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Perception and Quality of Life Associated With the Use of Olopatadine 0.2% (Pataday™) in Patients With Active Allergic Conjunctivitis

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ABSTRACT

This 28-d, open-label, multicenter, single-arm clinical study was designed to evaluate perceptions of olopatadine 0.2% in patients with active ocular allergic signs and symptoms. The study enrolled 330 patients, 5 to 94 y of age, who had previously used olopatadine 0.1% for active allergic conjunctivitis. Most patients were white (n=230; 70.1%) and female (n=239; 72.9%). Of all enrolled patients, 328 were evaluable for analysis. Throughout the study, patients instilled 1 drop of

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olopatadine 0.2% into each eye once daily; adverse events were documented and ocular evaluations were conducted to ensure patient safety. Direct evaluations of efficacy were not performed. On days 1 and 7, patients completed the Rhinoconjunctivitis Quality of Life Questionnaire, recorded their perceptions of olopatadine 0.1% (day 1) or 0.2% (day 7), and had their ocular allergies assessed globally. On each of the first 6 d of treatment, patients also completed a telephone-based perception questionnaire. On day 28, patients returned to the study center, reported their treatment perceptions, had their ocular allergies assessed, and exited the trial. Overall, patients had a positive perception of olopatadine 0.2%. Patients were more satisfied with olopatadine 0.2% than they remembered being with olopatadine 0.1% (289 vs 257 patients; 87.6% vs 77.8%; $P<.05$). The majority of the 48 patients who wore contact lenses (n=42; 88%) believed that they could wear their contacts as desired. Significant improvement was noted in all categories of the Rhinoconjunctivitis Quality of Life Questionnaire ($P<.0001$). No unexpected safety findings were reported. Patients perceived olopatadine 0.2% to be effective and well tolerated.

Keywords: allergic conjunctivitis; olopatadine; Patanol; Pataday; quality of life; perception

INTRODUCTION

Approximately 15% to 20% of the US population suffers from allergic conjunctivitis each year.[1] Allergic conjunctivitis is caused by an allergen-induced inflammatory response in which allergens bind to specific immunoglobulin (Ig)E antibodies on mast cells in the conjunctiva, triggering the release of preformed chemical mediators such as histamine. Histamine regulates numerous actions, but with respect to allergic conjunctivitis, important functions include vasodilation, induction of increased vascular permeability, and stimulation of nociceptors. Histamine-induced modulations are therefore a primary mediator of the classic signs and symptoms of ocular allergy: itching, redness, chemosis, and tearing.[2]

Olopatadine is the active ingredient in Patanol® (olopatadine 0.1%; Alcon Laboratories, Inc., Fort Worth, Tex), a topical ocular antiallergy product that has been approved in the United States, Canada, and the European Union (as Opatanol®). It is highly selective and functions via multiple distinct mechanisms of action, including antagonism of histamine H_1 receptors[3-5] and stabilization of mast cells.[6-8] Together, these mechanisms inhibit the release of both preformed and newly synthesized mediators.

The activity of olopatadine is rapid, with an onset of 3 min,[9] and its duration of action is prolonged. Pharmacologic testing of olopatadine demonstrated that protection from allergens could be observed for up to 24 h in sensitized animals.[3] On the basis of these data, a more concentrated formulation of olopatadine was developed (olopatadine 0.2% [Pataday™]; Alcon Laboratories, Inc.) to provide patients with a more convenient once-daily dosing regimen.

Several studies have been conducted to evaluate the safety and demonstrate the efficacy of olopatadine 0.2%[10-12] when used in the treatment of patients with itching associated with allergic conjunctivitis. These studies have also shown that olopatadine 0.2% is effective for up to 24 h after instillation when dosed once daily, and that it is safe and well tolerated in adults and children 3 y of age and older. Because safe-

ty and efficacy data for olopatadine 0.2% can be found in the literature, the current study was not designed to evaluate these parameters, but rather was designed to assess patient perceptions of olopatadine 0.2% when used once daily to treat patients with allergic conjunctivitis.

