Effectively Treating *Demodex* Blepharitis

The patient journey with XDEMVY (lotilaner ophthalmic solution) 0.25%.

BY LAURA M. PERIMAN, MD

Demodex blepharitis (DB) is dramatically underdiagnosed.[1] An estimated 25 million eye care patients in the United States alone are affected by DB.[1,2] Signs of DB including eyelid redness, collarettes, irritation, and inflammation are commonly overlooked by patients because they are similar to symptoms from other eye conditions.[3] The presence of *Demodex*, however, is important to identify, particularly now that we have such a targeted and specific treatment to address it. Lotilaner ophthalmic solution, 0.25% (XDEMVY, Tarsus Pharmaceuticals) was created specifically to treat DB. It paralyzes and kills *Demodex* mites with a 6-week course of treatment. The drops are taken twice daily in each eye, 12 hours apart.[4]

IDENTIFYING PATIENTS

According to a recent multicenter study, 58% of patients presenting for eye examinations had the presence of collarettes.[1] In my comprehensive clinic, every patient completes a detailed questionnaire. They answer questions about conditions such as facial flushing, dandruff of the scalp or the eyebrows, and a history of significant acne in teenage and early adulthood years. Their answers provide clues that DB may be present. Patients also undergo a careful examination. I ask them to look down so that I can check for collarettes around the lash base; that is the pathognomonic sign for DB.[1,3] I also look for significant inflammation of the lid margin, telangiectasias, redness, thickening, swelling, and cuffing around the eyelash follicle. I also tell them that we have an FDA-approved treatment that kills *Demodex* mites.

Often, patients want to know why they have DB. I reassure them that they've done nothing wrong; these mites just overpopulate in some individuals and create inflammation. I explain it's important for us to work together to reduce the population load with an integrated treatment plan. Depending on the severity of the local-regional problem, I offer an in-office deep clean of the eyelids and lashes, intense pulsed light (IPL) treatments, and, now that it's available, XDEMVY.

In my experience, patients have felt that XDEMVY is tolerable and have seen improvements in lid margin erythema and other signs associated with DB. In both the SATURN-1 and SATURN-2 clinical trials, ~90% of patients reported the drop as neutral to very comfortable.[5] The most common adverse event—in only 10% of patients—was stinging and burning at the instillation site.[4] Additionally, in pivotal trials at Day 43, 19% (N = 212) and 30% (N = 203) of patients receiving XDEMVY in SATURN-1 and SATURN-2, respectively, achieved erythema cure compared to 7% (N = 209) and 9% (N = 209) taking vehicle ($P<0.01$ for both studies).[5]

Some clinicians might feel uneasy talking to patients about *Demodex* mites. It's important to not shy away from the conversation, though, because patients come to us looking for a solution to their problems. There may have been some reluctance talking about DB because we didn't have a definitive way to treat it. Yes, there's lid hygiene to address the collarettes, hypochlorous acid sprays to control the bacterial component of DB, and IPL to kill mites on the face,[6] but nothing was FDA-approved to directly eradicate the mites. Now that we have something to offer them that readily addresses the mites in a 6-week course of treatment, the conversation with patients becomes streamlined. XDEMVY is an easy, straight-line option for patients, targeting the root cause of the disease. It is the only FDA-approved treatment for DB.

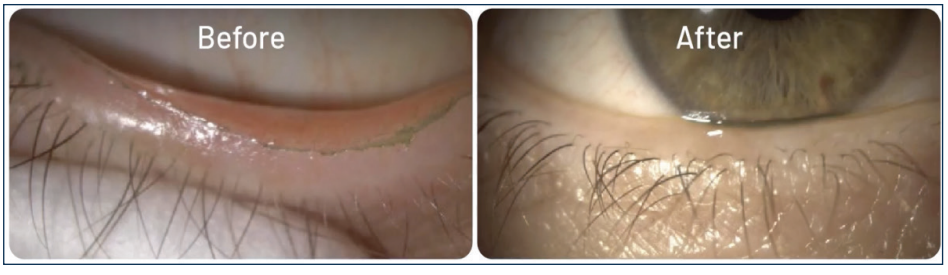

Figure. Scott's pre-treatment (left) and 6 weeks post-treatment (right) case images.

