Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Olopatadine Misom 1 mg/mL eye drops, solution

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

1 mL of solution contains olopatadine hydrochloride equivalent to 1 mg olopatadine.
One drop of solution (approximately 0.03 mL) contains 0.03 mg of olopatadine.

Excipient(s) with known effect:
Each ml contains 0.1 mg benzalkonium chloride and disodium phosphate equivalent to 3.34 mg of phosphates.
One drop of solution (approximately 0.03 mL) contains 0.003 mg of benzalkonium chloride and disodium phosphate equivalent to 0.1 mg of phosphates.

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Eye drops, solution (eye drops)
Clear, colourless solution practically free from particles, with a pH of 5.5 to 7.5 and an osmolality of 260 to 340 mOsmol/kg.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Treatment of ocular signs and symptoms of seasonal allergic conjunctivitis.

4.2 Posology and method of administration

Posology

The dose is one drop of Olopatadine Misom 1 mg/ml Eye drops, solution in the conjunctival sac of the affected eye(s) twice daily (8 hourly). Treatment may be maintained for up to four months, if considered necessary.

Use in elderly
No dosage adjustment in elderly patients is necessary.

Paediatric patients

Olopatadine Misom 1 mg/ml Eye drops, solution may be used in paediatric patients three years of age and older at the same dose as in adults. The safety and efficacy of Olopatadine Misom 1 mg/ml Eye drops, solution in children aged under 3 years has not been established. No data are available.

Use in hepatic and renal impairment
Olopatadine in the form of eye drops (Olopatadine Misom 1 mg/ml Eye drops, solution) has not been studied in patients with renal or hepatic disease. However, no dosage adjustment is expected to be necessary in hepatic or renal impairment (see section 5.2).

Method of administration
For ocular use only.

When using nasolacrimal occlusion or closing the eyelids for 2 minutes, the systemic absorption is reduced. This may result in a decrease in systemic side effects and an increase in local activity.
To prevent contamination of the dropper tip and suspension, care must be taken not to touch the eyelids, surrounding areas or other surfaces with the dropper tip of the bottle. Instruct patients to keep the bottle tightly closed when not in use.

In case of concomitant therapy with other topical ocular medicines, an interval of five minutes should be allowed between successive applications. 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.

4.4 Special warnings and precautions for use

Olopatadine Misom 1 mg/ml Eye drops, solution is an antiallergic/antihistaminic agent and, although administered topically, is absorbed systemically. If signs of serious reactions or hypersensitivity occur, discontinue the use of this treatment.

Benzalkonium chloride
This medicinal product contains 0.1 mg benzalkonium chloride in each ml of solution.
From the limited data available, there is no difference in the adverse event profile in children compared to adults.
Generally, however, eyes in children show a stronger reaction for a given stimulus than the adult eye. Irritation may have an effect on treatment adherence in children.
Benzalkonium chloride has been reported to cause eye irritation, symptoms of dry eyes and may affect the tear film and corneal surface. Should be used with caution in dry eye patients and in patients where the cornea may be compromised. Patients should be monitored in case of prolonged use.

Benzalkonium chloride and Contact lenses

Benzalkonium chloride may be absorbed by soft contact lenses and may change the colour of the contact lenses. You should remove contact lenses before using this medicine and put them back 15 minutes afterwards.

Phosphate buffer
This medicine contains 3.34 mg phosphates in each ml of solution. (See section 4.8 Undesirable effects, corneal calcification)

4.5 Interaction with other medicinal products and other forms of interaction

No interaction studies with other medicinal products have been performed.

In vitro studies have shown that olopatadine did not inhibit metabolic reactions which involve cytochrome P-450 isozymes 1A2, 2C8, 2C9, 2C19, 2D6, 2E1 and 3A4. These results indicate that olopatadine is unlikely to result in metabolic interactions with other concomitantly administered active substances.

4.6 Fertility, pregnancy and lactation

Pregnancy

There are no or limited amount of data from the use of ophthalmic olopatadine in pregnant women.
Studies in animals have shown reproductive toxicity following systemic administration (see section 5.3). Olopatadine is not recommended during pregnancy and in women of childbearing potential not using contraception.

