation *Rare:* rash
General disorders and administration site conditions	*Uncommon:* drug intolerance, feeling hot

Additional adverse reactions identified from post-marketing surveillance include the following. Frequencies cannot be estimated from the available data. Within each System Organ Class adverse reactions are presented in order of decreasing seriousness.

System Organ Classification	**MedDRA Preferred Term**
Cardiac disorders	palpitation

Reporting suspected adverse effects

Reporting suspected adverse reactions after registration of the medicinal product is important. It allows continued monitoring of the benefit-risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions at www.tga.gov.au/reporting-problems.

4.9 OVERDOSE

Due to the characteristics of this preparation, toxic effects are unlikely following an ocular overdose of this product. In the event of an ocular overdose, flush from the eye with lukewarm water.

In case of accidental ingestion of doses of 0.1 mg to 10.0 mg of lodoxamide, the following adverse 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 and 10.0 mg of oral lodoxamide, but they resolve spontaneously after a short time. Other possible adverse effects after an oral overdose are headache, dizziness, fatigue and loose stools.

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

For information on the management of overdose, contact the Poison Information Centre on 13 11 26 (Australia).

5 PHARMACOLOGICAL PROPERTIES

5.1 PHARMACODYNAMIC PROPERTIES

Mechanism of action

Lodoxamide trometamol is a mast cell stabiliser that inhibits the *in vivo* Type I, IgE-mediated (immediate) hypersensitivity reaction. Lodoxamide inhibits the increase in cutaneous vascular permeability that is associated with reagin or IgE and antigen-mediated reactions.

In vitro studies have demonstrated the ability of lodoxamide to stabilise rodent mast cells and prevent antigen-stimulated release of histamine. In addition, lodoxamide prevents the release of other mast cell inflammatory mediators (i.e. SRS-A, slow-reacting substances of anaphylaxis, also known as the peptido-leukotrienes) and inhibits eosinophil chemotaxis. Although lodoxamide's precise mechanism of action is unknown, the drug has been reported to prevent calcium influx into mast cells upon antigen stimulation.

Lodoxamide has no intrinsic vasoconstrictor, antihistaminic, cyclo-oxygenase inhibition or other anti-inflammatory activity.

Clinical trials

The safety (915 patients) and efficacy (723 patients) of LOMIDE Eye Drops in the treatment of allergic ocular disorders were studied in a series of nine clinical studies; 336 of the patients evaluated for safety were treated for seasonal allergic conjunctivitis while 389 of the patients evaluated for safety were treated for vernal keratoconjunctivitis. Patients four years of age and older were enrolled, with no upper age limit. The demographic features of the study population reflected the expected age-sex distribution of the conditions studied.

Fifty six patients were treated up to 12 months, with no evidence of rebound exacerbation of disease on cessation of therapy or tachyphylaxis.

Seasonal allergic conjunctivitis

LOMIDE Eye Drops were demonstrated to be at least as efficacious as sodium cromoglycate 2% and 4% in the treatment of seasonal allergic conjunctivitis with significant improvement in many symptoms and signs occurring within the first three to seven days of treatment. Treatment effect continued to increase up to 4 weeks after initiation of therapy.

Vernal keratoconjunctivitis

LOMIDE Eye Drops were shown to be superior to placebo and sodium cromoglycate 2% and 4% in the treatment of vernal keratoconjunctivitis with resolution of some of the major clinical signs (corneal papillae, follicles and corneal staining) of this condition. In a 7-week study LOMIDE Eye Drops significantly reduced the need for adjunctive topical steroid therapy in patients with moderate to severe vernal keratoconjunctivitis in comparison to sodium cromoglycate 2% (Week 3 - Week 7 of the study).

5.2 PHARMACOKINETIC PROPERTIES

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 (83%). The elimination half-life of ^{14}C-lodoxamide was estimated from urinary excretion data to be 8.5 hours.

The administration of LOMIDE Eye Drops to twelve healthy adult volunteers (one drop in each eye four times per day for ten days) resulted in only 3 plasma samples (from a total of 108) with detectable levels of lodoxamide (level of detection 2.5 ng/mL). It is, therefore, possible that minute amounts of lodoxamide might be absorbed systemically in some patients.

5.3 PRECLINICAL SAFETY DATA

Carcinogenicity

A long-term study with lodoxamide trometamol in rats (two-year oral administration) showed no neoplastic or tumourigenic effects at doses up to 100 mg/kg/day (more than 5,000 times the proposed human clinical dose).

Genotoxicity

No evidence of mutagenicity or genetic damage was seen in assays for gene mutations and chromosomal damage. In the BALB/c-3T3 Cells Transformation Assay, some increase in the number of transformed foci was seen at high concentrations.

6 PHARMACEUTICAL PARTICULARS

6.1 LIST OF EXCIPIENTS

Mannitol, hypromellose, sodium citrate, citric acid monohydrate, tyloxapol, disodium edetate, benzalkonium chloride, hydrochloric acid, sodium hydroxide and water-purified.

6.2 SHELF LIFE

In Australia, information on the shelf life can be found on the public summary of the Australian Register of Therapeutic Goods (ARTG). The expiry date can be found on the packaging.

6.3 SPECIAL PRECAUTIONS FOR STORAGE

Store below 25°C. Do not freeze.

Discard 28 days after opening.

6.4 NATURE AND CONTENTS OF CONTAINER

LOMIDE Eye Drops 0.1% are a clear, colourless solution in an LDPE 10 mL dispenser bottle.

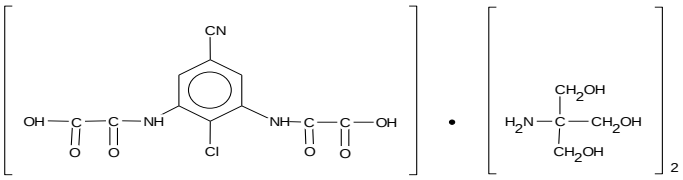
6.5 SPECIAL PRECAUTIONS FOR DISPOSAL

In Australia, any unused medicine or waste material should be disposed of by taking to your local pharmacy.

6.6 PHYSICOCHEMICAL PROPERTIES

Lodoxamide trometamol is a white crystalline powder, freely soluble in water.

Chemical structure:



Molecular weight: 553.91

Empirical formula: $C_{19}H_{28}O_{12}N_5Cl$

Chemical names: Lodoxamide: N,N'-(2-chloro-5-cyano-m-phenylene)dioxamic acid.

Trometamol: 2-amino-2-(hydroxymethyl)-1,3-propanediol.

CAS number:

CAS-63610-09-3

7 MEDICINE SCHEDULE (POISONS STANDARD)

Pharmacy Only Medicine (Schedule 2).

8 SPONSOR

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13 February 1997

10 DATE OF REVISION

12 January 2021

SUMMARY TABLE OF CHANGES

Section Changed	Summary of new information
All	Product Information reformat
8	Sponsor contact details added

6.5	Delete tradename DROP-TAINER®

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