


# National Agency for Food & Drug Administration & Control (NAFDAC)

## Registration & Regulatory Affairs (R & R) Directorate

## SUMMARY OF PRODUCT CHARACTERISTICS (SmPC)

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# SUMMARY OF PRODUCT CHARACTERISTICS

## 1. NAME OF THE FINISHED PHARMACEUTICAL PRODUCT

RAPIDON EYE DROPS

Olopatadine Hydrochloride Ophthalmic Solution USP 0.1% w/v

## 2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains:

Olopatadine Hydrochloride 1.11mg equivalent to Olopatadine 1 mg

Benzalkonium Chloride Solution USNF 0.01%

(As preservative)

Water for injection USP q.s to 1 ml

For the full list of excipients, see section 6.1.

## 3. PHARMACEUTICAL FORM

Ophthalmic Solution

Clear, colorless solution practically free from particles.

## 4. CLINICAL PARTICULARS

### 4.1 Therapeutic indications

Treatment of ocular signs and symptoms of seasonal allergic conjunctivitis.

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## 4.2 Posology and method of administration

**Posology**

The dose is one drop of Olopatadine Hydrochloride Ophthalmic 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.

**Pediatric population**

Olopatadine Hydrochloride Ophthalmic Solution may be used in pediatric patients three years of age and older at the same dose as in adults. The safety and efficacy of Olopatadine Hydrochloride Ophthalmic 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 Hydrochloride Ophthalmic 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.

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.

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### 4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1

### 4.4 Special warnings and special precautions for use

Olopatadine Hydrochloride Ophthalmic 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.

Olopatadine Hydrochloride Ophthalmic Solution 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 discolor 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 reinserting 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.

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### 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 newborn/infants cannot be excluded.

Olopatadine Hydrochloride Ophthalmic 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 Hydrochloride Ophthalmic 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.

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**4.8 Undesirable effects**

**Summary of safety profile**

In clinical studies involving 1680 patients, Olopatadine Hydrochloride Ophthalmic 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 Hydrochloride Ophthalmic 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 Hydrochloride Ophthalmic Solution 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, hypo aesthesia |
| | 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 hyperemia |
| | 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 disorder 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.

**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 Hydrochloride Ophthalmic 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 repolarization.

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 antagonizes 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 Hydrochloride Ophthalmic Solution 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-dimethyl 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 hemodialysis (with no urinary output), plasma olopatadine concentrations were significantly lower on the hemodialysis day than on the non-hemodialysis day suggesting olopatadine can be removed by hemodialysis.

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 Hydrochloride Ophthalmic 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, Geno toxicity, 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
Dibasic sodium phosphate anhydrous
Sodium hydroxide for pH adjustment
Hydrochloric acid for pH adjustment

### 6.2 Incompatibilities:

Not applicable

### 6.3 Shelf life:

36 Months
Use solution within 28 days after opening the bottle

### 6.4 Special precautions for storage:

Store below 30°C.
Protect from light.
Keep out of reach of children.

### 6.5 Nature and contents of container:

5 ml filled in 5 ml 3-Piece container and packed in a single carton.

### 6.6 Instructions for use and handling and disposal

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

## 7. MARKETING AUTHORISATION HOLDER

Micro Labs Limited,
No. 31, Race Course Road,
Bangalore-560 001, India.

**Manufacturing Site:**

**MICRO LABS LIMITED**
Plot NO. 113-116, IV
Phase, KIADB Industrial
Area, Bommasandra,
Bangalore -560099
INDIA.

Applicant: MICRO NOVA PHARMACEUTICALS IND LTD, Plot 3, Billings Way, Oregun

## 8. NUMBER(S) IN THE NATIONAL REGISTER OF FINISHED PHARMACEUTICAL PRODUCTS

B4-9668

## 9. DATE OF FIRST AUTHORISATION/RENEWALOF THE AUTHORISATION

28.02.2019

## 10. DATE OF REVISION OF THE TEXT

July 2023