Breast-feeding
Available data in animals have shown excretion of olopatadine in milk following oral administration (for details see section 5.3).

A risk to the new-born/infants cannot be excluded.

Olopatadine Misom 1 mg/ml Eye drops, solution should not be used during breast-feeding.

Fertility
Studies have not been performed to evaluate the effect of topical ocular administration of olopatadine on human fertility.

4.7 Effects on ability to drive and use machines

Olopatadine Misom 1 mg/ml Eye drops, solution has no or negligible influence on the ability to drive and use machines.

As with any eye drop, 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 Undesirable effects

Summary of safety profile

In clinical studies involving 1680 patients, Olopatadine Misom 1 mg/ml Eye drops, solution was administered one to four times daily in both eyes for up to four months as monotherapy or adjunctive therapy to loratadine 10 mg. Approximately 4.5% of patients can be expected to experience adverse reactions associated with the use of Olopatadine Misom 1 mg/ml Eye drops, solution; however, only 1.6% of patients discontinued from the clinical studies due to these adverse reactions. No serious ophthalmic or systemic adverse reactions related to olopatadine were reported in clinical studies. The most frequent treatment-related adverse reaction was eye pain, reported at an overall incidence of 0.7%.

Tabulated list of adverse reactions

The following adverse reactions have been reported during clinical studies and post-marketing data and 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 <1/1000), 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.

System Organ Classification	Frequency	Adverse Reactions
Infections and infestations	Uncommon	rhinitis
Immune system disorders	Not known	hypersensitivity, swelling face
Nervous system disorders	Common	headache, dysgeusia
	Uncommon	dizziness, hypoaesthesia
	Not known	somnolence
Eye disorders	Common	eye pain, eye irritation, dry eye, abnormal sensation in eyes
	Uncommon	corneal erosion, corneal epithelium defect, corneal epithelium disorder, punctate keratitis, keratitis, corneal staining, eye discharge, photophobia, vision blurred, visual acuity reduced, blepharospasm, ocular discomfort, eye pruritus, conjunctival follicles, conjunctival disorder, foreign body sensation in eyes, lacrimation increased, erythema of eyelid, eyelid oedema, eyelid disorder, ocular hyperaemia
	Not known	corneal oedema, eye oedema, eye swelling, conjunctivitis, mydriasis, visual disturbance, eyelid margin crusting
Respiratory, thoracic, and mediastinal disorders	Common	nasal dryness
	Not known	dyspnoea, sinusitis
Gastrointestinal disorders	Not known	nausea, vomiting,
Skin and subcutaneous tissue disorders	Uncommon	dermatitis contact, skin burning sensation, dry skin
	Not known	dermatitis, erythema
General disorders and administration site conditions	Common	fatigue
	Not known	asthenia, malaise

Cases of corneal calcification have been reported very rarely in association with the use of phosphate containing eye drops in some patients with significantly damaged corneas (See Section 4.4).

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation 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 via the HPRA Pharmacovigilance Website: www.hpra.ie.

4.9 Overdose

No data are available in humans regarding overdose by accidental or deliberate ingestion. olopatadine has a low order of acute toxicity in animals. Accidental ingestion of the entire contents of a bottle of Olopatadine Misom 1 mg/ml Eye drops, solution would deliver a maximum systemic exposure of 5 mg olopatadine. This exposure would result in a final dose of 0.5 mg/kg in a 10 kg infant, assuming 100% absorption.

Prolongation of the QTc interval in dogs was observed only at exposures considered sufficiently in excess of the maximum human exposure indicating little relevance to clinical use. A 5 mg oral dose was administered twice-daily for 2.5 days to 102 young and elderly male and female healthy volunteers with no significant prolongation of QTc interval compared to placebo. The range of peak steady-state olopatadine plasma concentrations (35 to 127 ng/ml) seen in this study represents at least a 70-fold safety margin for topical olopatadine with respect to effects on cardiac repolarisation.