To that end, patients who presented with active signs and symptoms of ocular allergy, as confirmed by the investigators (ie, patients who were in need of treatment), who had a reported or documented history of ocular allergy, and who had been treated during the current year with olopatadine 0.1% were recruited into the study and were asked to provide their impressions of olopatadine 0.2%.

PATIENTS AND METHODS

Test Article

The test article, olopatadine hydrochloride ophthalmic solution 0.2% (olopatadine 0.2%), was supplied in open-label DROP-TAINER® bottles identified by protocol number and patient number. These bottles were filled with 2.5 mL of the test article (the same volume that is contained within the currently marketed product).

Study Design

This 28-d, multicenter (10 sites), single-arm, open-label clinical trial was designed to evaluate perceptions of olopatadine 0.2%, dosed once daily, in patients with allergic conjunctivitis who were previously exposed to olopatadine 0.1%. For the duration of the study, patients were instructed to instill 1 drop of the test article into each eye every morning. Patients were seen for in-office visits on days 1, 7, and 28.

Patient perceptions of previous olopatadine 0.1% use (day 1) and current olopatadine 0.2% use (days 7 and 28) were collected on paper questionnaires during the appropriate study visit(s). In addition, on each evening from days 1 through 6, patients completed a telephone-based questionnaire regarding their experience with olopatadine 0.2%. The paper-based questionnaires asked patients up to 5 questions regarding their use of olopatadine, their satisfaction with the 0.1% or the 0.2% formulation, their ability to wear contact lenses (if applicable), the comfort of the medication, and the ease of its use. All questions were constructed in a multiple-choice format, and some items required that patients evaluate given assertions using a 5-point scale that ranged from 1 (strongly agree) to 5 (strongly disagree). The telephone-based questionnaire included only 2 questions: one queried medication usage, and the other asked patients to assess 6 individual statements using a scale that ranged from 1 (strongly agree) to 5 (strongly disagree).

In addition to the perception questionnaires, on days 1 and 7, patients completed the Rhinoconjunctivitis Quality of Life Questionnaire (RQLQ), a validated assessment that measures the physical, emotional, and social problems encountered as a result of allergic rhinoconjunctivitis.[13] Each RQLQ domain variable was rated in whole-unit increments with the use of a scale that ranged from 0 (not troubled) to 6 (extremely troubled).

At all 3 study visits, the investigators assessed global signs and symptoms of allergic conjunctivitis (categorized as absent, trace, mild, moderate, or severe) after reviewing the results of a slit-lamp examination, conducting a general observation

of the patient, and evaluating the patient's allergy complaints. Best-corrected visual acuity was tested at every visit. To evaluate each patient's ocular health before entry into the study on day 1, intraocular pressure (IOP) was measured and the fundus was examined. At each visit, adverse events (AEs), changes in medical history, concomitant medication use, and dosing compliance were recorded.

The protocol for this trial was approved by the Institutional Review Board (IRB; IntegReview, Austin, Tex), and the study was conducted in accordance with Good Clinical Practices and the ethical principles described within the Declaration of Helsinki. All participating patients gave written informed consent. A parent or legal guardian signed the consent document for children younger than 18 y; the individual patient separately signed or otherwise marked an assent form as approved by the IRB. Enrollment was targeted at 300 evaluable patients. The number of patients was not supported statistically but rather was chosen to provide a sample size large enough to achieve the purposes of the study.

