Summary of Product Characteristics for Pharmaceutical Products

1. Name of the medicinal product:

Olapo eye drops

2. Qualitative and quantitative composition

Each mL of solution contains 1.10 mg of Olopatadine Hydrochloride equivalent to 1 mg of Olopatadine.

Excipients with known effect:
Each mL of solution contains 0.1 mg benzalkonium chloride.

For a full list of excipients, see section 6.1.

3. Pharmaceutical form

Eye drops, solution (eye drops).

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 Olapo 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

Olapo may be used in paediatric patients three years of age and older at the same dose as in adults. The safety and efficacy of Olapo 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 (Olapo) 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. After the bottle cap is removed, if the tamper evident snap collar is loose, remove before using the product. To prevent contamination of the dropper tip and solution, care must be taken not to touch the eyelids, surrounding areas, or other surfaces with the dropper tip of the bottle. 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

4.4 Special warnings and precautions for use

Olapo 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.

Olapo contains benzalkonium chloride which may cause eye irritation.
Benzalkonium chloride has also been reported to cause punctate keratopathy and/or toxic ulcerative keratopathy. Close monitoring is required with frequent or prolonged use in dry eye patients, or in conditions where the cornea is compromised.

Contact lenses

Benzalkonium is known to discolour soft contact lenses. Avoid contact with soft contact lenses. Patients should be instructed to remove contact lenses prior to administration of the eye drop and wait at least15 minutes after instillation before re-inserting contact lenses.

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 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 newborn/infants cannot be excluded.

Olapo 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

Olapo 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, Olapo 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 Olapo; 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 Olapo 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.

Reporting of suspected adverse reactions: Healthcare professionals are requested to report any suspected adverse reactions via National Pharmacovigilance Electronic Reporting Systems' to the respective National Regulatory Authorities.

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 Olapo 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 Olapo 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 Olapo 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 solution BP
Di sodium Hydrogen Orthophosphate BP
Sodium Dihydrogen Orthophosphate BP
Sodium Chloride BP
Disodium EDTA BP
Propylene Glycol BP

6.2 Incompatibilities

None known.

6.3 Shelf-Life

2 years

6.4 Special Precautions for storage

Store below 30°C in a dry place, protect from light.

6.5 Nature and Content of container

5 mL sterile white color plastic vial along with the pack insert is packed in Primary Carton.

6.6 Special precautions for disposal and other handling

No special requirements.

7. Marketing Authorization Holder
Hanuchem Laboratories
1317 – 20, Manpura, Baddi, Dist. Solan (HP.)
173205. India.

8. Marketing Authorization Number
H2022/CTD8764/18555

9. Date of first authorization/renewal of the authorization
19/11/2022

10. Date of revision of the text
19/11/2022