

Alcaftadine for the Prevention of Itching Associated with Allergic Conjunctivitis

Tracy D Mahvan, Whitney A Buckley, and Jaime R Hornecker

Allergic rhinitis affects approximately 60 million people in the US, including 10-30% of all adults and up to 40% of children.¹ Allergic rhinoconjunctivitis is often referred to as allergic rhinitis because nasal symptoms are a more common complaint than ocular symptoms. The prevalence of ocular symptoms alone hasn't been well studied, but is estimated to affect 20-40% of the US population.^{2,3} Data collected in the third National Health and Nutrition Examination Survey (NHANES III) between 1988 and 1994 indicated that 6% of the US population had isolated ocular symptoms over the course of 1 year, while up to 40% reported symptoms at least once during the 6-year period. Ocular symptoms are prevalent in all decades of adult life, whereas nasal symptoms alone or in combination with ocular symptoms are more common at younger ages.²

Ocular allergic disease, or allergic conjunctivitis, is the result of ocular exposure to an antigen that causes cross-linkage of membrane-bound immunoglobulin E (IgE), resulting in mast cell degranulation.⁴ Mast cell degranulation causes the release of preformed mediators such as histamine, as well as newly formed mast cell mediators such as prostaglandins,

OBJECTIVE: To evaluate the safety and efficacy of alcaftadine for the prevention of itching associated with allergic conjunctivitis.

DATA SOURCES: A medical literature search was conducted in MEDLINE/PubMed (2006-February 2012) and EMBASE (2006-February 2012) using the search terms alcaftadine and Lastacaft. References from these publications were reviewed for additional resources. Additional information was collected from Web sites of the US government (<http://www.clinicaltrials.gov>, <http://www.fda.gov>) and of Allergan Inc., the manufacturer of Lastacaft (<http://www.lastacaft.com>).

STUDY SELECTION AND DATA EXTRACTION: All identified articles and publications in English were reviewed for pharmacology, pharmacokinetics, efficacy, and safety data. Priority was placed on clinical trials.

DATA SYNTHESIS: Two published clinical trials evaluated the efficacy of alcaftadine in the prevention of ocular itching and conjunctival redness associated with allergic conjunctivitis. One trial compared alcaftadine to placebo, and another trial compared alcaftadine to placebo and olopatadine HCl to placebo. Both studies showed superior efficacy, both clinically and statistically, in the prevention of ocular itching associated with allergic conjunctivitis compared to placebo. Although conjunctival redness was evaluated in the 2 trials, neither trial demonstrated both clinical and statistical significance. Both trials demonstrated a rapid onset of action of less than 15 minutes, as well as a duration of action greater than 16 hours, which supports the use of once-daily administration. Overall, alcaftadine was well tolerated, and common adverse effects, reported in less than 4% of patients, included ocular irritation, pruritus, erythema, and stinging or burning upon instillation. Ocular adverse effects were typically mild in severity and self-limiting.

CONCLUSIONS: Alcaftadine is a safe and effective option for the prevention of ocular itching associated with allergic conjunctivitis, is dosed once daily, and is competitively priced among prescription medications for allergic conjunctivitis. Additional studies are needed to further evaluate the comparative efficacy among ocular antihistamine/mast cell stabilizing medications.

KEY WORDS: alcaftadine, ocular antihistamine, ocular antihistamine/mast cell stabilizer, seasonal allergic conjunctivitis.

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Author information provided at end of text.

leukotrienes, and platelet-activating factor. Allergic conjunctivitis is characterized by pruritus, hyperemia, chemosis, tearing, and lid swelling. Interestingly, histamine is the only mediator that can reproduce the entire clinical presentation and the only mediator that produces pruritus.³ Pruritus is the key feature that distinguishes between allergic and infectious causes of conjunctivitis.⁴ Relief of pruritus is the principal objective of treatment options available today.⁵