STARTING THE JOURNEY

When I hear patients have tried so hard for so long to control their symptoms, that drives me to look for treatment options. I get excited to follow a patient's journey, especially with XDEMVY because it gets to the root cause of the problem. Scott, one of my longtime patients, initially presented to my clinic with significant eyelid margin redness and a 30-year history of symptoms associated with blepharitis (Figure). I knew it was important to find out whether *Demodex* was present or not. When we confirmed it was, I immediately prescribed XDEMVY and had high hopes that the treatment would improve his irritation and eyelid health. DB can affect patients' daily activities, but we don't always realize it until they come in for treatment.

Taking 10 seconds to ask your patient to look down and look for the presence of collarettes around the lash base is crucial. The presence of collarettes can help us to make

SCOTT'S JOURNEY WITH XDEMVY (LOTILANER OPHTHALMIC SOLUTION) 0.25%

I'm in my early 60s, and I have been dealing with *Demodex* blepharitis for many years. My symptoms came on suddenly in the late 1990s, but no one could tell me what caused them. My eyes became red and swollen toward the edge, and they were constantly bothersome. Eventually, I learned that I had blepharitis, but no one ever used the term *Demodex* blepharitis. The basics of lid hygiene, including using baby shampoo, warm compresses, and eyedrops, seemed to have an impact, but my eyes still bothered me. I had no idea what to do, and nothing provided lasting relief.

About 3 years ago, my symptoms got worse, and I was referred to Dr. Periman. At my first appointment, she handed me a large rubber *Demodex* model that she kept in her office to show patients. That was the most vivid description for me. She explained that *Demodex* blepharitis was inside my eyelash follicles, and it is a chronic condition that can be controlled with lid hygiene, intense pulsed light (IPL), and eyelid cleansers and wipes to reduce the *Demodex* on the rest of my face.

Learning about *Demodex* blepharitis gave me additional insight into what I was dealing with—a mite overgrowth that was causing issues for me. One of the hardest parts about having *Demodex* blepharitis is that you can't hide it. My eyelids were red, irritated, and inflamed. The constant maintenance was also an issue. I cleaned my eyelids at least twice a day with tea tree oil and used hypochlorous sprays several times a day. I had IPL on a regular schedule, and I used ivermectin cream on my face.

Dr. Periman told me about the FDA approval and availability of lotilaner ophthalmic solution 0.25% (XDEMVY, Tarsus Pharmaceuticals). I was so excited to hear that an FDA-approved treatment was available to treat the root cause of my disease.

I love the fact that it is easy to use and fits easily into my daily routine. I simply instill a drop in each eye in the morning when I first wake up and again at night before bedtime.

Early on, I had the suspicion that something was happening. My lid margin was less inflamed, and I wasn't rubbing my eyes as often. When you've been living with *Demodex* blepharitis for as long as I have, these improvements are a fabulous thing.

In just 6 weeks, XDEMVY reduced my eyelid redness.

a recommendation to treat DB in a targeted, specific, efficient manner with XDEMVY.

TARGETED TREATMENT

Treatment for DB should be tailored to the individual patient and account for the severity of their disease and any comorbid conditions. XDEMVY provides a direct solution to treating patients' *Demodex* blepharitis. I plan on using the medication anytime I see appropriate patients who report symptoms and have telltale signs, including lid thickening, redness of the lid, and collarettes at the lash base. We have treated about 100 DB cases since XDEMVY was approved by the FDA, and we are impressed with the clinical results.

