New Allergy And Glaucoma Agents Debut

Learn how top physicians use the latest treatments in ocular disease and what therapies they look forward to using to optimize patient care.

By Sheree Crute, *Contributing Editor*

With new treatments for ocular disease awaiting FDA approval, it appears 2007 may be a promising year for ophthalmic pharmaceuticals. A handful of new, innovative drugs have the potential to make significant advances in allergy, glaucoma and dry eye treatment. Medications in the nonsteroidal anti-inflammatory drug (NSAID) category are offering new possibilities to reduce complications in postoperative retinal care.

Read on to find out how leading physicians are optimizing current treatments and integrating new therapies into practice, and get their take on what's in the pipeline.

Allergy: Raising the Bar

Each year, millions of patients seek relief from the itching, burning and inflammation associated with ocular allergies. For more than a decade, physicians have had drugs like olopatadine hydrochloride ophthalmic solution 0.1% (Patanol) to provide relief. Currently the market leader for allergic conjunctivitis, olopatadine 0.1% was the first agent to combine antihistaminic and mast cell stabilizing properties. "It's a wonderful first-line drug for allergic conjunctivitis," says Martin Zitt, M.D., chief of allergy and immunology at the Queens-Long Island Medical Group. "It's very useful to have a highly effective eye drop in [the allergy] category that's not a steroid, and Patanol meets that need."

In November 2006, Alcon began marketing olopatadine 0.2% (Pataday), a formula that enhances the effects of olopatadine 0.1% with a longer duration of action. Unlike other ocular allergy medications, just one dose of olopatadine 0.2% provides

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Spreading agents

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24 hours of relief from ocular allergy symptoms, an added benefit that could improve patient compliance.

"I anticipate using Pataday for allergic conjunctivitis, atopic conjunctivitis, seasonal and perennial allergies — the same indications as Patanol," says Terry Kim, M.D., associate director for cornea and refractive surgery at the Duke University Eye Center, in Durham, NC. "Studies show Pataday has an immediate onset of action. I don't know of any patient who doesn't react well to Patanol," Dr. Kim added. "I expect the same excellent response to Pataday. Children and contact lens wearers also should benefit from single dosing as well as people who must take several other medications in addition to their eye drops."

In a 2006 study, published in *Investigative Ophthalmology & Visual Science*, comparing olopatadine 0.1% and olopatadine 0.2% with several other topical antiallergy drugs, the 0.2% formula showed a "superior ability to inhibit histamine-induced conjunctival vascular permeability."

Other studies report that olopatadine 0.2% significantly reduced mean itching scores and chemosis, and was found to be safe and well-tolerated. "I stress the fact that Patanol is very safe and highly effective, which is not all that common in a medication," Dr. Zitt says. "Patients can use Patanol and, therefore, Pataday with a high degree of self-assuredness."

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Glaucoma: A Patient-friendly Solution

Compliance remains a big issue among glaucoma patients who must instill medications daily to lower IOP. For that reason, the latest research on travoprost 0.004% (Travatan) is particularly good news. A study published in the *American Journal of Ophthalmology* in 2006 showed that travoprost 0.004% helped sustain lower IOP readings than latanoprost 0.005% (Xalatan) over a 24-hour period. Even better news for physicians who've heard complaints of eye irritation from patients using travoprost 0.004%, is the introduction of travoprost 0.004% made without the preservative benzalkonium chloride (BAK). A recent study shows the BAK-free formulation of travoprost 0.004% (Travatan Z) is equally safe and effective in reducing IOP while avoiding the risk of BAK-induced inflammatory dry eye and other ocular surface complications.

"The BAK-free formulation doesn't irritate the eye or provoke allergic reactions in the same manner as the previous formula," says Alan Robin, M.D., associate professor of ophthalmology at the Wilmer Eye Institute at Johns Hopkins University School of Medicine, in Baltimore. The ionic-buffered preservative system called *sof*Zia is what makes the new formulation less damaging to the ocular surface. Dr. Robin, who uses BAK-free travoprost 0.004% in his practice, says patients also benefit from the Travatan Dosing Aid (TDA), a unique device that helps patients instill the medication into their eyes.

The TDA makes things simpler for patients and physicians in several ways. The bottle of BAK-free travoprost 0.004% fits neatly into a tray that uses electronic monitoring to remind patients of the last dose taken and alerts them when it's time to take their medication. The device records the number of doses taken so physicians can retrieve that data. An ergonomic bottle design also prevents patients from wasting the medication. "It encourages compliance by making it much easier for patients to place the drops in their eyes," Dr. Robin says.

The topical prostaglandin analogues do an excellent job of reducing IOP by increasing uveoscleral aqueous outflow, clinicians say. Yet, preliminary research on a new type of treatment suggests it may surpass these drugs in sustaining reduced IOP for a longer period of time.