Current treatment options for allergic conjunctivitis include oral antihistamines, ophthalmic antihistamines, mast cell stabilizers, nonsteroidal antiinflammatory drugs (NSAIDs), decongestants, corticosteroids, and intranasal corticosteroid sprays. Oral antihistamines can relieve pruritus; however, ophthalmic antihistamines (eg, ketotifen, azelastine, bepotastine, epinastine, olopatadine, and alcaftadine) have a faster onset of action. Newer ophthalmic antihistamines are often dual-acting antihistamines and mast cell stabilizers and are considered a mainstay in pharmacotherapy. Ophthalmic mast cell stabilizers (eg, cromolyn, lodoxamide, nedocromil, and pemirolast) have a slower onset of action than antihistamines and are used in the treatment of mild to moderate symptoms. One ophthalmic NSAID (ketorolac) was found to be less effective in comparator studies with olopatadine and emedastine. An ophthalmic decongestant (naphazoline) is currently available in combination with ophthalmic antihistamines; however, it is not recommended because of a short duration of action and multiple adverse effects such as burning, stinging, rebound hyperemia, and conjunctivitis medicamentosa. Ophthalmic corticosteroids (eg, rimexolone, loteprednol) should be considered as a last resort because of the potential for exacerbation of viral infections of the conjunctiva and cornea, as well as increased intraocular pressure and cataract formation. Intranasal corticosteroid sprays may also be useful in relieving the symptoms of allergic conjunctivitis.⁶

Alcaftadine (Lastacaft, Allergan Inc.) is the newest dual-action antihistamine/mast cell stabilizer approved by the Food and Drug Administration (FDA) in 2010. The objective of this article is to review the pharmacology, pharmacokinetics, clinical studies, efficacy, and safety of alcaftadine.

Data Sources and Selection

A medical literature search was conducted in MEDLINE/PubMed (2006-February 2012) and EMBASE (2006-February 2012) using the search terms alcaftadine and Lastacaft. References from these publications were reviewed for additional resources. Additional information was collected from Web sites of the US government (<http://www.clinicaltrials.gov>, <http://www.fda.gov>) and the manufacturer (<http://www.lastacaft.com>). All articles and

publications identified were reviewed for information regarding pharmacology, pharmacokinetics, efficacy, and safety.

Pharmacology

Alcaftadine is an H₁-receptor antagonist and mast cell stabilizer.⁷ Recent developments in the molecular mechanism of action of H₁-antihistamines suggest that the term *receptor antagonist* is outdated. The process is more accurately described using the term *inverse agonist*. It has been shown that H₁-antihistamines combine with and stabilize the inactive conformation of the H₁-receptor, shifting the equilibrium toward the inactive state.⁸ Decreased chemotaxis and activation of eosinophils have been demonstrated.⁷ Alcaftadine has also shown activity at H₂- and H₄-receptors in vivo, although the clinical significance of these findings in the management of allergic conjunctivitis remains to be determined.⁵ In addition, a unique quality of alcaftadine may be its conjunctival epithelial stabilizing activity that was seen in a murine model.⁹ Alcaftadine also shows antiinflammatory activity in acute and late-phase allergic conjunctivitis in guinea pig models.¹⁰

Pharmacokinetics

The pharmacokinetic parameters of alcaftadine are summarized in Table 1.^{7,11} Metabolism of alcaftadine is mediated by non-CYP450 cytosolic enzymes to the active carboxylic acid metabolite. Neither alcaftadine nor the carboxylic acid metabolite substantially inhibited reactions catalyzed by major CYP450 enzymes. Peak levels of alcaftadine and the carboxylic acid metabolite are detected in

Table 1. Pharmacokinetics of Alcaftadine^{7,11}

Absorption	
median time to maximum concentration	
alcaftadine	15 minutes
carboxylic acid metabolite	1 hour
Distribution	
protein binding	
alcaftadine	39.2%
carboxylic acid metabolite	62.7%
Metabolism	
mediated by non-CYP450 cytosolic enzymes to the active carboxylic acid metabolite	
Elimination	
carboxylic acid metabolite	
half-life	~2 hours ^a
routes	Eliminated unchanged in the urine ^b
^a Following topical ocular administration.	
^b Following oral administration.	

plasma within 15 minutes and 1 hour after bilateral ocular administration, respectively. Plasma concentrations fall below the detectable limit for alcaftadine and the carboxylic acid metabolite at 3 and 12 hours following instillation, respectively. There is no indication that alcaftadine or the carboxylic acid metabolite accumulates systemically following daily topical ocular administration.^{7,11}