It's important to set expectations and ensure patients understand there is no single treatment that will fix all possible symptoms. However, I am excited that we have a targeted way to eradicate *Demodex* mites in the eyelashes and on the eyelids. Before XDEMVY became available, we could reduce the mite load around the eyes but never on the eyelids. Now, we can target the mites in *Demodex* blepharitis directly with XDEMVY. ■

1. Trattler W, Karpecki P, Rapoport Y, et al. The prevalence of Demodex blepharitis in US eye care clinic patients as determined by collarettes: a pathognomonic sign. *Clin Ophthalmol*. 2022;16:1153-1164.
2. O'Dell L, Dierker DS, Devries DK, et al. Psychosocial impact of demodex blepharitis. *Clin Ophthalmol*. 2022:16; 2979-2987.
3. Rhee MK, Yeu E, Barnett M, et al. Demodex blepharitis: a comprehensive review of the disease, current management, and emerging therapies. *Eye Contact Lens*. 2023;49(8):311-318.
4. XDEMVY [prescribing information]. Tarsus Pharmaceuticals, Inc; 2023.
5. Yeu E, Mun J, Vollmer P, et al. Treatment of Demodex blepharitis with lotilaner ophthalmic solution. 0.25%: combined analysis of two pivotal randomized, vehicle-controlled, multicenter trials. Saturn-1 and Saturn-2 combined data. Paper presented at: ARVO 2023; April 23-27, 2023; New Orleans, LA.
6. Fishman HA, Periman LM, Shah AA. Real-time videu microscopy of in vitro Demodex death by intense pulsed light. *Photobiomodul Photomed Laser Surg*. 2020;38(8):472-476.

LAURA M. PERIMAN, MD

- Director of Dry Eye Services and Clinical Research, Periman Eye Institute, Seattle, Washington
- dryeyemaster@gmail.com; X (formerly Twitter), Instagram, and YouTube @DryEyeMaster
- Financial disclosure: Clinical investigator, consultant, and speaker (Tarsus Pharmaceuticals)

XDEMVY™ (lotilaner ophthalmic solution) 0.25%, for topical ophthalmic use

BRIEF SUMMARY OF PRESCRIBING INFORMATION
Please see the XDEMVY™ package insert for full Prescribing Information.

INDICATIONS AND USAGE
XDEMVY is indicated for the treatment of *Demodex* blepharitis.

CONTRAINDICATIONS
None.

WARNINGS AND PRECAUTIONS
Risk of Contamination Do not allow the tip of the dispensing container to contact the eye, surrounding structures, fingers, or any other surface in order to minimize contamination of the solution. Serious damage to the eye and subsequent loss of vision may result from using contaminated solutions.

Use with Contact Lenses Contact lenses should be removed prior to instillation of XDEMVY and may be reinserted 15 minutes following its administration.

ADVERSE REACTIONS
Because clinical studies are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

XDEMVY was evaluated in 833 patients with *Demodex* blepharitis in two randomized, double-masked, vehicle-controlled studies (Saturn-1 and Saturn-2) with 42 days of treatment. The most common ocular adverse reaction observed in controlled clinical studies with XDEMVY was instillation site stinging and burning which was reported in 10% of patients. Other ocular adverse reactions reported in less than 2% of patients were chalazion/hordeolum and punctate keratitis.

USE IN SPECIFIC POPULATIONS
Pregnancy: Risk Summary There are no available data on XDEMVY use in pregnant women to inform any drug associated risk; however, systemic exposure to lotilaner from ocular administration is low. In animal reproduction studies, lotilaner did not produce malformations at clinically relevant doses.

Data *Animal Data* In an oral embryofetal developmental study in pregnant rats dosed during organogenesis from gestation days 6-19, increased post-implantation loss, reduced fetal pup weight, and incomplete skeletal ossification were observed at 50 mg/kg/day (approximately 1390 times the recommended human ophthalmic dose (RHOD) on a body surface area basis) in the presence of maternal toxicity (i.e., decreased body weight and food consumption). A rare malformation of situs inversus of the thoracic and abdominal viscera occurred in 1 fetus from a pregnant rat receiving 50 mg/kg/day; whether this finding was treatment-related could not be excluded. No maternal or embryofetal toxicity was observed at 18 mg/kg/day (approximately 501 times the RHOD on a body surface area basis). In an oral embryofetal development study in pregnant rabbits dosed during organogenesis from gestation days 7-19, no embryofetal toxicity or teratogenic findings were observed at 20 mg/kg/day (approximately 580-times the RHOD on an AUC basis), even in the presence of maternal toxicity (i.e., decreased food consumption and body weight).

