White Paper

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Pataday® Dual-Action Ophthalmic Drops for Ocular Allergies

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Key Messages

- Dual-action anti-allergy agents, including olopatadine, utilize two mechanism of action to provide ocular allergy itch relief: antihistamine and mast cell stabilization
- Pataday® (olopatadine hydrochloride ophthalmic solution) is available in three different strengths to provide rapid ocular allergy itch relief that lasts for up to 8 hours (Pataday® Twice Daily Relief), 16 hours (Pataday® Once Daily Relief), and 24 hours (Pataday® Once Daily Relief *Extra Strength*)
- Pataday® is the first over-the-counter dual-action ophthalmic solution to offer once-daily ocular allergy itch relief

Introduction

Ocular allergy is a common immunological inflammatory process on the anterior surface of the eye and can be triggered by many allergens, including ragweed, pollen, grass, and animal dander. Ocular exposure to these allergens can induce symptoms of itch and clinical signs of conjunctival redness, chemosis, swollen eyelids, and corneal staining. An estimated 40% of the United States population has had ocular allergy symptoms.[1] Only approximately 10% of patients with ocular allergies seek medical attention for their symptoms, while the remainder self-diagnose and may also self-medicate.[2] It is estimated that over-the-counter (OTC) ocular allergy medication sales are 10-fold higher than the combined ocular allergy prescriptions generated by primary care physicians (30%), eye care specialists (41%) and allergists (9%).[3]

Allergy Cascade

Ocular allergies are primarily mediated by the immunoglobulin E (IgE)-mast cell system, triggered by allergens (Figure 1).[4] The early phase reaction, which lasts about 30 minutes, involves the interaction of the allergens with IgE on the mast cell membrane.[4] Allergens cross-link the IgEs, leading to mast cell degranulation and release of histamine along with pro-inflammatory mediators such as prostaglandins, leukotrienes, and cytokines.[4] The late phase reaction of mast cell degranulation in the conjunctiva includes binding of histamine receptors (H1, H2, H3, and H4) on vascular endothelial cells, neuronal fibers, goblet cells, immune cells, and conjunctival epithelial cells, leading to expression of cellular mediators and activation of inflammatory cells (T lymphocytes, eosinophils, and neutrophils).[4]

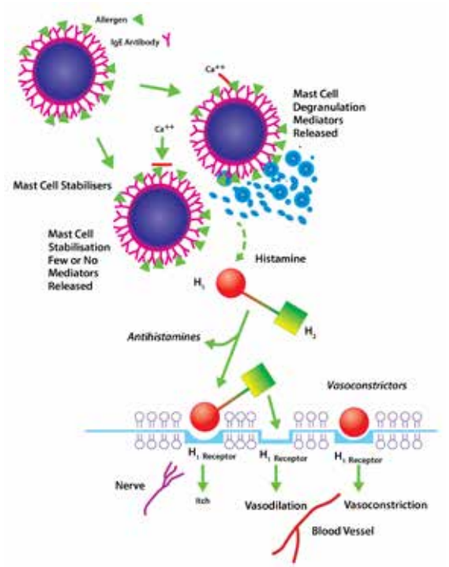


Figure 1: Mechanism of allergic conjunctivitis.

Common Therapeutic Options

Antihistamine drugs block histamine receptors on nerves and blood vessels and are designed to reduce itch and vasodilation.[4] Mast cell stabilizers inhibit mast cell degranulation and histamine release, reduce the recruitment of inflammatory cells, and reduce the allergic reaction cascade, but their activation can take 3-5 days.[4] Olopatadine is both a mast cell stabilizer and a histamine H1 antagonist and has demonstrated decreased chemotaxis and inhibition of eosinophil activation.

Olopatadine (Figure 2) is a dual-action selective histamine H1 receptor antagonist and mast cell stabilizer approved for the relief of ocular allergy itch in 1996. Other dual-action agents that have come to the ophthalmic prescription market since then include ketotifen, azelastine, epinastine, bepostatine, and alcaftadine.[5] Dual-action anti-allergy ophthalmic drops are indicated for 2-3 times daily dosing, except for olopatadine and alcaftadine, each of which have a formulation(s) for once daily dosing.[5]

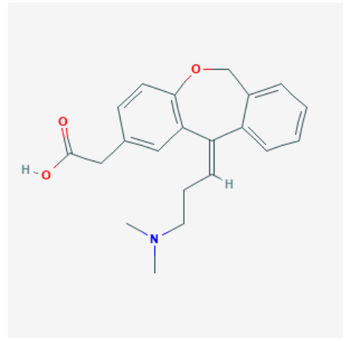


Figure 2: Olopatadine molecule.

