CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

206276Orig1s000

LABELING

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use PAZEO safely and effectively. See full prescribing information for PAZEO.

PAZEO (olopatadine hydrochloride ophthalmic solution) 0.7%
For topical ophthalmic administration.
Initial U.S. Approval: 1996

----------INDICATIONS AND USAGE----------
PAZEO 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: 7.76 mg of olopatadine hydrochloride in one mL of solution (0.7%) in a four mL bottle. (3)

----------CONTRAINDICATIONS----------
None.

----------WARNINGS AND PRECAUTIONS----------
Contamination of Tip and Solution. To prevent contaminating the dropper tip and solution, do not touch the eyelids or surrounding areas with the dropper tip of the bottle. (5.1)

----------ADVERSE REACTIONS----------
The most common adverse reactions (2-5%) were blurred vision, superficial punctate keratitis, dry eye, abnormal sensation in eye, and dysgeusia. (6)

To report SUSPECTED ADVERSE REACTIONS, contact Alcon Laboratories, Inc. at 1-800-757-9195 or FDA at 1-800-FDA-1088 or www fda.gov/medwatch.

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

Revised: 1/2015

FULL PRESCRIBING INFORMATION: CONTENTS*

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

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE
PAZEO is indicated for the treatment of ocular itching associated with allergic conjunctivitis.

2 DOSAGE AND ADMINISTRATION
The recommended dosage of PAZEO is to instill one drop in each affected eye once a day.

3 DOSAGE FORMS AND STRENGTHS
Ophthalmic solution: 7.76 mg of olopatadine hydrochloride in one mL solution (0.7%) in a 4 mL bottle.

4 CONTRAINDICATIONS
None.

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

5.2 Contact Lens Use
Patients should not wear a contact lens if their eye is red.

The preservative in PAZEO solution, 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 five minutes after instilling PAZEO before they insert their contact lenses.

6 ADVERSE REACTIONS
6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

In a randomized, double-masked, vehicle-controlled trial, patients at risk for developing allergic conjunctivitis received one drop of either PAZEO (N=330) or vehicle (N=169) in both eyes for 6 weeks. The mean age of the population was 32 years (range 2 to 74 years). Thirty-five percent were male. Fifty-three percent had brown iris color and 23% had blue iris color. The most commonly reported adverse reactions occurred in 2-5% of patients treated with either PAZEO or vehicle. These events were blurred vision, dry eye, superficial punctate keratitis, dysgeusia and abnormal sensation in eye.

8 USE IN SPECIFIC POPULATIONS
8.1 Pregnancy

Risk Summary
There are no adequate or well-controlled studies with PAZEO in pregnant women. Olopatadine caused maternal toxicity and embryofetal toxicity in rats at levels 1,080 to 14,400 times the maximum recommended human ophthalmic dose (MRHOD). There was no toxicity in rat offspring at exposures estimated to be 45 to 150 times that at MRHOD. Olopatadine should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Animal Data
In a rabbit embryofetal study, rabbits treated orally at 400 mg/kg/day during organogenesis showed a decrease in live fetuses. This dose is 14,400 times the MRHOD, on a mg/m^2 basis.

An oral dose of 600 mg/kg/day olopatadine (10,800 times the MRHOD) was shown to be maternally toxic in rats, producing death and reduced maternal body weight gain. When administered to rats throughout organogenesis, olopatadine produced cleft palate at 60 mg/kg/day (1080 times the MRHOD) and decreased embryofetal viability and reduced fetal weight in rats at 600 mg/kg/day. When administered to rats during late gestation and throughout the lactation period, olopatadine produced decreased neonatal survival at 60 mg/kg/day and reduced body weight gain in offspring at 4 mg/kg/day. A dose of 2 mg/kg/day olopatadine produced no toxicity in rat offspring. An oral dose of 1 mg/kg olopatadine in rats resulted in a range of systemic plasma area under the curve (AUC) levels that were 45 to 150 times higher than the observed human exposure [9.7 ng·hr/mL] following administration of the recommended human ophthalmic dose.

8.3 Nursing Mothers
Olopatadine has been identified in the milk of nursing rats following oral administration. Oral administration of olopatadine doses at or above 4 mg/kg/day throughout the lactation period produced decreased body weight gain in rat offspring; a dose of 2 mg/kg/day olopatadine produced no toxicity. An oral dose of 1 mg/kg olopatadine in rats resulted in a range of systemic plasma area under the curve (AUC) levels that were 45 to 150 times higher than the observed human exposure [9.7 ng·hr/mL] following administration of the recommended human ophthalmic dose. 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 PAZEO is administered to a nursing mother.

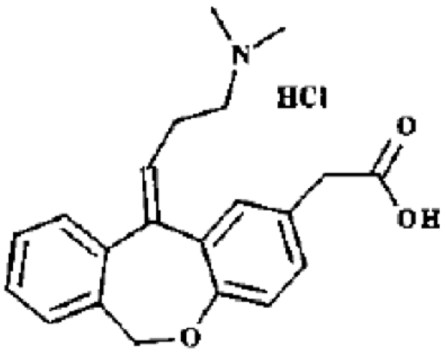
8.4 Pediatric Use
The safety and effectiveness of PAZEO have been established in pediatric patients two years of age and older. Use of PAZEO in these pediatric patients is supported by evidence from adequate and well-controlled studies of PAZEO in adults and an adequate and well controlled study evaluating the safety of PAZEO in pediatric and adult patients.

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

11 DESCRIPTION

PAZEO is a sterile ophthalmic solution containing olopatadine, which is a mast cell stabilizer, for topical administration to the eyes. Olopatadine hydrochloride is a white, crystalline, water-soluble powder with a molecular weight of 373.88 and a molecular formula of $C_{21}H_{23}NO_3$•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 PAZEO solution contains an active ingredient [7.76 mg of olopatadine hydrochloride (7 mg olopatadine)] and the following inactive ingredients: povidone; hydroxypropyl-gamma-cyclodextrin; polyethylene glycol 400; hydroxypropyl methylcellulose; boric acid; mannitol; benzalkonium chloride 0.015% (preservative); hydrochloric acid/sodium hydroxide (to adjust pH); and purified water.

PAZEO solution has a pH of approximately 7.2 and an osmolality of approximately 300 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

In healthy subjects, topical ocular dosing of 1 drop of PAZEO once daily for 7 days into both eyes resulted in mean ± SD (range) steady state plasma olopatadine C_{max} and AUC_{0-12} of 1.6 ± 0.9 ng/mL (0.6 to 4.5 ng/mL) and 9.7 ± 4.4 ng*h/mL (3.7 to 21.2 ng*h/mL), respectively. The olopatadine C_{max} and AUC_{0-12} after the first dose were similar to those measured on day 7 in these subjects, suggesting that there was no systemic accumulation of olopatadine after repeated topical ocular dosing with PAZEO. The median (range) time to achieve peak olopatadine concentrations (T_{max}) was 2.0 hours (0.25 to 4 hours). The mean ± SD (range) elimination half-life of olopatadine was 3.4 ± 1.2 hours (2 to 8 hours). N-oxide olopatadine (M3) was

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