APOTEX
ADVANCING GENERICS

PRINTED PACKAGING MATERIAL MASTER

Material Code: TBD	ECL Common Text#: N/A	Description: INS USA OLOPATADINE OP/SLN 0.2%2.5ML	
Material Code REF: N/A			
Previous Code: 275523	QA Rev#: 0	C of A: PKGP-CA-INSERT-RH	Change Control #: N/A
Pantone Colours: BLACK DIELINE			
Dimensions/Dieline#: Flat: 133 mm x 200 mm (5,24" x 7,87") Folded: 133 mm x 26 mm (5,24" x 1,02")		Minimum Font Size: 6 PT	Prepared by: DEEPAK K Date: OCT 26, 2016

NOTE: Pharmacode is vendor specific information and may vary.

133 mm

26 mm

200 mm

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HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use Olopatadine Hydrochloride Ophthalmic Solution USP safely and effectively. See full prescribing information for Olopatadine Hydrochloride Ophthalmic Solution USP.

Olopatadine Hydrochloride Ophthalmic Solution USP, 0.2%

Initial U.S. Approval: 1996

---------- INDICATIONS AND USAGE ----------

Olopatadine hydrochloride ophthalmic solution, 0.2% is a mast cell stabilizer indicated for the treatment of ocular itching associated with allergic conjunctivitis. (1)

----------DOSAGE AND ADMINISTRATION ----------

The recommended dose is one drop in each affected eye once a day. (2)

---------- DOSAGE FORMS AND STRENGTHS----------

Ophthalmic solution 0.2%: each ml contains 2.22 mg of olopatadine hydrochloride. (3)

----------WARNINGS AND PRECAUTIONS----------

For topical ocular use only. Not for injection or oral use. (5.1)

---------- ADVERSE REACTIONS ----------

Symptoms similar to cold syndrome and pharyngitis were reported at an incidence of approximately 10%. (6)

To report SUSPECTED ADVERSE REACTIONS, contact Apotex Corp. at 1-800-667-4708 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling.

Revised: 10/2016

FULL PRESCRIBING INFORMATION:

CONTENTS*

*Sections or subsections omitted from the full prescribing information are not listed

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

Olopatadine hydrochloride ophthalmic solution, 0.2% is indicated for the treatment of ocular itching associated with allergic conjunctivitis.

2 DOSAGE AND ADMINISTRATION

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3 DOSAGE FORMS AND STRENGTHS

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4 CONTRAINDICATIONS

None.

5 WARNINGS AND PRECAUTIONS

5.1 For topical ocular use only. Not for injection or oral use.

5.2 Contamination of Tip and Solution

As with any eye drop, to prevent contaminating the dropper tip and solution, care should be taken not to touch the eyelids or surrounding areas with the dropper tip of the bottle. Keep bottle tightly closed when not in use.

5.3 Contact Lens Use

Patients should be advised not to wear a contact lens if their eye is red.

Olopatadine hydrochloride ophthalmic solution, 0.2% should not be used to treat contact lens related irritation.

The preservative in olopatadine hydrochloride ophthalmic solution, 0.2%, benzalkonium chloride, may be absorbed by soft contact lenses. Patients who wear soft contact lenses and **whose eyes are not red**, should be instructed to wait at least ten minutes after instilling olopatadine hydrochloride ophthalmic solution, 0.2% before they insert their contact lenses.

6 ADVERSE REACTIONS

Symptoms similar to cold syndrome and pharyngitis were reported at an incidence of approximately 10%.

The following adverse experiences have been reported in 5% or less of patients:

Ocular: blurred vision, burning or stinging, conjunctivitis, dry eye, foreign body sensation, hyperemia, hypersensitivity, keratitis, lid edema, pain and ocular pruritus.

Non-ocular: asthenia, back pain, flu syndrome, headache, increased cough, infection, nausea, rhinitis, sinusitis and taste perversion.

Some of these events were similar to the underlying disease being studied.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Teratogenic effects: Pregnancy Category C

Olopatadine was found not to be teratogenic in rats and rabbits. However, rats treated at 600 mg/kg/day, or 150,000 times the MROHD and rabbits treated at 400 mg/kg/day, or approximately 100,000 times the MROHD, during organogenesis showed a decrease in live fetuses. In addition, rats treated with 600 mg/kg/day of olopatadine during organogenesis showed a decrease in fetal weight.

133 mm

26 mm

200 mm

Further, rats treated with 600 mg/kg/day of olopatadine during late gestation through the lactation period showed a decrease in neonatal survival and body weight. There are, however, no adequate and well-controlled studies in pregnant women. Because animal studies are not always predictive of human responses, this drug should be used in pregnant women only if the potential benefit to the mother justifies the potential risk to the embryo or fetus.

8.3 Nursing Mothers

Olopatadine has been identified in the milk of nursing rats following oral administration. It is not known whether topical ocular administration could result in sufficient systemic absorption to produce detectable quantities in the human breast milk. Nevertheless, caution should be exercised when olopatadine hydrochloride ophthalmic solution, 0.2% is administered to a nursing mother.