In 2006, ketotifen 0.025% (Zaditor; Alcon, Fort Worth, TX) was the first dual-action anti-allergy drop available OTC in the United States. Nearly 15 years later, olopatadine was approved by the FDA to be only the second dual-action agent available OTC as Pataday® Twice Daily Relief (olopatadine hydrochloride 0.1%), Pataday® Once Daily Relief (olopatadine hydrochloride 0.2%), and Pataday® Once Daily Relief *Extra Strength* (olopatadine hydrochloride 0.7%). The prescription-to-OTC switch made both Pataday® Once Daily Relief and Pataday® Once Daily Relief *Extra Strength* the only once-daily dosing dual-action anti-allergy ophthalmic drops available OTC in the United States.

Pataday® Efficacy and Safety

The Pataday® products can provide temporary relief of itchy eyes due to pollen, ragweed, grass, and animal hair and dander, in patients 2 years or older for up to 8 hours (Pataday® Twice Daily Relief), 16 hours (Pataday® Once Daily Relief), and 24 hours (Pataday® Once Daily Relief *Extra Strength*) after drug instillation.[6-8] They have a neutral pH of approximately 7.0, which is similar to the average pH of the normal ocular surface.[9]

Pataday® Twice Daily Relief (Olopatadine hydrochloride ophthalmic solution, 0.1%)

Pataday® Twice Daily Relief (formerly Patanol®) was the first olopatadine ophthalmic solution approved by the FDA. In addition to ocular allergy itch relief, Pataday® Twice Daily Relief is approved for temporary relief of red eyes due to the allergens described above for up to 8 hours. In two randomized, double-masked, vehicle controlled conjunctival allergen challenge (CAC) model studies of 85 subjects, Pataday® Twice Daily Relief was reported to be significantly more effective than vehicle in reducing itch and redness at all evaluation times at onset (27 minutes) and 8 hours after drug administration (all $P < .05$), demonstrating its efficacy in reducing ocular allergy itch and redness.[7]

Pataday® Once Daily Relief (Olopatadine hydrochloride ophthalmic solution, 0.2%)

Pataday® Once Daily Relief (formerly Pataday®) was originally approved by the FDA in 2004 for the relief of itchy allergic eyes for up to 16 hours. When compared to vehicle in a randomized, double-masked, parallel group CAC study of 90 subjects, Pataday® Once Daily Relief was reported to have significantly lower itch scores at all evaluation times at onset (27 minutes) and at 16 hours after drug instillation (Figure 3).[6]

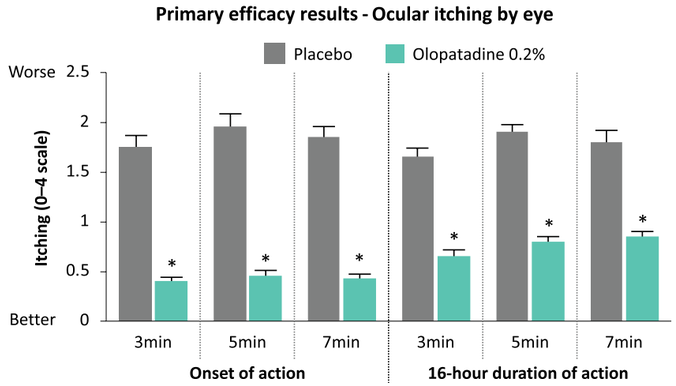
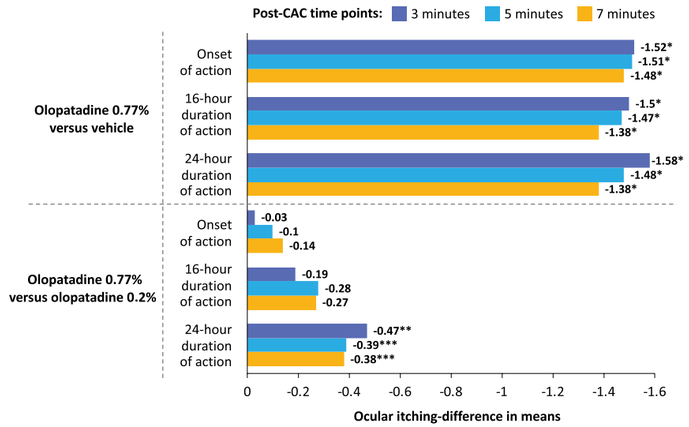


