**ITCHY ALLERGY EYES?**

Use this short questionnaire as a conversation starter for you and your doctor to see if a prescription eyedrop may be right for you.

<table>
<thead>
<tr>
<th>Background</th>
</tr>
</thead>
<tbody>
<tr>
<td>Is there a history of allergies in your family, especially eye allergies?</td>
</tr>
<tr>
<td>Do your allergies mainly affect your eyes, nose, or both?</td>
</tr>
<tr>
<td>How long have you had them?</td>
</tr>
<tr>
<td>Do they occur only at certain times of the year?</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Do your allergies cause your eyes to itch?</td>
</tr>
<tr>
<td>If yes, please explain:</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Location</th>
</tr>
</thead>
<tbody>
<tr>
<td>Where does your eye allergy itch usually occur?</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Timing</th>
</tr>
</thead>
<tbody>
<tr>
<td>When does your eye allergy itch bother you?</td>
</tr>
<tr>
<td>Please explain:</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Treatments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Do you use medication for your eye allergies?</td>
</tr>
<tr>
<td>If yes, is it prescription or over-the-counter?</td>
</tr>
<tr>
<td>What product(s) do you use?</td>
</tr>
</tbody>
</table>

**INDICATION AND DOSING**

PAZEO® Solution is a prescription medicine used to treat eye itching associated with eye allergies. The recommended dosage is to put one drop in each affected eye once a day.

**IMPORTANT SAFETY INFORMATION**

Do not touch dropper tip to eyelids or surrounding areas. Touching may contaminate the dropper tip and PAZEO® Solution. Keep the bottle tightly closed when it is not in use.

Do not wear contact lenses if your eyes are red. PAZEO® Solution should not be used to treat contact lens-related irritation. Always remove your contact lenses before administering PAZEO® Solution.
IMPORTANT SAFETY INFORMATION (cont’d)

PAZEO® Solution contains the preservative benzalkonium chloride (BAK). BAK may be absorbed by soft contact lenses. If you wear soft contacts, you should wait at least five minutes after administering PAZEO® Solution before inserting your contacts.

In a clinical study with PAZEO® Solution, the most common side effects occurred in approximately 2% to 5% of patients. These side effects were blurred vision, dry eye, superficial punctate keratitis (a type of inflammation on the front part of the eye), impaired taste, and abnormal sensation in the eye.

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch, or call 1-800-FDA-1088.

For additional information on PAZEO® Solution, please refer to the accompanying full Prescribing Information.

REFERENCE: 1. PAZEO® Solution Package Insert.
Pazeo (olopatadine hydrochloride ophthalmic solution) 0.7%

For topical ophthalmic administration.

Initial U.S. Approval: 1996

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 is a mast cell stabilizer indicated for the treatment of ocular itching associated with allergic conjunctivitis. (1).

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

Ophthalmic solution: 7.76 mg of olopatadine hydrochloride in one mL solution (0.7%) in a four mL bottle. (3)

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

HIGHLIGHTS OF PRESCRIBING INFORMATION

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FULL PRESCRIBING INFORMATION: CONTENTS*

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2 DOSAGE AND ADMINISTRATION
3 DOSAGE FORMS AND STRENGTHS
4 CONTRAINDICATIONS
5 WARNINGS AND PRECAUTIONS
6 ADVERSE REACTIONS
7 USE IN SPECIFIC POPULATIONS
8 USE IN SPECIFIC POPULATIONS
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13 NONCLINICAL TOXICOLOGY
14 HOW SUPPLIED/STORAGE AND HANDLING
15 ADVERSE REACTIONS

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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_{22}N_2O_3·HCl.

The chemical structure is presented below:

![Chemical Structure]

Chemical Name: 11-[(Z)-3(dimethylamino) propylidene]-6,11-dihydro dibenz[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; hydroxpropyl-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 H1 antagonist. Decreased chemotaxis and inhibition of eosinophil activation has also been demonstrated.

12.2 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_{ssmax} and AUC_{ss} 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_{ssmax} and AUC_{ss} 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_{ss}) was 2.0 hours (0.25 to 4.0 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 detected during the first 4 hours after topical ocular dosing of PAZEO in approximately half of the subjects in less than 10% of the total plasma samples collected, at concentrations not exceeding 0.121 ng/mL on day 1 and 0.174 ng/mL on day 7. None of the plasma samples from these subjects had mono-desmethyl olopatadine (M1) concentrations that were above the lower limit of quantitation (0.05 ng/mL) of the PK assay.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Carcinogenicity

Olopatadine administered orally was not carcinogenic in mice and rats in doses up to 1500 mg/kg/day (approximately 900 times the MRHOD) on a mg/m² basis.

Mutagenesis

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.

Impairment of fertility

Olopatadine administered at an oral dose of 400 mg/kg/day (approximately 7,200 times the MRHOD) produced toxicity in male and female rats, and resulted in a decrease in the fertility index and reduced implantation rate. No effects on reproductive function were observed at 150 mg/kg/day (approximately 900 times the MRHOD).

14 CLINICAL STUDIES

The efficacy of PAZEO was established in two randomized, double-masked, placebo-controlled, conjunctival allergen challenge (CAC) clinical studies in patients with a history of allergic conjunctivitis (Studies 1 and 2).