In the case of overdose, appropriate monitoring and management of the patient should be implemented.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: ophthalmologicals; decongestant and antiallergics; other antiallergics, ATC code: S01GX 09

Olopatadine is a potent selective antiallergic/antihistaminic agent that exerts its effects through multiple distinct mechanisms of action. It antagonises histamine (the primary mediator of allergic response in humans) and prevents histamine induced inflammatory cytokine production by human conjunctival epithelial cells. Data from in vitro studies suggest that it may act on human conjunctival mast cells to inhibit the release of pro-inflammatory mediators. In patients with patent nasolacrimal ducts, topical ocular administration of olopatadine was suggested to reduce the nasal signs and symptoms that frequently accompany seasonal allergic conjunctivitis. It does not produce a clinically significant change in pupil diameter.

5.2 Pharmacokinetic properties

Absorption

Olopatadine is absorbed systemically, as are other topically administered medicinal products. However, systemic absorption of topically applied olopatadine is minimal with plasma concentrations ranging from below the assay quantitation limit (<0.5 ng/ml) up to 1.3 ng/ml. These concentrations are 50-to 200-fold lower than those following well tolerated oral doses.

Elimination

From oral pharmacokinetic studies, the half-life of olopatadine in plasma was approximately eight to 12 hours, and elimination was predominantly through renal excretion. Approximately 60-70% of the dose was recovered in the urine as active substance. Two metabolites, the mono-desmethyl and the N-oxide, were detected at low concentrations in the urine.

Since olopatadine is excreted in urine primarily as unchanged active substance, impairment of renal function alters the pharmacokinetics of olopatadine with peak plasma concentrations 2.3-fold greater in patients with severe renal impairment (mean creatinine clearance of 13.0 ml/min) compared to healthy adults. Following a 10 mg oral dose in patients undergoing haemodialysis (with no urinary output), plasma olopatadine concentrations were significantly lower on the haemodialysis day than on the non-haemodialysis day suggesting olopatadine can be removed by haemodialysis.

Studies comparing the pharmacokinetics of 10 mg oral doses of olopatadine in young (mean age 21 years) and elderly (mean age 74 years) showed no significant differences in the plasma concentrations (AUC), protein binding or urinary excretion of unchanged parent drug and metabolites.
A renal impairment study after oral dosing of olopatadine has been performed in patients with severe renal impairment. The results indicate that a somewhat higher plasma concentration can be expected with Olopatadine Misom 1 mg/ml Eye drops, solution in this population. Since plasma concentrations following topical ocular dosing of olopatadine are 50-to 200-fold lower than after well-tolerated oral doses, dose adjustment is not expected to be necessary in the elderly or in the renally impaired population. Liver metabolism is a minor route of elimination. Dose adjustment is not expected to be necessary with hepatic impairment.

5.3 Preclinical safety data

Non-clinical data reveal no special hazard for humans based on conventional studies of safety, pharmacology, repeated dose toxicity, genotoxicity, carcinogenic potential and toxicity to reproduction.

Studies in animals have shown reduced growth of nursing pups of dams receiving systemic doses of olopatadine well in excess of the maximum level recommended for human ocular use. Olopatadine has been detected in the milk of nursing rats following oral administration.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Benzalkonium chloride
Sodium chloride
Disodium phosphate (E339)
Hydrochloric acid, concentrated (E507) (for pH adjustment)
Sodium hydroxide (E524) (for pH adjustment)
Water for injections

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

2 years
Shelf life after first opening: *4 weeks*

6.4 Special precautions for storage

This medicinal product does not require any special storage conditions.

6.5 Nature and contents of container

5 ml white LDPE bottle with white LDPE dropper and white HDPE screw cap with temper evident seal.
Approximately 160 drops are delivered from a single 5 ml container.

Pack sizes: 1 x 5 ml
3 x 5 ml

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7 MARKETING AUTHORISATION HOLDER

Misom Labs Limited
Malta Life Sciences Park
Ls2.01.06 Industrial Estate
San Gwann
SGN 3000
Malta

8 MARKETING AUTHORISATION NUMBER

PA23377/001/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 9th May 2025

10 DATE OF REVISION OF THE TEXT