In an oral two-generation reproductive toxicity study, F0 male and female rats were administered lotilaner at doses up to 40 mg/kg/day for 10 weeks before pairing and during the 2-week pairing period (3 weeks for males). Dosing for F0 females continued through lactation day 22. F1 male and female rats were administered lotilaner at 1 and 5 mg/kg/day post-weaning from day 23 for 10 weeks before pairing and during the 2-week pairing period (3 weeks for males). Dosing for F1 parenteral females continued through lactation day 22. There were no clear adverse effects on the F1 generation, and a slightly lower mean body weight during lactation was noted for F2 pups at 5 mg/kg/day. The no observed adverse effect level (NOAEL) was determined to be 5 mg/kg/day (approximately 139 times the RHOD on a body surface area basis).

Lactation: Risk Summary There are no data on the presence of XDEMVY in human milk, the effects on the breastfed infant, or the effects on milk production. However, systemic exposure to lotilaner following 6 weeks of topical ocular administration is low and is >99% plasma protein bound, thus it is not known whether measurable levels of lotilaner would be present in maternal milk following topical ocular administration. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for XDEMVY and any potential adverse effects on the breast-fed child from XDEMVY.

Pediatric Use: Safety and effectiveness in pediatric patients below the age of 18 years have not been established.

Geriatric Use: No overall differences in safety or effectiveness have been observed between elderly and other adult patients.

NONCLINICAL TOXICOLOGY
Carcinogenesis, Mutagenesis, Impairment of Fertility
Carcinogenesis Long-term studies in animals have not been performed to evaluate the carcinogenic potential of lotilaner.

Mutagenesis Lotilaner was not genotoxic in the following assays: Ames assay for bacterial gene mutation, *in vitro* chromosomal aberration assay in cultured human peripheral blood lymphocytes, and *in vivo* rat micronucleus test.

Impairment of fertility In a two-generation study of reproductive performance in rats, F0 male and female rats were administered lotilaner at oral doses of 40 mg/kg/day for 80 days reduced to 20 mg/kg/day for 47-50 supplementary days. Reduced pregnancy rates and decreased implantation rates were observed in F0 females at doses 20 mg/kg/day) (approximately 556 times the RHOD on a body surface area basis), which were also associated with maternal toxicity (i.e., decreased body weight and food consumption). No effects on fertility were observed in F0 females at the dose of 5 mg/kg/day (approximately 139 times the MRHOD on a body surface area basis). No effects on fertility were observed in F0 males at the oral dose of 20 mg/kg/day (approximately 556 times the RHOD on a body surface area basis), and no effects on fertility were observed in F1 males and females at the oral dose of 5 mg/kg/day (approximately 139 times the RHOD on a body surface area basis).

PATIENT COUNSELING INFORMATION
Handling the Container Instruct patients to avoid allowing the tip of the dispensing container to contact the eye, surrounding structures, fingers, or any other surface in order to minimize contamination of the solution. Serious damage to the eye and subsequent loss of vision may result from using contaminated solutions.

When to Seek Physician Advice Advise patients that if they develop an intercurrent ocular condition (e.g., trauma or infection), have ocular surgery, or develop any ocular reactions, particularly conjunctivitis and eyelid reactions, they should immediately seek their physician's advice concerning the continued use of XDEMVY.

Use with Contact Lenses Advise patients that XDEMVY contains potassium sorbate, which may discolor soft contact lenses. Contact lenses should be removed prior to instillation of XDEMVY and may be reinserted 15 minutes following its administration.

Use with Other Ophthalmic Drugs Advise patients that if more than one topical ophthalmic drug is being used, the drugs should be administered at least 5 minutes between applications.

Missed Dose Advise patients that if one dose is missed, treatment should continue with the next dose.

RX only

US--2300345 9/23