Clinical Trials

Two published clinical trials have established the efficacy and safety of alcaftadine (Table 2).^{12,13} Both trials used the conjunctival allergen challenge (CAC) model. The CAC model has been developed to evaluate antiallergy agents in a controlled setting instead of an environmental setting with multiple confounding factors. The standard CAC design involves 2 baseline visits: the first to titrate the allergen dose to achieve the desired clinical response and a second visit to confirm the initial result. Patients who have reproducible results and demonstrate the desired clinical response to the allergen challenge are able to move forward to a third visit. In the third and fourth visits the onset and duration of action are measured by instilling the study medications (active ingredient, placebo, and comparator) in any combination and then challenging the patient with the appropriate dose of allergen. The eyes are then evaluated at specified times for the desired signs and symptoms, such as pruritus, hyperemia, and chemosis. Depending on

the symptom being evaluated, patients or study personnel rate the response on a scale from 1 to 4, with 1 being the least symptomatic and 4 being the most symptomatic. The onset of action can be measured within minutes after medication administration and the allergen challenge. At a separate visit, the duration of action can be measured by performing the allergen challenge again at a specific time, usually hours after administration of the medication.¹⁴ The CAC model has been validated and used as a standard clinical method by the FDA in the evaluation of allergic diseases for over 20 years.¹³

ALCAFTADINE, OLOPATADINE, AND PLACEBO

Greiner and colleagues conducted a 5-week, prospective, single-center, double-masked, randomized, active- and placebo-controlled trial using the CAC model.¹² The intent-to-treat analysis consisted of 170 patients; 164 patients completed the study. The efficacy of alcaftadine 0.05%, 0.1% and 0.25% ophthalmic solutions in relieving the symptoms of allergic conjunctivitis, ocular itching, and conjunctival redness was compared with placebo. The same efficacy and symptoms were also evaluated comparing olopatadine HCl 0.1% ophthalmic solution to placebo. Patients were included if they were 18 years of age or older, had a history of ocular allergies and/or a positive skin test reaction to specified allergens within the last 24 months, had a best-corrected visual acuity of 0.6 logMAR

Table 2. Alcaftadine Clinical Trials

Reference	Design	Duration (weeks)	Treatment Arm	Primary End Point	Results
Greiner (2011) ¹²	N = 170 DM, R, SC, APC, CAC	5	Placebo (n = 34) Alcaftadine 0.05% (n = 34) Alcaftadine 0.1% (n = 34) Alcaftadine 0.25% (n = 34) Olopatadine 0.1% (n = 34)	Ocular itching 5 minutes after an allergen challenge and conjunctival redness 15 minutes after an allergen challenge	Ocular itching at 5 minutes ^{a,b} alcaftadine 0.05%: -1.61 alcaftadine 0.1%: -1.73 alcaftadine 0.25%: -1.92 Olopatadine 0.1%: -1.84 Conjunctival redness at 15 minutes ^{a,b} alcaftadine 0.05%: -0.34 alcaftadine 0.01%: -0.32 alcaftadine 0.25%: -0.94 olopatadine 0.1%: -0.87
Torkildsen (2011) ¹³	N = 58 Phase 3, DM, R, MC, PC, CAC	5	Placebo (n = 29) Alcaftadine 0.25% (n = 29)	Ocular itching at 3, 5, and 7 minutes after an allergen challenge; conjunctival redness at 7, 15, and 20 minutes after an allergen challenge	Ocular itching ^{a,c} alcaftadine 0.25% 3 minutes: -1.50 5 minutes: -1.49 7 minutes: -1.474 Conjunctival redness ^{a,b} alcaftadine 0.25% 7 minutes: -0.879 15 minutes: -0.612 20 minutes: -0.578

APC = active and placebo-controlled; CAC = conjunctival allergen challenge; DM = double-masked; MC = multicenter; PC = placebo-controlled; R = randomized; SC = single center.
^aMean difference vs placebo.
^bp < 0.05.
^cp < 0.001.

or better in each eye, as measured using an Early Treatment of Diabetic Retinopathy Study chart, and had not worn contact lenses for at least 3 days prior to and during the study period. Female subjects were required to have a negative pregnancy test at visit 1 and upon exit from the study. Baseline characteristics were described and no significant differences were reported. Characteristics described included average (SD) age 41.5 (11.5) years; 61.8% female; and 92.9% white, 1% Asian, 1% black, and 2.9% other race.¹²