Figure 3: Comparison of mean ocular itching scores between olopatadine 0.2%-treated eyes and vehicle-treated eyes assessed after conjunctival allergen challenges at onset (27 minutes post-dose administration) and 16 hours after drug instillation.

Pataday® Once Daily Relief *Extra Strength* (Olopatadine hydrochloride ophthalmic solution, 0.7%)

Finally, Pataday® Once Daily Relief *Extra Strength* (formerly Pazeo®) was originally approved by the FDA in 2015 for the relief of itchy allergy eyes for up to 24 hours. A phase III, randomized, double-masked, parallel group trial using the CAC model with 202 subjects reported that, compared to vehicle, Pataday® Once Daily Relief *Extra Strength* significantly lowered itch scores at all evaluation times at onset (27 minutes) and 24 hours after drug instillation (Figure 4).[8]



**P<0.001; **P<0.01; ***P<0.05.*

Figure 4: Treatment differences in means after conjunctival allergen challenge (CAC): primary endpoint of ocular itching at 27 minutes (onset), 16-hours, and 24-hours post-dose administration.

Safety

Combined data from nine clinical studies show that Pataday® Once Daily Relief has a favorable ocular safety profile, with few reports of ocular adverse events, the most commonly reported being ocular pain with Pataday® Once Daily Relief (1.1%) and decreased visual acuity, ocular discomfort, and dry eye with vehicle (1.0-1.3%).[10] Furthermore, for Pataday® Once Daily Relief *Extra Strength*, the most commonly reported adverse reactions occurred in 2-5% of patients treated with either Pataday® Once Daily Relieve *Extra Strength* or vehicle and included blurred vision, dry eye, superficial punctate keratitis, dysgeusia and abnormal sensation in eye.[11]

	Pataday® Twice Daily Relief	Pataday® Once Daily Relief	Pataday® Once Daily Relief Extra Strength
Olopatadine Concentration	0.1% (Twice Daily)	0.2% (Once Daily)	0.7% (Once Daily Extra Strength)
Mechanism	Dual action selective histamineH1 receptor antagonist and mast cell stabilizer		
Indication	Temporarily relieves itchy and red eyes due to pollen, ragweed, grass, animal hair and dander	Temporarily relieves itchy eyes due to pollen, ragweed, grass, animal hair and dander	Temporarily relieves itchy eyes due to pollen, ragweed, grass, animal hair and dander
Indicated For	Adults, children 2 years+		
Dosage	1 drop in the affected eye(s) twice daily, every 6-8 hours, no more than twice per day	1 drop in the affected eye(s) once daily, no more than once per day	1 drop in the affected eye once daily, no more than one drop in each eye per day
Duration of Action	8 hours	16 hours	24 hours
pH	Approximately 7.0		
Warnings and Precautions	• Do not touch tip of container to any surface to avoid contamination. • Remove contact lens before use. Wait at least 10 minutes before reinserting contact lenses after use. • If using other ophthalmic products while using this product, wait at least 5 minutes between each product.		

Table 1: Pataday® porfolio.

Conclusion

Dual-action (antihistamine/mast cell stabilizers) anti-allergic agents utilize two mechanisms of action to provide ocular allergy itch relief: antihistamine and mast cell stabilization. Nearly 15 years after FDA approval of the first OTC dual-action anti-allergy ophthalmic drop, olopatadine is now only the second dual-action agent available OTC for ocular allergy itch in the United States. Pataday® provides rapid ocular allergy itch relief in three different strengths to last up to 8 hours (Pataday® Twice Daily Relief), 16 hours (Pataday® Once Daily Relief), and 24 hours (Pataday® Once Daily Relief *Extra Strength*), offering patients the only dual-action once-daily 16- and 24-hour ophthalmic formulations OTC.

References

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Notes:

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