Inclusion and Exclusion Criteria

Eligible for inclusion in this study were patients 3 y of age or older with a history of allergic conjunctivitis (within the past 24 mo) who were able to reliably and accurately complete the patient perception questionnaires (paper- and telephone-based), and who satisfied all informed consent requirements. (For young children, parents or legal guardians may have assisted with completion of the questionnaires.) Patients must have been treated for allergic conjunctivitis with olopatadine 0.1% within the current year of study enrollment. Patients must have presented at the screening visit (day 1) with signs and symptoms of allergic conjunctivitis significant enough to warrant treatment and must not have used any topical ocular antiallergy medication between the last treatment with olopatadine 0.1% and the screening visit. Patients had to have a corrected visual acuity of 0.6 logMAR (logarithmic minimal angle resolution) or better in each eye and ocular health within normal limits. Women of childbearing potential were eligible if they had a negative urine pregnancy test at the screening visit, were not breast-feeding, did not intend to get pregnant during the course of the study, agreed to use adequate birth control throughout the trial, and agreed to take a urine pregnancy test upon exit. Contact lens wearers had to be willing to avoid wearing their lenses during each of the study visits, immediately prior to instillation of study medication, and for 10 min after dosing. Contact lens wearers also had to be stable and consistent for 3 mo prior to the screening visit.

Safety Analysis

All patients who received study medication were included in the safety analysis. The safety evaluation included reports on AEs (solicited and volunteered) and ocular parameters (best-corrected logMAR visual acuity and slit-lamp evaluation).

Statistics

Summary statistics were generated for the individual scores from patient perception questionnaires, as well as for global investigator assessments. Tabulations of patient compliance and reasons for discontinuation of study drug were also performed. Because this was a descriptive study, analysis was based solely on a modified

intent-to-treat data set in which all patients who were dosed with olopatadine 0.2% and who completed at least 1 questionnaire were considered evaluable. Summary statistics were also generated for best-corrected logMAR visual acuity measurements and assessment of ocular signs (in the cornea, iris/anterior chamber, or lens).

RESULTS

A total of 330 patients were enrolled and treated with study medication. For 2 patients, no on-therapy follow-up data were available; therefore, 328 patients were evaluable for the intent-to-treat analysis. The vast majority of patients (97%) reported compliance with study instructions and used olopatadine 0.2% once daily.

Of 330 enrolled patients, 26 (7.9%) were younger than 18 y of age and 92.1% were adults (total age range, 5 to 94 y). Mean age at enrollment was 46.3±19.9 y. Most patients in this study were white (69.7%), followed by black (20.3%), Hispanic (8.5%), and Asian (1.5%), and 72.7% of participants were female. A complete summary of the demographic characteristics of study patients is provided in the Table.