The primary end points were ocular itching (at visit 4, 5 minutes after allergen challenge) and conjunctival redness (at visit 4, 15 minutes after allergen challenge). Authors reported that results were considered clinically significant if the unit difference was ≥ 1 and statistically significant if the p value was < 0.001 . However, in the methods section, statistical significance was defined as $p < 0.017$ for primary end points and $p < 0.05$ for secondary end points. The mean score for ocular itching 5 minutes after the CAC was 2.76 and was similar for all treatment arms at visit 2. All active treatment groups were clinically (≥ 1 unit difference) and statistically ($p < 0.001$) superior to placebo for ocular itching measured at 5 minutes post-CAC at visit 4. The mean unit differences between placebo and alcaftadine 0.25% and placebo and olopatadine 0.1% were -1.92 and -1.84 , respectively. Duration of action was measured at visit 3, 16 hours after medication instillation. The mean unit differences were clinically superior to placebo for both alcaftadine 0.25% and olopatadine 0.1%, at -1.47 and -1.08 , respectively.¹²

Ocular redness was the second primary end point evaluated in this study. Ocular redness was measured 15 minutes after the CAC. Both olopatadine 0.1% and alcaftadine 0.25% had statistically significant ($p < 0.05$) improvement of ocular redness 15 minutes post-CAC compared to placebo; however, neither achieved clinically significant improvement (alcaftadine 0.25%, 0.94; olopatadine 0.1%, 0.87). Ocular redness measured at visit 3, 16 hours after medication instillation, showed statistically significant improvement with both olopatadine 0.1% and alcaftadine 0.25% compared to placebo. Only alcaftadine 0.25% showed a clinically significant improvement compared to placebo (1.01 vs 0.9).¹²

Secondary end points included ciliary and episcleral redness, chemosis, lid swelling, tearing, ocular mucous discharge, and nasal symptoms (sneezing, rhinorrhea, nasal congestion, nasal pruritus, and ear or palate pruritus). At both 15-minute and 16-hour postinstillation evaluations, both alcaftadine 0.25% and olopatadine 0.1% exhibited statistically significant ($p < 0.05$) lower mean scores than placebo for all secondary end points.¹²

While this study included olopatadine 0.1% as an active control, it was not designed to compare olopatadine HCl 0.1% and alcaftadine 0.25%. The data indicate that both

agents are effective for the prevention of signs and symptoms of allergic conjunctivitis and have a longer duration of action that requires less frequent dosing than earlier ophthalmic antihistamines. Although alcaftadine 0.25% significantly improved ocular redness at 16 hours postinstillation in this study,¹² it was not granted FDA approval to prevent conjunctival redness.¹⁵ Olopatadine 0.2% (once daily dosing) was not available at the time the study was conducted and would have been a more similar comparator if superiority were to be determined between the 2 medications. The formulation used in this study for alcaftadine and the vehicle placebo were not the same formulation currently being used in the commercial product. According to FDA reports, the vehicle formulation was modified to improve overall comfort after pre-New Drug Application studies had been conducted. These modifications included a reduction in the buffer concentration, preservative, and chelating agent.¹⁶ The newer formulation was used in a later Phase 3 multicenter CAC to confirm similar efficacy.¹⁵

ALCAFTADINE AND PLACEBO

Torkildsen and colleagues conducted a 5-week, 2-arm, double-masked, multicenter, randomized placebo-controlled CAC Phase 3 study.¹³ Fifty-eight patients were enrolled in the study: 29 patients in the alcaftadine 0.25% group and 29 patients in the placebo group. Patients were included if they were 10 years of age or older with a history of ocular allergies and a positive skin test reaction to cat hair dander, grasses, ragweed, dog dander, cockroaches, dust mites, Japanese cedar, and/or tree pollen within the past 24 months, had a best-corrected visual acuity of 0.6 logMAR or better in each eye, and had a positive bilateral CAC reaction within 10 minutes of instillation of the last titration of allergen at the first visit. Negative pregnancy tests and approved birth control were required in women of childbearing age.¹³

