Lotilaner Ophthalmic Solution (XDEMVY)
National Drug Mini-monograph
January 2024

VA Pharmacy Benefits Management Services, Medical Advisory Panel, and VISN Pharmacist Executives

The purpose of VA PBM Services drug monographs is to provide a focused drug review for making formulary decisions. Updates will be made if new clinical data warrant additional formulary discussion. The Product Information or other resources should be consulted for detailed and most current drug information.

FDA APPROVAL

Description / MOA	Anti-parasitic: causes spastic paralysis in ectoparasites resulting in death
Indication Under Review[1]	Treatment of Demodex blepharitis
Dosage Regimen	One drop in each eye twice daily for 6 weeks
Dosage Forms Under Review	Ophthalmic solution, 0.25%, 10 mL bottle

EFFICACY CONSIDERATIONS

Trial	**Saturn-1**	**Saturn-2**
Design	Phase 2b/3, multicenter, double-blind, vehicle-controlled RCT - Primary outcome: % subjects cured based on collarette score zero at day 43 - Secondary: eradication of *Demodex* mites from eyelid margin, erythema cure (post-hoc)	Phase 3, multicenter, double-blind, vehicle-controlled RCT - Primary outcome: % subjects cured based on collarette score zero at day 43 - Secondary: eradication of *Demodex* mites from eyelid margin, **erythema score 0**, elimination of collarettes and erythema of eyelid
Population	Adults with evidence of significant *Demodex* infection*	Adults with evidence of significant *Demodex* infection*
Intervention	1 drop lotilaner or inactive vehicle in each eye twice daily for 43 days	1 drop lotilaner or inactive vehicle in each eye twice daily for 43 days
Results	411 subjects who completed study, mean age 67 yrs., 43% male, 91% white. Collarette scores, eyelid erythema and mite density comparable. **Cure: 44% lotilaner vs. 7% vehicle** **Mite eradication: 68% vs. 17%** **Erythema cure: 19% vs 7%**	412 subjects randomized, mean age 64 yrs., 51% male, 88% white. Collarette scores, eyelid erythema and mite density comparable. **Cure: 56% lotilaner vs. 13% vehicle (p<0.0001)** **Mite eradication: 52% vs. 15% (p<0.0001)** **Erythema cure: 31% vs 9% (p<0.0001)**

**Significant Demodex infection defined as each of the following in at least 1 eye: > 10 lashes with collarettes on upper eyelid (collarette score ≥ 2); at least mild erythema of upper eyelid margin; and Demodex density, upper and lower eyelids combined, ≥ 1.5 mites per lash.*

SAFETY CONSIDERATIONS

Boxed Warnings	None
Contraindications	None
Other Warnings	Risk of contamination – do not allow tip of container to contact eye, fingers, or other surfaces. Contact lenses should be removed prior to instillation -may be reinserted 15 minutes after administration
Common Adverse events	Installation site stinging and burning in 10% of patients (7% with vehicle). Chalazion/hordeolum and punctate keratitis in less than 2% and were similar in vehicle group SATURN-2: ocular treatment-emergent AE in 19% Lotilaner vs. 12% control patients. None were considered serious.
Drug Interactions	None

ALTERNATIVE THERAPY

DRUG	VANF	GUIDELINES
Lotilaner	NF	Incidence of Demodex blepharitis unclear but thought to be common and underdiagnosed. Often chronic and recurrent with goal to manage symptoms rather than cure, but no clear consensus about optimal management.
Tea tree oil and derivatives (terpinen 4-ol)	NF	Available as OTC and prescription formulations (gel, shampoo, ointment, lid wipe/scrub) No clear regimen or concentration and side effects of ocular irritation, allergy and contact dermatitis, particularly with higher concentration preparations. May be toxic to meibomian gland cells.
Blepharoexfoliation	NF	Done in-office and typically combined with daily at-home eyelid hygiene
Topical ivermectin + metronidazole gel	NF	Single small RCT – compounded product vs. placebo applied 3 times: day 1, 15 and day 30 associated with marked improvement in redness and mite density by 30 days No mention of adverse events
Oral ivermectin +/- metronidazole	PA-F	Single RCT showed improvement in mite density with ivermectin alone and in combination with metronidazole with combination showing greater reduction No mention of adverse events, but systemic therapy

VHA PLACE IN THERAPY

Potential Use in VHA

1. Blepharitis is a common ophthalmologic condition that is typically incurable and is managed symptomatically with good lid hygiene (warm compresses with massage, eyelid cleansing, hypochlorous acid or tea tree oil lid scrubs, , antibiotics and topical anti-inflammatory agents).
2. Demodex species are commonly found on human skin, with increasing frequency by age, but are suggested may be pathogenic in some patients with non-responding blepharitis but their overall role in blepharitis is unclear. Of note, patients with evidence of ocular rosacea have a higher incidence of *Demodex* blepharitis and may benefit from earlier treatment to avoid topical steroids over a longer term.
3. Currently no FDA approved alternatives exist for management of blepharitis due to *Demodex spp.*
4. Good lid hygiene, tea tree oil wipes, systemic or topical ivermectin and/or systemic or topical metronidazole have been used to treat *Demodex* blepharitis although evidence is limited. Other options are in office procedures such as blepharoexfoliation.
5. Lotilaner offers a convenient topical therapy that has been shown to be more effective than placebo at reduction of mites, cure by collarette scores and erythema. Observation of mites or evidence of persistent symptomatic blepharitis, such as scrub/debris in tear film, blocked meibomian glands or eroded lid margins that persists in symptomatic patients after failure of conservative measures may help identify patients most likely to benefit from lotilaner. In some cases, earlier use may be warranted in those unable to reliably use conservative measures (e.g., homeless patients).
6. Given the specificity, use should be restricted to eye specialists (optometrists and ophthalmologists) to use after other measures for blepharitis have been ineffective, in patients with documented *Demadex spp* or pathognomonic findings (collarettes).

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References

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3. Gaddie I, Donnenfeld E, Karpecki P, et al. Lotilaner ophthalmic solution 0.25% for *Demodex* blepharitis. Randomized, vehicle-controlled, multicenter, phase 3 trial (SATURN-2). *Ophthalmology* 2023;130(10):1015-23.
4. Ayres B, Donnenfeld E, Farid M, et al. Clinical diagnosis and management of *Demodex* blepharitis: the *Demodex* expert panel on treatment and eyelid health (DEPTH). *Eye* 2023;37:3249-55.
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6. Blepharitis Preferred Practice Patterns. American Academy of Ophthalmology. November 2018. *Blepharitis PPP-2018 - American Academy of Ophthalmology (aao.org)*