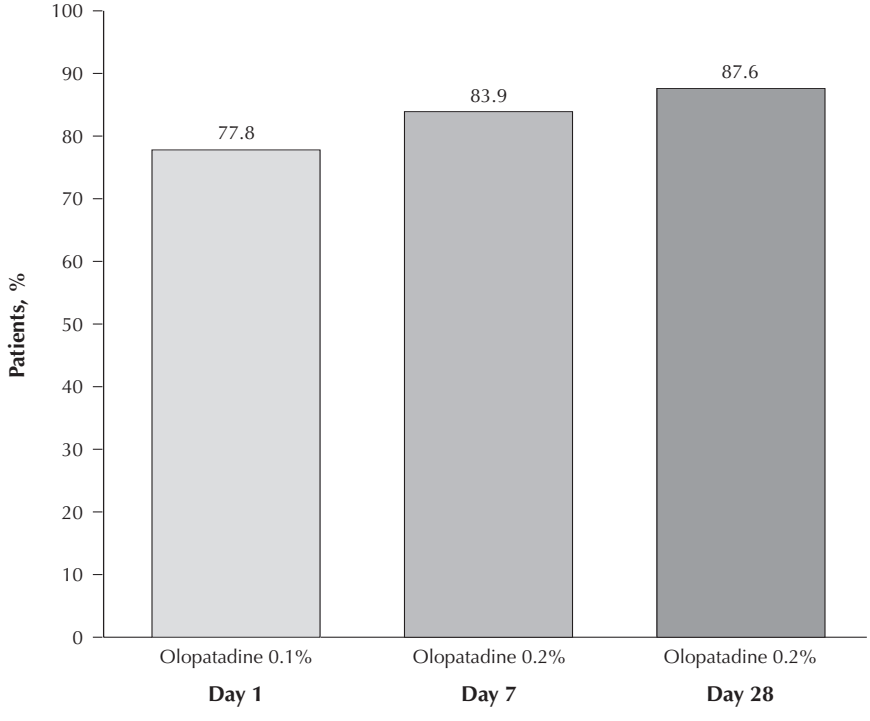
Summary of Demographic Characteristics

	Olopatadine 0.2% **(N=330)**
Age, y	
Mean	46.3
Standard deviation	19.9
Min to max	5–94
Race, n (%)	
White	230 (69.7)
Black	67 (20.3)
Asian	5 (1.5)
Hispanic	28 (8.5)
Sex, n (%)	
Male	90 (27.3)
Female	240 (72.7)
Iris color, n (%)	
Brown	169 (51.2)
Hazel	43 (13.0)
Green	26 (7.9)
Blue	87 (26.4)
Gray	5 (1.5)

A total of 73% of patients had used olopatadine 0.1% within 1 mo of study enrollment and 89% reported using it within 4 mo of study enrollment. Most patients (58.2%) also reported that they had used olopatadine 0.1% 2 or more times each day. When asked to rate their satisfaction from very dissatisfied to very satisfied, 77.8% of patients

perceived their prior use of olopatadine 0.1% as satisfactory (Fig 1). After 1 week of using olopatadine 0.2%, 83.9% of patients reported that they were satisfied with the treatment; this number increased to 87.6% by the end of the treatment period.

Fig 1. Patient satisfaction with olopatadine 0.1% and 0.2%.

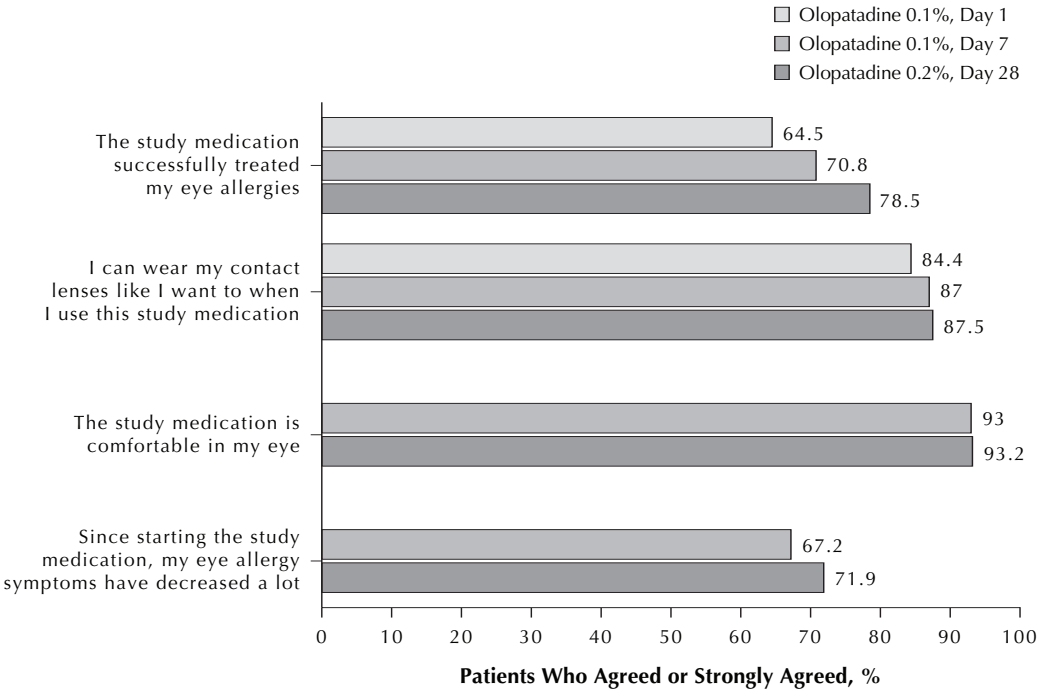


Note: Patient satisfaction with olopatadine 0.1% as reported on day 1 was based on recall. Patient satisfaction reported with olopatadine 0.2% was based on current use.

