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BONDPATADINE

Olopatadine Hydrochloride Ophthalmic solution 0.1 % w/v

Summary of Product Characteristics

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1 NAME OF THE MEDICINAL PRODUCT

Olopatadine Hydrochloride Ophthalmic Solution 0.1 % w/v

2 QUALITATIVE AND QUANTITATIVE COMPOSITIONS

Composition:
Each ml contains
Olopatadine Hydrochloride
Eq. to Olopatadine……... 1 mg
Benzalkonium Chloride BP…… 0.01 % w/v
Sterile Aqeous Vehicle…… Q.S.

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORMS

Eye Drops

4 CLINICAL PARTICULARS

4.1 Therapeutic Indication.

Treatment of ocular signs and symptoms of seasonal allergic conjunctivitis.

4.2 Posology and method of administration.

The dose is one drop of BONDPATADINE 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.

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 to ten minutes should be allowed between successive applications.

Use in elderly

No dosage adjustment in elderly patients is necessary.

Paediatric patients

BONDPATADINE may be used in paediatric patients (three years of age and older) at the same dose as in adults.

Use in hepatic and renal impairment

Olopatadine in the form of eye drops (BONDPATADINE) 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.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients.

4.4 Special warnings and precaution for use.

BONDPATADINE 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, which is commonly used as a preservative in ophthalmic products, has been reported to cause punctate keratopathy and/or toxic ulcerative keratopathy. Since BONDPATADINE 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

Patients should be instructed to wait 10-15 minutes after instillation of BONDPATADINE before inserting contact lenses. BONDPATADINE should not be administered while wearing contact lenses.

4.5 Interaction with other medicinal product and other forms of interaction.

No interaction studies 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

For olopatadine, no clinical data on exposed pregnancies are available.

Animal studies do not indicate direct or indirect harmful effects with respect to pregnancy, embryonal/foetal development, parturition or postnatal development.

Caution should be exercised when prescribing to pregnant women.

Breast-feeding mothers

BONDPATADINE is not recommended for breast-feeding mothers.

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 administration to humans could result in sufficient systemic absorption to produce detectable quantities in human breast milk.

4.7 Effect on the ability to drive and use machine.

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 effect.

In clinical studies involving 1680 patients, BONDPATADINE 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 undesirable effects associated with the use of BONDPATADINE; however, only 1.6% of patients discontinued from the clinical studies due to these undesirable effects. No serious ophthalmic or systemic undesirable effects related to BONDPATADINE were reported in clinical studies. The most frequent treatment-related undesirable effect was eye pain, reported at an overall incidence of 0.7%.

The following undesirable effects were assessed to be treatment-related 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), or very rare (≤1/10,000). Within each frequency grouping, undesirable effects are presented in decreasing order of seriousness.

Infections and infestations

Uncommon: rhinitis

Nervous system disorders

Common: headache, dysgeusia

Uncommon: dizziness, hypoaesthesia

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, eyelids pruritus, erythema of eyelid, eyelid oedema, eyelid disorder, conjunctival hyperaemia, ocular hyperaemia

Respiratory, thoracic, and mediastinal disorders

Common: nasal dryness

Skin and subcutaneous tissue disorders

Uncommon: dermatitis contact, skin burning sensation, dry skin

General disorders and administration site conditions

Common: fatigue

Not known (cannot be estimated from the available data):

Adverse reactions identified from post-marketing experience that have not been reported previously in clinical trials with BONDPATADINE include those detailed below. Unlike data from clinical trials, due to the nature of post-marketing surveillance, the frequency at which these events occur is not known and cannot be estimated based upon the available data.

Ocular: corneal oedema, conjunctivitis, eye oedema, eye swelling, mydriasis, visual disturbance, eyelid margin crusting

Systemic: hypersensitivity, dyspnea, somnolence, swelling face, dermatitis, erythema, nausea, vomiting, sinusitis, asthenia, malaise

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 BONDPATADINE 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 BONDPATADINE 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.

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. 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 BONDPATADINE 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.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Benzalkonium Chloride *BP*

Polyvinyl Alcohol	*BP*
Sodium Chloride	*USP*
Citric Acid (Monohydrate)	*BP*
Sodium Citrate	*BP*
Sodium Hydroxide	*BP*
Water for Injection	*BP*

6.2 Incompatibilities
unknown

6.3 Shelf-life

24 months

28 days after opening the container.

6.4 Special precautions for storage
Do not store above 25ºC. Store in a dry place.

6.5 Nature and composition of immediate packaging

A clear, colourless solution filled in 5 ml HDPE container pluged with dropper attachment plug, sealed with screw cap closure.

6.6 Special precautions for the disposal of unused veterinary medicinal products or waste materials
None.

7 MARKETING AUTHORISATION HOLDER

8 MARKETING AUTHORISATION NUMBER(S)

9 AUTHORISATION/RENEWAL OF THE AUTHORISATION

10 DATE OF REVISION OF THE TEXT

20th Feb 2012