The primary end points were ocular itching at 3, 5, and 7 minutes after CAC and conjunctival redness at 7, 15, and 20 minutes after CAC. Patients were asked to rate their ocular itching on a scale of 0–4, with 0 referring to no itching and 4 to an incapacitating itch with an irresistible urge to rub. A slit lamp was used to evaluate conjunctival redness on a scale of 0–4, with 0 equaling no redness and 4 equaling extremely severe redness. Clinical efficacy for itching and conjunctival redness was defined as a 0.5-unit improvement over placebo at all measured time points, or at least 1 unit for the majority (2 of 3) of all measured time points. A clinically and statistically significant ($p < 0.001$) reduction in ocular itching was seen in the alcaftadine treatment group compared to placebo at all time points following allergen challenge at 15 minutes and 16 hours after medication administration. For conjunctival redness, there was a statistically significant improvement ($p < 0.05$) for

alcaftadine compared to placebo at all measured time points post-CAC at 15 minutes and 16 hours. However, this change was not considered clinically significant.¹³

Secondary end points including ciliary redness, episcleral redness, chemosis, lid swelling, tearing, and rhinorrhea were significantly improved with alcaftadine compared to placebo. There was also a lower incidence of nasal congestion at most time points.¹³

Safety

ADVERSE EFFECTS

The incidence of adverse drug effects associated with alcaftadine instillation was small, and, in original safety studies, they were reported more frequently in placebo-treated patients.¹³ Overall, alcaftadine is well tolerated, and common adverse effects, reported in less than 4% of patients, include ocular irritation, pruritus, erythema, and stinging or burning upon instillation.^{7,12,17} Ocular adverse effects are typically mild in severity and self-limiting.¹⁴ Headache, nasopharyngitis, and influenza are the most commonly reported nonocular adverse effects. Dysgeusia is frequently associated with ophthalmic preparations and was also reported with the use of alcaftadine.^{7,12}

DRUG INTERACTIONS

In vitro interaction studies indicate that alcaftadine is metabolized via non-CYP450 cytosolic enzymes to an active carboxylic acid metabolite and that neither agent substantially inhibits the CYP450 enzyme system.⁷ Biotransformation of alcaftadine to its carboxylic acid metabolite was not inhibited by incubation with beclomethasone, budesonide, codeine, diphenhydramine, albuterol, or theophylline. Metabolism of alcaftadine was inhibited by 25–33% in the presence of erythromycin, loratadine, and ketotifen at in vitro concentrations 5–8 times the therapeutic plasma concentration.¹¹ No significant drug interactions involving the CYP enzymes or alterations in serum protein binding have been identified.^{7,11}

SPECIAL POPULATIONS

Alcaftadine appears to be safe and well tolerated for the treatment of allergic conjunctivitis in both pediatric and geriatric populations. Because children younger than 10 years of age cannot reliably describe the subjective end point of itching and the disease is the same in pediatric and adult patients, the efficacy data established for children aged 10 years or older were extrapolated down to age 3 years. In all of the studies conducted for FDA approval that included pediatric patients aged 3–17 years, alcaftadine was safe and well tolerated, with no unexpected safety issues.¹⁶

Geriatric patients (>64 years) were included in clinical studies throughout the development process. No clinically significant differences were detected in the adverse effect profile or efficacy data between geriatric subjects and younger patients.¹⁶

Alcaftadine is the only agent in its class that is rated pregnancy category B. It has been evaluated in animal reproduction studies in rats and rabbits. There was no evidence of impaired female reproduction or harm to the fetus with plasma exposure levels 200–9000 times the plasma exposure expected with the usual human ocular dose. There have been no adequate or well-controlled studies in the human population, and this drug should be used during pregnancy only if clearly indicated.⁷

Dosage and Administration

Alcaftadine is approved by the FDA as a topical ophthalmic antihistamine for the prevention of itching associated with allergic conjunctivitis in children older than 2 years of age and in adults.^{7,17} Use in children less than 2 years is not recommended, primarily because safety and efficacy have not been established in this population. A reliable diagnosis of allergic conjunctivitis is also challenging in patients of this age.¹⁸

Alcaftadine should be administered as 1 drop instilled in each eye once daily. The product is available as a 3-mL fill in a 5-mL bottle and should be stored at room temperature.⁷ Refrigeration of topical ophthalmic products before use may help decrease stinging and burning in patients who experience these adverse effects.¹⁷

Patients should be counseled on the proper administration of ophthalmic drops, including the prevention of contamination of the dropper tip. Touching the tip to the eye or eyelid, the surrounding area of the face, or to another surface could potentially contaminate the dropper and solution. Alcaftadine should be used only as a topical preparation for the eye.