Figure 2 shows the proportion of patients who agreed or strongly agreed with a series of statements about olopatadine 0.2% and 0.1%. Overall, most patients (>70%) agreed with statements that olopatadine 0.2% successfully treated their eye allergies, allowed them to wear contact lenses as desired, and was comfortable in their eyes, and that their eye allergy symptoms had decreased significantly after olopatadine 0.2% use. Eighty-two percent of patients indicated that they would use olopatadine 0.2% again to treat their eye allergies. In general, the proportion of subjects who agreed or strongly agreed with each of the statements regarding olopatadine 0.2% increased from day 7 to day 28.

The daily telephone-based questionnaire revealed opinions that were generally similar to those reported on the paper-based questionnaires, and a trend toward increased satisfaction with olopatadine 0.2% use over time was also observed. Specifically, in evaluating the statement, "The study medication successfully treats

Fig 2. Patient perceptions of olopatadine 0.1% and 0.2% from the paper-based questionnaire.



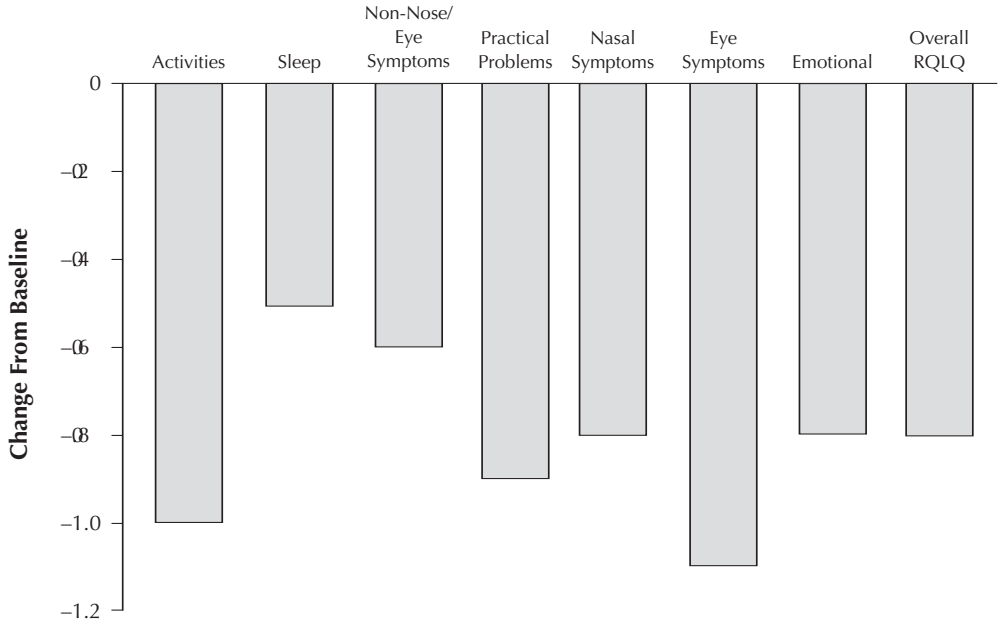
Note: Patient perceptions of olopatadine 0.1% on day 1 were based on recall; perceptions of olopatadine 0.2% were based on current use. Responses to the contact lens statement were limited to those patients who reported wearing contacts. The statement regarding comfort was evaluated only for olopatadine 0.2%.

my eye allergies," 42.8% of patients agreed or strongly agreed after 1 day of treatment. After 6 d of treatment, the percentage was 79.2%. The percentage of patients who agreed or strongly agreed that olopatadine 0.2% was comfortable grew from 89.8% on day 1 to 92.5% on day 28. Likewise, the proportion of subjects who believed that their ocular allergies had decreased "a lot" since they started the study medication was 24.6% at day 1 and 65% on day 6. In addition, after 1 day of treatment, 34.4% of contact lens wearers were undecided about whether they could wear their contact lenses as desired, but by day 6, only 7.1% were still undecided (all other contact lens wearers agreed or strongly agreed by day 6 that they could wear their contacts as needed).

