OptometryTimesOptometryAlcon

Shire gets FDA nod for Xiidra (lifitegrast) for dry eye

Courtesy of Shire

July 15, 2016
By Gretchyn M. Bailey, NCLC, FAAO, Editor in Chief, Content Channel Director

Lexington, MA—Shire plc obtained U.S. Food and Drug Administration (FDA) approval for Xiidra (lifitegrast ophthalmic solution) 5%, a twice-daily eye drop indicated for the treatment of the signs and symptoms of dry eye disease in adult patients. Shire expects to launch Xiidra in the United States in the third quarter of 2016.

Xiidra is the only prescription eye drop indicated for the treatment of signs and symptoms of dry eye. It joins Restasis (cyclosporine ophthalmic emulsion, Allergan) 0.05%, which since its launch in 2003 had been the only prescription therapy for dry eye. Restasis is indicated to increase tear production in patients whose tear production is presumed to be suppressed due to ocular inflammation associated with keratoconjunctivitis sicca

"The FDA's approval of Shire's Xiidra is the biggest news to hit eye care in quite awhile and the biggest news in the dry eye arena in over a decade," says *Optometry Times* Chief Optometric Editor Ernie Bowling, OD, FAAO. "After countless drugs failed to make it through the FDA pipeline, at long last we have another prescription medication for our dry eye patients. I look forward to offering this medication to my patients, many of whom have long suffered with this disease and have anticipated this drug's approval."

According to Shire, about 16 million adults in the U.S. are diagnosed with dry eye disease.

The company was expecting to hear from the FDA on July 23, which was the Prescription Drug User Fee Act (PDUFA) date—or deadline for the FDA to review a new drug application (NDA).

Bob Dempsey, vice president and head of ophthalmics at Shire, says to have approval come early on July 11 was a tremendous accomplishment by the team and the FDA.

"Xiidra is the first treatment to be approved for both signs and symptoms of dry eye disease," he says. "To meet that extremely high bar is a tremendous accomplishment to address this very common condition.

"I've been involved with Allergan, Inspire, Bausch + Lomb, and now Shire, with the trials and tribulations of the condition in that there's a discordance of signs and symptoms—they often don't run together. It can be a very different development path. It was enhanced by Shire's entrance into the space. We looked at what had been done in previous research and looked at it through a different lens. Symptoms are what's driving patients in to see the optometrist or ophthalmologist."

Newcomer vs. veteran

Milton Hom, OD, FAAO, who consults with both Shire and Allergan and is an *Optometry Times* Editorial Advisory Board member, says that with any new drug comes a lot of questions.

"In one corner, we have the proven option, Restasis. How does Xiidra compare with Restasis? Does Xiidra work for meibomian gland dysfunction? Should Xiidra be a first-line choice instead of artificial tears, or should it be a last resort? Is it compatible with Restasis or Lotemax (loteprednol 0.5%, Bausch + Lomb)? How does it fit into the dry eye algorithm? Which patients does it work with? Which patients doesn't it work with?"

Dr. Hom says the industry should be prepared for a deluge of marketing information.

"I think we are one the cusp of a huge marketing war between the new challenger and the veteran champion. It reminds me of the numbers war between Zymar (gatiifloxacin, Bausch + Lomb) and Vigamox (moxifloxacin, Alcon)," he says.

"We were deluged with study after study showing differences between the two. This new war will have a different flavor. Instead of numbers, it will be an alphabet war: NFK-B, iCAM, LFA, T-cell, MMP-9, etc. It will be all about the intricacies of inflammation. People always want to simplify and simplify. If you think inflammation is complicated now, you ain't seen nothing yet. The dialogue is going to be several levels higher in complexity."

However, he says that patients will benefit the most from a new development to treat dry eye.

"And that's the way it should be," he says.

ODs looking ahead to treating patients

Paul Karpecki, OD, FAAO, was involved with lifitegrast studies OPUS-2, SONATA, and OPUS-3 studies and says Xiidra shows great clinical efficacy with improvement in symptoms close to two weeks after therapy began. That improvement was maintained while patients remained on Xiidra. In addition, corneal staining improved after a month. Burning and/or abnormal taste (dysgeusia) occurred in about one in five patients—most cases were mild and transient.

"I still have patients who say their eyes felt better while in the study (on study drug) than any other time," he says.

Dr. Karpecki is a clinical investigator and consultant for Shire.

Optometry Times Editorial Advisory Board member Ben Gaddie, OD, FAAO, says it's a milestone to see another medication approved for the treatment of dry eye disease.

"The novel mechanism of action for Xiidra builds on our anti-inflammatory armamentarium as another excellent option for the management of this debilitating condition," he says. "I'm excited to gain some clinical experience with Xiidra and hope it will benefit my patients with dry eye disease."

Walt Whitley, OD, FAAO, *Optometry Times* Editorial Advisory Board member, was involved with OPUS-1 and OPUS-2 studies.

"Many investigational drugs attempted but were unable to meet both primary endpoints for symptom and sign," he says. "I think the biggest benefit of Xiidra will be for our patients—it will bring more awareness of dry eye disease, more options for treatment, and more opportunities to address this chronic condition which affects so many."

Dr. Whitley has received honoraria and funding for advisory board, research, and speaking.

Looking at the science

Xiidra is dosed twice per day, approximately 12 hours apart, in each eye. The safety and efficacy of Xiidra was studied in 1,181 patients (of which 1,067 patients received lifitegrast 5%) in four placebo-controlled 12-week trials. Each of the four studies assessed the effect of Xiidra on both the signs and symptoms of dry eye disease at baseline and Weeks Two, Six and 12. Assessment of symptoms was based on change from baseline in patient reported eye dryness score (EDS; 0-100 visual analogue scale). Assessment of signs was based on inferior corneal staining score (ICSS; 0-4 scale).

In all four studies, a larger reduction in EDS was observed with Xiidra at six and 12 weeks. In two of the four studies, an improvement in EDS was seen with Xiidra at two weeks. At Week 12, a larger reduction in ICSS favoring Xiidra was observed in three of the four studies. The most common adverse reactions reported in five to 25 percent of patients were instillation site irritation, altered taste sensation (dysgeusia), and reduced visual acuity.

"The clinical program supporting the approval of Xiidra is the largest for an investigational-stage dry eye disease candidate to date, including more than 2,500 patients," says Edward Holland, MD, professor of clinical ophthalmology at University of Cincinnati and a clinical trial investigator for Xiidra. "The clinical trial program design took into consideration many of the challenges of past dry eye research."

The inflammation associated with dry eye is thought to be primarily mediated by T-cells and associated cytokines. One effect of this process may be increased expression of intracellular adhesion molecule-1 (ICAM-1); ICAM 1 may be overexpressed in corneal and conjunctival tissues in dry eye disease. Lifitegrast is a small-molecule integrin antagonist that binds to the integrin lymphocyte function-associated antigen-1 (LFA-1), a cell surface protein found on leukocytes, and blocks the interaction of LFA-1 with its cognate ligand intercellular adhesion molecule−1 (ICAM−1). LFA−1/ICAM−1 interaction can contribute to the formation of an immunological synapse resulting in T−cell activation and migration to target tissues. In vitro studies demonstrated that lifitegrast may inhibit T−cell adhesion to ICAM−1 in a human T-cell line and may inhibit secretion of inflammatory mediators (cytokines) in human peripheral blood mononuclear cells. The exact mechanism of action of lifitegrast in dry eye disease is not known.