Alcaftadine contains the preservative benzalkonium chloride, which may be absorbed by soft contact lenses. Contact lenses should be removed before using alcaftadine to avoid changes to lens integrity and may be reinserted 10 minutes after drop administration.^{7,18} Patients should not use alcaftadine to treat irritation of the eye associated with contact lens use.

Therapeutic and Economic Issues

Two European studies have evaluated the economic impact of allergic conjunctivitis as well as the impact on quality of life (QOL) among patients who sought medical attention for allergic conjunctivitis. Both studies found that patients with allergic conjunctivitis reported a lower QOL as well as an increased economic burden with work absences.

teism and money spent on items to help alleviate symptoms.^{19,20} In 2002, patients in Spain spent an average (SD) of 133.28 (141.66) minutes seeking and receiving medical care from eye clinics for allergic conjunctivitis. Patients with allergic conjunctivitis also reported a worse self-perception on QOL questionnaires regarding self-care, usual activities, pain/discomfort, anxiety/depression, and general health compared to patients in the control group who had never been diagnosed with allergic conjunctivitis. Between the annual direct costs and the costs of reduced productivity, it is estimated that the total per-patient cost is approximately €348.50 (US \$461.08) per year.¹⁹

In 2001, a study of patients with allergic conjunctivitis in Oxfordshire, England, showed a significantly worse perception of pain/discomfort, daily activities, sleep, practical problems, nasal and eye symptoms, and emotions in QOL questionnaires, as well as a worse overall self-perception of their health compared to the control group without allergic conjunctivitis. The estimated annual economic costs of allergic conjunctivitis were estimated to be £64.61 (\$99.92) for retirees and £123.69 (\$191.29) for patients currently employed.²⁰

One advantage that alcaftadine has over most of the other agents is once-daily dosing. In 2003, the World Health Organization identified medication nonadherence as a significant cause of preventable morbidity, mortality, and health care costs.²¹ While there are no studies evaluating the impact of medication adherence in allergic conjunctivitis, there are data regarding medication adherence in another ophthalmic condition, glaucoma. Most studies indicate that medications taken once daily have higher rates of adherence than do medications dosed twice or more daily.²² Once-daily dosing of alcaftadine has the potential to improve patient adherence and QOL issues, as well as the economic burden described above.

Alcaftadine has several other potential advantages over other medications in this class (Table 3).^{7,23-29} First, alcaftadine is available at a slightly lower cost than most of the other brand-name prescription agents in this class, regardless of dosing frequency. However, over-the-counter (OTC) medications containing ketotifen fumarate, which require twice-daily dosing, are significantly less expensive than the prescription medications. Secondly, alcaftadine is approved for use in children as young as 2 years. Although bepotastine also has an indication for children as young as 2 years, all of the other agents are approved for use in children 3 years and older. Finally, alcaftadine is the only agent that is pregnancy category B.⁷ All other medications in this class are pregnancy category C and showed harm to an-

imal fetuses, with plasma concentrations ranging from 10,000 to 150,000 times higher than the plasma concentration expected with ocular administration in humans.²³⁻²⁸ Based on data provided for all of the medications, it is possible that the same types of harm were undetectable in the alcaftadine studies because of the use of lower animal doses, which achieved lower plasma concentrations. In general, the potential to cause fetal harm with the usual ocular administration of any of these agents appears to be low.

One potential disadvantage of alcaftadine is the presence of multiple agents already available to treat allergic conjunctivitis. More specifically, there are 5 prescription medications, 2 generic equivalents, and 1 OTC medication with multiple generic versions that are available. Another potential disadvantage is cost. Although alcaftadine is priced slightly below the brand-name medications, it is slightly more expensive than the 2 generic prescription medications.

Summary

Alcaftadine was approved by the FDA in 2010 as the newest agent in the class of ophthalmic dual-acting antihistamines and mast cell stabilizers. Alcaftadine works on H₁ and H₂ receptors and may demonstrate some action on H₄ receptors, although the clinical significance of this is unknown at this time. Two published trials have demonstrated that alcaftadine is safe and effective for the prevention of itching associated with allergic conjunctivitis. Because

Table 3. Comparison of Dual-Acting Antihistamine/Mast Cell Stabilizing Ophthalmic Medications^{7,23-29}