The RQLQ queries patients about the impact of their nose/eye symptoms on daily activities, sleep patterns, practical problems (eg, the need to rub their eyes), and emotional problems (eg, frustration, embarrassment); the questionnaire uses a scale that ranges from 0 (not troubled) to 6 (extremely troubled) in whole-unit increments. The RQLQ also questions patients about how bothered they are by their symptoms. Patients judged the impact of their symptoms to be less severe across all

variables tested on day 7 compared with day 1. This is illustrated by statistically significant changes in mean scores ranging from –0.5 to –1.1 ($P<.0001$). Mean overall quality of life improved by –0.8 units after 1 wk of olopatadine 0.2% use (Fig 3).

Fig 3. RQLQ results.



Note: The RQLQ results are for changes from baseline (day 1) to day 7; all results were statistically significant ($P<.0001$).

At day 1, 54% of patients were judged as having mild or moderate signs and symptoms of allergic conjunctivitis. After 4 wk of olopatadine 0.2% use, 87.4% of patients were judged as having absent or trace ocular allergy signs and symptoms; this change was statistically significant ($P<.05$).

The safety analysis was conducted with all 330 enrolled patients. No treatment-related, clinically relevant changes from baseline were identified for visual acuity (best-corrected logMAR) or ocular sign parameters (cornea, iris/anterior chamber, and lens). No deaths or treatment-related serious AEs were reported during this study.

Five cases of treatment-related ocular AEs (1.5%) and 9 cases of headache (2.7%) were reported. Four patients discontinued study participation because of nonserious AEs.

DISCUSSION

Olopatadine 0.2% was formulated to improve upon the convenience of twice-daily olopatadine 0.1% (Patanol), which has been established as a well-tolerated and effective treatment for allergic conjunctivitis; olopatadine 0.2% contains the same active ingredient at twice the concentration and is dosed once daily. Several studies using the conjunctival antigen challenge (CAC) model have already demonstrated that olopatadine 0.2% is effective in treating itching associated with allergic conjunctivitis.[10-12] Therefore, although physician assessments of allergic signs and symptoms were obtained to provide a context in which patient-reported outcomes could be considered, the current study was not designed to demonstrate efficacy. Rather, this study was conducted solely to evaluate perceptions of olopatadine 0.2% (Pataday).

In particular, this study was designed to allow patients under "real world" conditions to report their perceptions of olopatadine 0.2%. Outside of a clinical trial, patients seek medical attention only when their allergic condition includes signs and symptoms substantial enough to be especially troublesome or to interfere with their daily activities. Thus, to participate in this study, patients were not screened using an antigen challenge or skin test, but rather must have presented only with active signs and symptoms sufficient to necessitate the use of a prescription topical antiallergy medication.

It has been shown that dosing compliance increases as the dosing regimen decreases, and that healthcare costs decrease, in particular, with once-daily dosing.[14,15] It has further been reported that once-daily medications are perceived to be as safe and effective as treatments with more frequent dosing regimens, and their use can result in improved dosing compliance and overall patient outcomes.[16,17] Thus, it is valuable to investigate how patients who already use olopatadine 0.1% perceive the effectiveness of olopatadine 0.2%. To that end, patients in the current study must have had recent exposure (within the same calendar year) to olopatadine 0.1% and must not have used any other topical ocular antiallergy treatment between their last use of olopatadine 0.1% and the start of the study. Most patients (89%) used olopatadine 0.1% within 4 mo of study entry.

Overall, the results of this trial indicate that once-daily olopatadine 0.2% was well accepted by patients who had recently used olopatadine 0.1%; patients generally reported high levels of satisfaction with both products. Most patients had favorable opinions about the effect of olopatadine 0.2% in terms of ocular comfort, contact lens wear, and eye allergy symptoms. More than 80% of patients in this study expressed a desire to use olopatadine 0.2% again to treat their eye allergies.