In Study 1, patients were randomized to receive one of the following study treatments: PAZEO, PATADAY, or vehicle ophthalmic solutions. In Study 2, patients were randomized to receive one of the following study treatments: PAZEO, PATADAY, PATANOL, or vehicle ophthalmic solutions. Patients were evaluated with an ocular itching severity score ranging from 0 (no itching) to 4 (incapacitating itch) at several time points after CAC administration. Table 1 displays the mean ocular itching severity scores after ocular administration of a specific antigen using the CAC model in Studies 1 and 2, respectively. A one unit difference compared to vehicle is considered a clinically meaningful change in the ocular itching severity score.

PAZEO demonstrated statistically significantly improved relief of ocular itching compared to vehicle at 30-34 minutes, 16 hours, and 24 hours after study treatment. PATADAY demonstrated statistically significantly improved relief of ocular itching compared to PATADAY at 24 hours after study treatment, but not at 30-34 minutes after study treatment.

Table 1. Itching Scores by Treatment Group and Treatment Difference* in Mean Itching

<table>
<thead>
<tr>
<th>Time Point</th>
<th>PAZEO (Olopatadine, 0.7%)</th>
<th>PATADAY (Olopatadine, 0.2%)</th>
<th>Vehicle</th>
<th>Mean</th>
<th>Mean Difference (95% CI)</th>
<th>Mean Difference (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Onset</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3 mins</td>
<td>0.36</td>
<td>0.39</td>
<td>1.90</td>
<td>-0.02 (-0.31, 0.26)</td>
<td>-1.54 (-1.82, -1.25)</td>
<td></td>
</tr>
<tr>
<td>5 mins</td>
<td>0.53</td>
<td>0.61</td>
<td>2.06</td>
<td>-0.08 (-0.39, 0.22)</td>
<td>-1.53 (-1.84, -1.22)</td>
<td></td>
</tr>
<tr>
<td>7 mins</td>
<td>0.48</td>
<td>0.61</td>
<td>1.97</td>
<td>-0.13 (-0.44, 0.17)</td>
<td>-1.49 (-1.89, -1.18)</td>
<td></td>
</tr>
<tr>
<td>16h</td>
<td>0.70</td>
<td>0.87</td>
<td>2.20</td>
<td>-0.17 (-0.44, 0.11)</td>
<td>-1.50 (-1.77, -1.23)</td>
<td></td>
</tr>
<tr>
<td>24h</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3 mins</td>
<td>0.79</td>
<td>1.04</td>
<td>2.27</td>
<td>-0.24 (-0.55, 0.07)</td>
<td>-1.48 (-1.79, -1.16)</td>
<td></td>
</tr>
<tr>
<td>5 mins</td>
<td>0.75</td>
<td>0.98</td>
<td>2.13</td>
<td>-0.23 (-0.54, 0.08)</td>
<td>-1.38 (-1.69, -1.07)</td>
<td></td>
</tr>
<tr>
<td>7 mins</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>24h</td>
<td>0.93</td>
<td>1.41</td>
<td>2.54</td>
<td>-0.48 (-0.76, -0.20)</td>
<td>-1.61 (-1.88, -1.33)</td>
<td></td>
</tr>
<tr>
<td>5 mins</td>
<td>1.10</td>
<td>1.52</td>
<td>2.05</td>
<td>-0.42 (-0.72, -0.12)</td>
<td>-1.51 (-1.81, -1.21)</td>
<td></td>
</tr>
<tr>
<td>7 mins</td>
<td>1.09</td>
<td>1.50</td>
<td>2.50</td>
<td>-0.51 (-0.72, -0.10)</td>
<td>-1.41 (-1.72, -1.11)</td>
<td></td>
</tr>
</tbody>
</table>

* Mean score estimates, treatment differences and corresponding 95% confidence intervals (CI) were based on analysis of repeated measures using a mixed model with itching scores from each eye (left or right) as the dependent variable and fixed effect terms for investigator, treatment, eye-type (left or right), time, and treatment-by-time interaction; The ocular itching score range is 0-4, where 0 is none and 4 is incapacitating itch.

16 HOW SUPPLIED/STORAGE AND HANDLING

PAZEO (olopatadine hydrochloride ophthalmic solution) 0.7% is supplied in a white, oval, low density polyethylene DROP-TAINER® dispenser with a natural low density polyethylene cap. Tapner evidence is provided with a shrink band around the closure and neck area of the package. PAZEO is supplied in a 4 mL bottle that contains 2.5 mL of olopatadine hydrochloride ophthalmic solution [7.76 mg of olopatadine hydrochloride in one mL of solution (0.7%)].

NDC 0065-4273-25

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

17 PATIENT COUNSELING INFORMATION

- Risk of Contamination: Advise patients not to touch dropper tip to eyelids or surrounding areas, as this may contaminate the dropper tip and ophthalmic solution.

- Concomitant Use of Contact Lenses: Advise patients not to wear contact lenses if their eyes are red. Advise patients that PAZEO should not be used to treat contact lens-related irritation. Advise patients to remove contact lenses prior to instillation of PAZEO.

The preservative in PAZEO solution, benzalkonium chloride, may be absorbed by soft contact lenses. Lenses may be reinserted 5 minutes following administration of PAZEO.

Patents: 8,791,154

*Trademark of Novartis