Medication, Generic (Brand)	Usual Dosage	Patient Age, years	Pregnancy Category	Cost of 1-Month Supply, \$ (bottle size)
Prescription only				
Alcaftadine 0.25% (Lastacft) ^a	1 drop once daily	≥2	B	112.32 (3 mL)
Azelastine 0.05% ^b (Optivar) ^a	1 drop twice daily	≥3	C	95.99 ^c (6 mL) 121.79 (6 mL)
Bepotastine 1.5% (Bepreve) ^a	1 drop twice daily	≥2	C	118.04 (5 mL)
Epinephrine 0.05% ^b (Elestat) ^a	1 drop twice daily	≥3	C	99.99 ^c (5 mL) 124.99 (5 mL)
Olopatadine 0.1% (Patanol) ^a	1 drop twice daily	≥3	C	130.81 (5 mL)
Olopatadine 0.2% (Pataday) ^a	1 drop once daily			126.65 (2.5 mL)
Over-the-counter				
Ketotifen 0.025% ^b (Zaditor) (Alaway)	1 drop twice daily	≥3	C	\$25.99 (5 mL) \$19.69 (5 mL)
^a Contains preservative benzalkonium chloride.				
^b Generic available.				
^c Generic cost.				

published data from the trials regarding the prevention of ocular redness were inconsistent, alcaftadine did not gain FDA approval for this indication. The adverse effect data suggest that alcaftadine is very well tolerated and that adverse effects are mild and self-limiting when they do occur. Alcaftadine appears to be safe and effective in both pediatric and geriatric populations.

Potential advantages of alcaftadine over existing medications include the convenience of once-daily dosing, pregnancy category B rating, and approval for use in children as young as 2 years of age. It is comparably priced with brand-name prescription medications and slightly more expensive than generic prescription medications. Two medications in this class are approved for once-daily dosing: alcaftadine and olopatadine 0.2%. Of these, alcaftadine appears to be slightly less expensive. The OTC medications containing the active ingredient ketotifen fumarate are significantly less expensive than all other prescription medications in this class but require twice-daily dosing. Because there have been no true head-to-head trials comparing alcaftadine to any other medications in the class, no conclusions can be made regarding comparative efficacy. Future research should be directed toward establishing the role of alcaftadine compared to similar medications, as well as determining the importance of once-daily ophthalmic administration.

Tracy D Mahvan PharmD, Associate Professor of Pharmacy Practice, School of Pharmacy, University of Wyoming, Laramie, WY; Clinical Pharmacy Specialist, Salud Family Health Centers, Longmont, CO

Whitney A Buckley PharmD, Clinical Assistant Professor of Pharmacy Practice, School of Pharmacy, University of Wyoming; Clinical Pharmacist, University of Wyoming Family Medicine Residency Program at Cheyenne

Jaime R Hornecker PharmD BCPS, Clinical Assistant Professor of Pharmacy Practice, School of Pharmacy, University of Wyoming; Clinical Pharmacist, University of Wyoming Family Medicine Residency Program at Casper

Correspondence: Dr. Mahvan, tbaher@uwoyo.edu

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EXTRACTO

Alcaftadina para la Prevención del Picor Asociado a la Conjuntivitis Alérgica

TD Mahvan, WA Buckley, y JR Hornecker

Ann Pharmacother 2012;46:1025-32.

OBJETIVO: Evaluar la seguridad y la eficacia de alcaftadina para la prevención del picor asociado a la conjuntivitis alérgica (CA).

FUENTES DE INFORMACIÓN: Se llevó a cabo una búsqueda bibliográfica en las bases de datos de MEDLINE/PubMed y EMBASE (enero de 2006-febrero de 2012) mediante los términos de búsqueda alcaftadina y Lastacaft. Se revisaron las referencias de estas publicaciones en busca de recursos suplementarios. También se obtuvo información adicional de páginas web gubernamentales de Estados Unidos (<http://www.clinicaltrials.gov>, <http://www.fda.gov>) y del fabricante de Lastacaft, Allergan (<http://www.lastacaft.com>).

SELECCIÓN DE FUENTES DE INFORMACIÓN Y MÉTODO DE EXTRACCIÓN DE INFORMACIÓN: Se revisaron todos los artículos y las publicaciones identificadas escritas en inglés para la obtención de datos farmacológicos, farmacocinéticos, de eficacia, y seguridad. Se dio prioridad a los ensayos clínicos en humanos.