In addition to direct patient reports of satisfaction, the RQLQ was used to evaluate quality-of-life outcomes after use of olopatadine 0.2%. The RQLQ consists of a validated scale that measures not only the severity of rhinoconjunctivitis symptoms, but also the physical, emotional, and social problems that arise because of them.[13] It is important to note that differences from baseline on the RQLQ that equal or exceed 0.5 have been shown to be clinically meaningful to patients.[18] In the present study, the improvement observed in each of the variables from baseline to day 7 ranged in magnitude from a low of 0.5 (sleep problems) to a high of 1.1 (eye symptoms). Thus, patients experience clinically meaningful improvement in quality of life after just 1 wk of olopatadine 0.2% treatment. On the basis of previously

cited papers,[14-17] this may lead to greater patient compliance, which, in turn, could reduce healthcare costs and improve patient outcomes.

Because this study sought to evaluate "real world" perceptions of olopatadine 0.2%, the results are limited. For example, as previously indicated, patients were not tested for specific allergic reactions; thus, their allergic symptoms may not have been conclusively confirmed. Additionally, pollen counts were not obtained or monitored during the course of the study, and thus it is possible that observed and reported improvements in ocular allergies were simply due to the fact that the offending pollen was no longer present in the environment. Thus, although global assessments of ocular allergic severity showed statistically significant reductions from baseline to day 28, these results must be evaluated carefully. Further, patient perceptions of olopatadine 0.1% were based on recall, whereas perceptions of olopatadine 0.2% were based on current use of an open-label product in a clinical trial. As such, it is possible that perceptions of olopatadine 0.2% were artificially greater than perceptions of olopatadine 0.1%. In general, however, the fact that a substantial proportion of subjects perceived olopatadine 0.2% to be comfortable, convenient to use (in the case of contact lens wearers), and effective in the treatment of ocular allergies is meaningful. The fact that patients perceived the 2 formulations favorably is important. Similarly, the observed improvement in quality of life after 1 wk of use and the desire of most patients to use olopatadine 0.2% again are both clinically relevant, "real world" findings.

Given the effectiveness of olopatadine 0.2%, as reported in the literature, and the favorable perceptions of the product reported in this study, once-daily dosing could lead to improved patient adherence to dosing schedules and could consequently reduce healthcare costs. In this study, most patients (58.2%) stated that they had previously used olopatadine 0.1%, on average, 2 or more times per day; during this study, 97% of patients stated that they had used olopatadine 0.2% just once per day, as instructed. Similar dosing compliance with olopatadine formulations has been shown in a separately published clinical study,[19] as well as in a survey of actual patient use.[20] Specifically, the published study reported that 77% of patients (n=105) used olopatadine 0.1% twice daily (as instructed), compared with 100% of patients who used olopatadine 0.2% once daily (as instructed). The actual use survey reported that 74% of patients (n=688) used olopatadine 0.1% 2 or more times each day.

Finally, in agreement with other published reports, olopatadine 0.2% had a favorable safety profile in this study. No treatment-related serious AEs or deaths were reported; very few (less than 3%) treatment-related AEs were observed. AEs in the total population of 330 patients were predominantly nonserious and were generally mild or moderate in intensity. They typically resolved with or without treatment and did not result in patient discontinuation. Additionally, no clinically relevant treatment-related ocular changes were observed in any patient. Results from this study coupled with other published data support the conclusion that olopatadine 0.2% is safe and well tolerated.

CONCLUSION

Patients perceive olopatadine 0.2% to be an effective and well-tolerated treatment for allergic conjunctivitis. Use of olopatadine 0.2% may result in improvement in patient quality of life and dosing compliance, both of which could lead to improved

patient outcomes and lower healthcare costs. In this open-label study, patients who previously used olopatadine 0.1% concluded that olopatadine 0.2% is comfortable and effective, and that it is a medication that they would use again to treat their ocular allergies.

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