SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT
DUPATIN 0.1% Eye Drops, Solution

2. QUALITATIVE AND QUANTITATIVE COMPOSITION
Each ml solution contains:
Active substance(s):
Olopatadine hydrochloride 1.11 mg
(Equivalent to 1.0 mg olopatadine)
Excipient(s) with known effect:
Benzalkonium chloride 0.1 mg
For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM
Eye drops, solution.
Clear, colorless, particle-free solution.

4. CLINICAL PARTICULARS
4.1 Therapeutic indications
Indicated for the treatment of the signs and symptoms of seasonal allergic conjunctivitis.

4.2 Posology and method of administration
Posology/frequency and duration of administration
The dose is 1 drop of DUPATIN in the conjunctival sac of the affected eye(s) 2 times a day (every 8 hours). Treatment may be maintained for up to 4 months, if considered necessary.

Method of administration
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. The bottle should be kept tightly closed when not in use.

In case of concomitant therapy with other topical ocular medicines, an interval of 5-10 minutes should be allowed between successive applications.

Additional information on special populations
Renal/Hepatic impairment
Olopatadine in the form of eye drops has not been studied in patients with renal or hepatic impairment. However, no dosage adjustment is expected to be necessary in patients with hepatic or renal impairment (see section 5.2).

Pediatric population
DUPATIN may be used in pediatric patients (3 years of age and older) at the same posology as in adults. The safety and efficacy in children aged under 3 years has not been established.

Geriatric population
No dosage alteration in elderly patients is necessary.

4.3 Contraindications
Contraindicated in case of hypersensitivity to olopatadine or any of the excipients of the drug.

4.4 Special warning and precautions for use
FOR TOPICAL USE ONLY. NOT FOR INJECTION OR ORAL INGESTION.

DUPATIN is an antiallergic/antihistaminic agent and, although applied topically, is absorbed systemically. If signs of serious reactions or hypersensitivity occur, discontinue the use of this treatment.

Benzalkonium chloride, which is commonly used as a preservative in ophthalmic products, has been reported to cause punctate keratopathy and/or toxic ulcerative keratopathy. Because DUPATIN contains benzalkonium chloride, close monitoring is required with frequent or prolonged use in dry eye patients, or in conditions where the cornea is compromised.

Contact Lenses:
DUPATIN may cause eye irritation due to its benzalkonium chloride content. Contact with soft contact lenses should be avoided. Patients should be instructed to remove their lenses prior to instillation and wait at least 15 minutes before reinserting them. Benzalkonium is known to discolor soft contact lenses. (See "GUIDELINE ON EXCIPIENTS IN THE LABELLING AND PACKAGE LEAFLET OF MEDICINAL PRODUCTS FOR HUMAN USE").

4.5 Interaction with other medicinal products and other forms of interaction
No clinical trials on DUPATIN have been investigated. No interaction studies have been conducted.

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.

Additional information on special populations
Pediatric population
No interaction studies on pediatric population have been implemented.

4.6 Fertility, pregnancy and lactation
General recommendation
Pregnancy category is C.

Women of childbearing potential/Contraception
Women of childbearing potential must use efficient contraceptive methods during treatment.

Pregnancy
There are no adequate data from the use of olopatadine in pregnant women. Animal studies are insufficient with respect to effects on pregnancy / and-or / embryonal/fetal development / and-or / parturition / and-or / postnatal development (see section 5.3). The potential risk for humans is unknown.

DUPATIN should not be used during pregnancy unless it is absolutely necessary. It should only be used if the potential benefit during pregnancy outweighs the potential fetal risk.

Caution is advised when prescribing this product to pregnant patients.

Breast-feeding
DUPATIN must not be used during breastfeeding.

Olopatadine has been detected in the milk of nursing rats following oral administration. 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. It is not known whether topical ocular administration could result in sufficient systemic absorption to produce detectable quantities in human breast milk.

It is not known whether olopatadine is excreted in human breast milk. Excretion of olopatadine in milk has not been investigated in animals. When deciding whether to stop breastfeeding or whether to stop/avoid treatment with DUPATIN, the benefit of breastfeeding for the child and the benefit of DUPATIN treatment for the nursing mother should be taken into account.

Reproductive ability / Fertility
No studies have been carried out to evaluate the effect of topical ocular administration of olopatadine on human fertility.

4.7 Effects on ability to drive and use machines
Olopatadine is a non-sedative antihistamine. 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
In clinical studies involving 1680 patients, olopatadine was administered 1 to 4 times daily in both eyes for up to 4 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; 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%.

The following adverse reactions were assessed as administration-related and classified according to the following rule: 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.

Infections and infestations
Uncommon : Rhinitis

Immune system disorders
Not known : Hypersensitivity, swelling face

Nervous system disorders
Common : Headache, dysgeusia
Uncommon : Dizziness, hypoesthesia
Not known : Somnolence

Eye disorders
Common : Eye pain, eye irritation, dry eye, abnormal sensation in eyes
Uncommon : Corneal abrasion, 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, eyelid pruritus, eyelid edema, eyelid disorder, ocular hyperemia
Not known : Corneal edema, eye edema, eye swelling, conjunctivitis, mydriasis, visual disturbance, eyelid margin crusting

Respiratory, thoracic, and mediastinal disorders
Common : Nasal dryness
Not known : Shortness of breath (dyspnea), 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
Reporting suspected adverse reactions after authorization 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 national reporting system.

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 DUPATIN 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.

Treatment
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; decongestants and antiallergics; other antiallergics.
ATC code: S01GX09

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 DUPATIN 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

General 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.

Distribution
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 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. Dose adjustment is not expected to be necessary with hepatic impairment.

Biotransformation
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.

Elimination
From oral pharmacokinetic studies, the half-life of olopatadine in plasma was approximately 8 to 12 hours, and elimination was predominantly through renal excretion. Olopatadine is eliminated essentially unchanged in the urine. Liver metabolism is a minor route of elimination.

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.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients
Benzalkonium chloride
Sodium chloride
Dibasic sodium phosphate dodecahydrate
Hydrochloric acid (for pH adjustment)
Sodium hydroxide (for pH adjustment)
Water for injections

6.2 Incompatibilities
There is no evidence that DUPATIN is incompatible with any medication or substance.

6.3 Shelf life
24 months.

6.4 Special precautions for storage
Store at room temperature below 25°C.
Once the bottle is opened, the medicine should be used within 28 days.

6.5 Nature and contents of container
An opaque white low-density polyethylene (LDPE) dropper bottle containing 5 mL solution, closed with a white screw cap, is presented along with a package leaflet in a cardboard box.

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 AUTHORIZATION HOLDER

DEVA Holding A.Ş.
Halkalı Merkez Mah. Basın Ekspres Cad. No:1
34303 Küçükçekmece – İSTANBUL / TÜRKİYE

8. MARKETING AUTHORIZATION NUMBER

2015/871

9. DATE OF FIRST AUTHORIZATION/RENEWAL OF THE AUTHORIZATION

Date of first authorization : 13.11.2015
Date of renewal :

10. DATE OF REVISION OF THE TEXT

12.02.2024