SÍNTESIS: Dos ensayos clínicos publicados evaluaron la eficacia de alcaftadina en la prevención del picor ocular y el enrojecimiento conjuntival asociado a la CA. Un ensayo comparó alcaftadina con un placebo, y un ensayo comparó alcaftadina y olopatadina HCL con un placebo. Ambos estudios mostraron una eficacia superior, tanto clínica como estadísticamente, en la prevención del picor ocular asociado a la CA en comparación con el placebo. El enrojecimiento conjuntival fue evaluado en los 2 ensayos; sin embargo, ningún ensayo mostró significancia clínica y estadística. Ambos ensayos mostraron un inicio rápido de acción de menos de 15 minutos, así como una duración de la acción superior a las 16 horas, lo cual apoya una posología de una vez al día. En general, alcaftadina se tolera muy bien, y los efectos adversos comunes, notificados en menos del 4% de los pacientes, incluyen irritación ocular, prurito, eritema, y escozor o quemazón tras la instilación. Los efectos adversos oculares son normalmente leves y autolimitados.

CONCLUSIONES: Alcaftadina tiene un precio competitivo entre los medicamentos prescritos para la CA, se administra una vez al día, y resulta una opción segura y efectiva para la prevención del picor ocular asociado con la CA. Es necesario la realización de nuevos estudios para evaluar la eficacia comparativa entre los medicamentos oculares antihistamínicos/estabilizadores de mastocitos.

Traducido por Enrique Muñoz Soler

RÉSUMÉ

L'Alcaftadine pour la Prévention des Démangeaisons Associées avec la Conjonctivite Allergique

TD Mahvan, WA Buckley, et JR Hornecker

Ann Pharmacother 2012;46:1025-32.

OBJECTIFS: Évaluer la sécurité et l'efficacité de l'alcaftadine pour la prévention des démangeaisons associées avec la conjonctivite allergique (CA).

SOURCE DE L'INFORMATION: Une recherche de la littérature médicale a été réalisée sur MEDLINE/PubMed (janvier 2006-février 2012) et EMBASE (janvier 2006-février 2012) en utilisant les mots clés alcaftadine et Lastacaft. Les bibliographies de ces publications ont aussi été révisées à la recherche de ressources informationnelles supplémentaires. De l'information additionnelle a aussi été retrouvée sur les sites internet du gouvernement des États-Unis (<http://www.clinicaltrial.gov>, <http://www.fda.gov>) et sur le site du fabricant de Lastacaft, la compagnie Allergan (<http://www.lastacaft.com>).

SÉLECTION DES ÉTUDES ET EXTRACTIONS DE L'INFORMATION: Tous les articles identifiés et les publications de langue anglaise ont été révisés pour retracer les données sur la pharmacologie, la pharmacocinétique, l'efficacité, et la sécurité. La priorité a été placée sur les études cliniques réalisées chez les sujets humains.

SYNTHÈSE DE L'INFORMATION: Deux études cliniques publiées ont évalué l'efficacité de l'alcaftadine dans la prévention des démangeaisons oculaires et de la rougeur conjonctivale associée à la CA. Une étude a comparé l'alcaftadine au placebo, et une étude a comparé l'alcaftadine au placebo et l'olopatadine HCL au placebo. Les 2 études ont démontré une efficacité supérieure, tant cliniquement que statistiquement, dans la prévention de la démangeaison oculaire associée à la CA par rapport au placebo. La rougeur conjonctivale a été évaluée dans 2 études; cependant aucune de ces études n'a pu démontrer de différence, tant au point de vue clinique que statistique. Les 2 études ont démontré un début d'action rapide de moins de 15 minutes, de même qu'une durée d'action supérieure à 16 heures, ce qui supporte son administration une fois par jour. De façon globale, l'alcaftadine est très bien tolérée, et les effets secondaires les plus fréquents, sont rapportés chez moins de 4% des patients, et incluent une irritation oculaire, de la démangeaison, de l'érythème, et une sensation de picotements ou de brûlures lors de l'instillation. Les effets secondaires oculaires sont typiquement légers et auto limités.

CONCLUSIONS: L'alcaftadine est vendu à un prix compétitif parmi les médicaments sous ordonnance visant à traiter la CA, et son administration une fois par jour, sa sécurité et son efficacité en font un choix valable pour la prévention des démangeaisons oculaires associées à la CA.

Traduit par Marc Parent