

THE ALLERGY HUDDLE



The OD's playbook for therapeutics commonly used to treat ocular allergy.

BY MICHAEL S. COOPER, OD

With allergy season about to hit its spring peak, now is a good time to get reacquainted with the players on the allergy grid-iron. On defense, we have an aggressive bunch, including pollen, mold, and dust mites. On offense, we have a strong lineup ready and waiting to complement the quarterback—a.k.a. us, our patients' eye care professionals.

Football analogy aside, we have to ask ourselves how we can best take care of our patients' needs in prevention and rapid relief. The answers lie in our ability to understand the gravity of the patient's condition and to prescribe appropriate treatment. This article offers an overview of some of the players available for us to draft according to our patients' individual treatment needs.

A GREAT OFFENSE

Avoidance is the only sure way to prevent the signs and symptoms of ocular allergy (Figure). This may mean keeping windows closed and cleaning air conditioning systems annually and at least a month before, if not regularly during, peak season. A 30-second cold shower after being outside will wash away outdoor allergens. Additionally, ice cold compresses can relieve symptoms. However, these techniques aren't always enough. In such cases, medical therapies such as ocular therapeutic agents become necessary.

The Veteran (Mast Cell Stabilizer)

As one of the original allergy medications indicated for treatment of vernal keratoconjunctivitis, cromolyn sodium ophthal-

mic solution USP 4% (various vendors) inhibits the degranulation of sensitized mast cells.¹ That being said, it has limited clinical efficacy in relieving signs and symptoms of allergic conjunctivitis.² Essentially, if you are in a bind and need a cost-effective option, this might be a choice.

Wide and Slot Receivers (Antihistamines and Antihistamine/Mast-Cell Stabilizers)

The drugs in this category can be sorted into two groups: those dosed once daily and those dosed twice daily.

Once Daily Options

Olopatadine HCl first gained approval in a 0.1% formulation in 1996 as Patanol (Novartis). The drug provides both H1-selective receptor antagonism and relatively selective mast-cell stabilization, a combination that has been successful in managing ocular itch for the past 20-plus years through two reformulations. This novel mechanism prevents the release of mast-cell mediators such as histamines by not allowing these antagonistic molecules to degranulate within the conjunctival

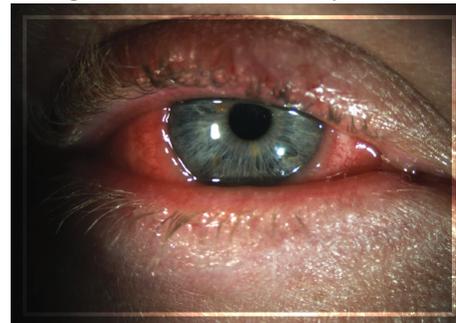


Figure. An eye showing signs typical of ocular allergy (ie, redness, tearing, conjunctival chemosis, and swollen eyelids) as noted on external examination.

Photo courtesy of Jacob Lang, OD, FAAO



Allergy has a significant impact from an epidemiologic standpoint as the sixth leading cause of chronic illness affecting more than 50 million Americans each year.^{1,2}



Estimated percentage of the general US population that experiences some form of allergic conjunctivitis.³

1. Allergy Facts. American College of Allergy, Asthma & Immunology website. January 9, 2018. <http://acaai.org/news/facts-statistics/allergies>. Accessed February 28, 2019.
2. Gateway to Health Communication & Social Marketing Practice. Centers for Disease Control and Prevention. September 15, 2017. www.cdc.gov/healthcommunication/ToolsTemplates/EntertainmentEd/Tips/Allergies.html. Accessed February 28, 2019.
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epithelium mucosa.³ It is important to note that this drug displays some anticholinergic and antimuscarinic capabilities, causing potentially more dryness and other unwanted side effects, including hypersensitivity.^{4,5}

Olopatidine HCl 0.2% (Pataday, Novartis) is a topical drug with a recommended dosage of once daily in each affected eye. Clinical studies of up to 12 weeks duration have shown that, when dosed once daily, olopatadine HCl 0.2% is effective in the treatment of ocular itching associated with allergic conjunctivitis.² Olopatadine HCl ophthalmic solution 0.7% (Pazeo, Novartis) is labeled for once daily dosing.

Alcaftadine ophthalmic solution 0.25% (Lastacaft, Allergan) is

another once daily option. It is the only commercially available ocular allergy medication that is labeled with the old designation Pregnancy Category B. Torkildsen and Shedden were the first to describe the efficacy and safety profile in the literature.⁶ The molecule exerts the triple threat of H1-selective receptor antagonistic behavior along with H2 and H4 activity, and this activity is combined with mast-cell stabilization and minimal anticholinergic activity. Decreased chemotaxis and inhibition of eosinophil activation are other novel features of this molecule, which acts as a stabilizer of conjunctival epithelium.⁷

I favored this medication when it first came out several years ago

for its rapid onset and prolonged duration of action reducing ocular itch. However, anecdotally, I found that patients had a repeated history of hypersensitivity and profound periorbital angioedema at approximately 6 months to 1.5 years after initiation of therapy.