8.4 Pediatric Use

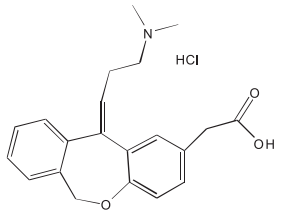
Safety and effectiveness in pediatric patients below the age of 2 years have not been established.

8.5 Geriatric Use

No overall differences in safety and effectiveness have been observed between elderly and younger patients.

11 DESCRIPTION

Olopatadine Hydrochloride Ophthalmic Solution USP, 0.2% is a sterile ophthalmic solution containing olopatadine for topical administration to the eyes. Olopatadine hydrochloride is a white to off-white, crystalline, water-soluble powder with a molecular weight of 373.88 and a molecular formula of $C_{21}H_{23}NO_3 \bullet HCl$. The chemical structure is presented below:



Chemical Name: 11-[(Z)-3-(Dimethylamino) propylidene]-6-11dihydrodibenz[b,e] oxepin-2-acetic acid, hydrochloride

Each mL of Olopatadine Hydrochloride Ophthalmic Solution USP, 0.2% contains: **Active:** 2.22 mg olopatadine hydrochloride equivalent to 2 mg olopatadine. **Inactives:** povidone; sodium chloride; sodium phosphate dibasic (anhydrous); edetate disodium dihydrate; benzalkonium chloride 0.01% **(preservative)**; hydrochloric acid/ sodium hydroxide (to adjust pH); and water for injection.

It has a pH of approximately 5.0 - 8.0 and an osmolality range of 260 - 320 mOsm/kg.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Olopatadine is a mast cell stabilizer and a histamine H_1 antagonist. Decreased chemotaxis and inhibition of eosinophil activation has also been demonstrated.

12.3 Pharmacokinetics

Systemic bioavailability data upon topical ocular administration of olopatadine hydrochloride ophthalmic solution, 0.2% are not available. Following topical ocular administration of olopatadine 0.15% ophthalmic solution in man, olopatadine was shown to have a low systemic exposure. Two studies in normal volunteers (totaling 24 subjects) dosed bilaterally with olopatadine 0.15% ophthalmic solution once every 12 hours for 2 weeks demonstrated plasma concentrations to be generally below the quantitation limit of the assay (< 0.5 ng/mL). Samples in which olopatadine was quantifiable were typically found within 2 hours of dosing and ranged from 0.5 to 1.3 ng/mL. The elimination half-life in plasma following oral dosing was 8 to 12 hours, and elimination was predominantly through renal excretion. Approximately 60 - 70% of the dose was recovered in the urine as parent drug. Two metabolites, the mono-desmethyl and the N-oxide, were detected at low concentrations in the urine.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Olopatadine administered orally was not carcinogenic in mice and rats in doses up to 500 mg/kg/day and 200 mg/kg/day, respectively. Based on a 40 µL drop size and a 50 kg person, these doses were approximately 150,000 and 50,000 times higher than the maximum recommended ocular human dose (MROHD). No mutagenic potential was observed when olopatadine was tested in an *in vitro* bacterial reverse mutation (Ames) test, an *in vitro* mammalian chromosome aberration assay or an *in vivo* mouse micronucleus test. Olopatadine administered to male and female rats at oral doses of approximately 100,000 times MROHD level resulted in a slight decrease in the fertility index and reduced implantation rate; no effects on reproductive function were observed at doses of approximately 15,000 times the MROHD level.

14 CLINICAL STUDIES

Results from clinical studies of up to 12 weeks duration demonstrate that olopatadine ophthalmic solution, 0.2% when dosed once a day is effective in the treatment of ocular itching associated with allergic conjunctivitis.

16 HOW SUPPLIED/STORAGE AND HANDLING

Olopatadine Hydrochloride Ophthalmic Solution USP, 0.2% is supplied in a white opaque ophthalmic bottle with a white translucent ophthalmic dropper and a white opaque plastic cap in the following size:

2.5 mL fill in 5 mL bottle: NDC 60505-0586-4

Storage

Store at 2° - 25°C (36° - 77°F). Keep bottle tightly closed when not in use.

Keep out of reach of children.

17 PATIENT COUNSELING INFORMATION

17.1 Topical Ophthalmic Use Only

For topical ophthalmic administration only.

17.2 Sterility of Dropper Tip

Patients should be advised to not touch dropper tip to any surface, as this may contaminate the contents.

17.3 Concomitant Use of Contact Lenses

Patients should be advised not to wear a contact lens if their eyes are red. Patients should be advised that olopatadine hydrochloride ophthalmic solution, 0.2% should not be used to treat contact lens-related irritation. Patients should also be advised to remove contact lenses prior to instillation of olopatadine hydrochloride ophthalmic solution, 0.2%. The preservative in olopatadine hydrochloride ophthalmic solution, 0.2%, benzalkonium chloride, may be absorbed by soft contact lenses. Lenses may be reinserted following administration of olopatadine hydrochloride ophthalmic solution, 0.2%.

Manufactured by:	Manufactured for:
Apotex Inc.	Apotex Corp.
Toronto, Ontario	Weston, FL
Canada M9L 1T9	33326
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