Anecortave acetate (Retaane), a sub-Tenon's injectable for instance, dramatically lowered IOP in patients with open-angle glaucoma (OAG) in a small Phase 2 investigator-sponsored trial recently conducted by Dr. Robin. A single injection of the drug lowered IOP for as long as 6 months. "The results are very impressive," Dr. Robin notes. One study participant experienced a drop in IOP from 25 mm Hg at baseline to 12 mm Hg at 3 months. In another case, IOP decreased from 24 mm Hg to 15 mm Hg. More research is needed to replicate these results and learn more about the treatment, Dr. Robin says. But as it stands, anecortave acetate holds the promise to eliminate the need for daily IOP-lowering therapies.

NSAIDs: A Better Tool for Retina Care

Nonsteroidal anti-inflammatory drugs (NSAIDs) have long been considered the treatment of choice for postoperative inflammation or cystoid macular edema (CME). Safety concerns and reports of corneal melts led some physicians to stop using NSAIDs in the late 1990s. But new safety information and the introduction of bromfenac ophthalmic solution 0.09% (Xibrom), for instance, and other NSAIDs have provided additional opportunities for their use. Approved by the FDA in March 2005, bromfenac has demonstrated a superior ability to penetrate and remain in the eye longer than other NSAIDs.

"I have used ketorolac tromethamine ophthalmic solution 0.5% (Acular) for CME as my primary therapy," says Jeffrey S. Heier, M.D., a vitreoretinal specialist at Ophthalmic Consultants of Boston. "I've done a lot of research on the drug, and it's very safe. But there are patients who don't respond well to ketorolac, and in those cases I have begun using bromfenac." Patients are likely to be more comfortable with bromfenac's b.i.d. dosing as opposed to ketorolac's q.i.d. schedule, Dr. Heier says. In addition, ketorolac may burn upon instillation; bromfenac doesn't, he added.

David Rho, M.D., clinical associate professor of ophthalmology at University of Medicine and Dentistry of New Jersey, reported at the 2006 American Academy of Ophthalmology annual meeting that bromfenac dosed b.i.d. was at least as effective as either ketorolac or diclofenac sodium 0.1% (Voltaren) dosed q.i.d. for treatment of CME after cataract surgery, as evidenced by visual benefit.[1] "I generally use Xibrom to treat all cases of pseudophakic CME. The data from my study shows that it trends statistically toward superiority over either Acular or Voltaren for treatment of pseudophakic CME."

Other studies show bromfenac can be found in significant concentrations in the aqueous humor more than 12 hours after one dose, and in retinal tissue after 24 hours.[2] Bromfenac also was found to ease pain quickly after cataract surgery.[3] Furthermore, patients who have undergone selective laser trabeculoplasty for glaucoma also can benefit from bromfenac. It increases patient comfort post-op and lowers postsurgical pressure spikes.[4] It also relieves pain after retinal laser treatments, although this is an off-label use.[5]

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Dry Eye: Creating Synergy

Meeting the needs of patients with dry eye often requires a delicate balance of medications to address the evaporation of the lipid and aqueous layers of the tear film due to Sjögren's syndrome or other conditions, and hormonal fluctuations. That's why Soothe Emollient (Lubricant) eye drops from Alimera Sciences are such a welcome addition to the dry eye category, according to physicians.

Soothe, the only multidose, emollient-based artificial tear on the market, works by stabilizing the lipid layer of the tear film, thereby preventing rapid evaporation of the aqueous layer. "I use Soothe in various situations," says Gary Foulks, M.D., director of the ocular surface disease research unit at the University of Louisville Kentucky Lions Eye Center. "When there is a great deal of inflammation, I use Restasis in combination with Systane. I add Soothe to prevent evaporative dry eye or to address an unstable tear film."

Charles C. Ho, M.D., at the Marietta Eye Clinic in Georgia says, "Patients prefer Soothe, in part, because it doesn't sting or burn upon instillation and because it provides lasting relief." To treat allergic dry eye, Dr. Ho combines antihistamines with Soothe. "For many of my female patients in the 50-plus age range, I combine Restasis and Soothe to get the best result," Dr. Ho adds.

The drug diquafosol tetrasodium ophthalmic solution 2% (Prolacria) by Inspire has shown potential to treat dry eye using a different mechanism of action. Diquafosol is a P2Y2 receptor agonist that stimulates fluid and mucin secretion on the ocular surface. A 2004 study, published in *Cornea*, found that diquafosol was "superior to a placebo in reducing corneal staining and dry eye symptoms," but it still fell short of FDA requirements for approval.

"Diquafosol will actually help a tear gland that no longer functions properly," Dr. Ho says, "so I am optimistic about this drug." However, at this point, the review process has stalled. In October 2006, Inspire released a statement saying, "We plan to provide the FDA with additional information to facilitate discussions related to Prolacria."

Full Speed Ahead

Research and development efforts for ocular pharmaceuticals continue to move forward. New drug innovations and new-found uses for tried-and-true therapies will produce a variety of treatments in the allergy, glaucoma, NSAIDs and dry eye categories in 2007 and beyond that will allow physicians to optimize patient care. **OM**

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