Twice Daily Options

The twice daily dosing group contains bepotastine besilate ophthalmic solution 1.5% (Bepreve, Bausch + Lomb), epinastine HCl ophthalmic solution 0.05% (Elestat, Allergan), azelastine HCl ophthalmic solution 0.05% (Optivar, Akorn), ketotifen fumarate ophthalmic solution 0.035% (Zaditor, Alcon), and ketotifen fumarate ophthalmic solution 0.035% (Alaway, Bausch + Lomb). The highlight in this crowded class is bepostatine, in that the active molecule is a highly selective H1-receptor antagonist.⁸

Managed care plans may ask you to choose step therapies before bridging to the branded products with options such as epinastine and azelastine. Be aware that even though each has similar chemistry, the side effect profile is better for the former. Approximately one-third of patients report that azelastine eye drops sting transiently upon instillation.⁹ It is worth noting that, similar to many therapeutic agents, most antihistamine/mast-cell stabilizers carry some risk of tachyphylaxis or may hit a plateau in efficacy over time.

The Rookie

The expected launch of cetirizine ophthalmic solution 0.24% (Zerviate, Eye Vance Pharmaceuticals) will bring to market the first *topical ocular formulation* of cetirizine. The drug is known in oral form as Zyrtec (Johnson & Johnson/McNeil).¹⁰ The molecule is a selective H1-receptor antagonist, and in topical formulation it is dosed twice daily. This chemical entity effectively combines an antihistamine and



mast-cell stabilizer that actively seek to competitively bind with selected histamine receptor sites to reduce swelling, itching, and vasodilation.^{11,12} These characteristics alone may not seem too dissimilar from other available products, but when we dissect the biochemical properties of cetirizine's mechanism of action we see that there is negligible anticholinergic and antiserotonergic activity.¹³ This could mean that cetirizine will not potentiate the dryness symptoms that affect many of our patients with ocular surface disease.

Although serotonin agonism and antagonism are not widely described in the ophthalmic space, they do deserve mention, as most antihistamines share a common lineage with antipsychotics and antidepressants via the chemical group piperazine.¹⁴ This particular entity is a cyclic organic compound possessing two nitrogen atoms in opposite positions within a six-member heterocyclic ring that serves as a backbone for derivatives.¹⁵ The core molecule can be spliced into myriad applications, including antihelminthic activity, antihistamines, male erectile dysfunction, and recreational drugs such as MDMA (ecstasy).

Running Backs (Steroids)

Corticosteroids can be used off-label in many instances as a short-term boost during an acute allergic flareup. Top to bottom in the order of potency, choices include difluprednate ophthalmic emulsion 0.05% (Durezol, Alcon), prednisolone acetate ophthalmic suspension 1% (Pred Forte, Sandoz), loteprednol etabonate ophthalmic suspension 1% (Inveltys, Kala Pharmaceuticals), loteprednol etabonate ophthalmic gel 0.5% (Lotemax Gel, Bausch + Lomb), loteprednol etabonate ophthalmic gel 0.38% (Lotemax SM, Bausch + Lomb), fluorometholone acetate ophthalmic suspension 0.1%, (Flarex, Eyeavance Pharmaceuticals), and fluorometholone alcohol ophthalmic suspension 0.1% (FML, Allergan). I am not afraid to use these agents aggressively to

blunt signs and symptoms and provide maximum relief. The various molecules in this family act through the cytosolic glucocorticoid receptor and exert their effects predominantly at the genomic level, especially in long-term use.¹⁶⁻¹⁸

Topical corticosteroids can produce a number of local adverse side effects, notably cataract development, IOP elevation, and increased risk of infection.¹⁹ The extent of these side effects may vary significantly depending on the molecule used, the dose given, and the susceptibility of the patient. With this in mind, I recommend taking IOP measurements before and after treatment to ensure appropriate moderation of the therapy within 7 to 21 days.

Loteprednol etabonate ophthalmic suspension 0.2% (Alrex, Bausch + Lomb) is an ester-based molecule indicated for the temporary relief of the signs and symptoms of seasonal allergic conjunctivitis. The ketone group in this unique class of corticosteroids has been substituted by a chloromethyl ester in the C-20 position of the prednisolone acetate core structure.^{20,21} By virtue of this ketone replacement, loteprednol does not specifically facilitate the lens epithelial migration to the posterior lens pole that is responsible for steroid-related cataract formation.²² Multiple studies support the sentiment that this chemical alteration leads to limited steroid response after more than 28 days of use.^{23,24}

ADVICE FOR THE QB (DOCTOR): GO LONG

As clinicians we call the plays to orchestrate the best therapeutic result. In essence, it is our job to solve the acute or chronic allergic issue with a strong, clinically relevant value proposition. The head coach of the New England Patriots, Bill Belichick, is credited with saying, "Whatever success I've had, it is because I've tried to understand the situation of the player. I think the coach's duty is to avoid complicating matters." This applies to us as clinicians. We need to understand the situation of the different defensive players (eg, pollen, mold, and dust mites)

in order to appropriately manage signs and symptoms and deliver ultimate patient satisfaction. ■

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