BlueCross BlueShield Arizona

An Independent Licensee of the Blue Cross Blue Shield Association

PHARMACY COVERAGE GUIDELINE

XDEMVY™ (lotilaner) ophthalmic solution Generic Equivalent (if available)

This Pharmacy Coverage Guideline (PCG):
- Provides information about the reasons, basis, and information sources we use for coverage decisions
- Is not an opinion that a drug (collectively "Service") is clinically appropriate or inappropriate for a patient
- Is not a substitute for a provider's judgment (Provider and patient are responsible for all decisions about appropriateness of care)
- Is subject to all provisions e.g. (benefit coverage, limits, and exclusions) in the member's benefit plan; and
- Is subject to change as new information becomes available.

Scope
- This PCG applies to Commercial and Marketplace plans
- This PCG does not apply to the Federal Employee Program, Medicare Advantage, Medicaid or members of out-of-state Blue Cross and/or Blue Shield Plans

Instructions & Guidance
- To determine whether a member is eligible for the Service, read the entire PCG.
- This PCG is used for FDA approved indications including, but not limited to, a diagnosis and/or treatment with dosing, frequency, and duration.
- Use of a drug outside the FDA approved guidelines, refer to the appropriate Off-Label Use policy.
- The "Criteria" section outlines the factors and information we use to decide if the Service is medically necessary as defined in the Member's benefit plan.
- The "Description" section describes the Service.
- The "Definition" section defines certain words, terms or items within the policy and may include tables and charts.
- The "Resources" section lists the information and materials we considered in developing this PCG
- **We do not accept patient use of samples as evidence of an initial course of treatment, justification for continuation of therapy, or evidence of adequate trial and failure.**
- Information about medications that require prior authorization is available at www.azblue.com/pharmacy. You must fully complete the request form and provide chart notes, lab workup and any other supporting documentation. The prescribing provider must sign the form. Fax the form to BCBSAZ Pharmacy Management at (602) 864-3126 or email it to Pharmacyprecert@azblue.com.

Criteria:

➢ **Criteria for initial therapy:** Xdemvy (lotilaner) and/or generic equivalent (if available) is considered ***medically necessary*** and will be approved when **ALL** the following criteria are met:

1. Prescriber is a physician specializing in the patient's diagnosis or is in consultation with an Ophthalmologist or Optometrist

2. Individual is 18 years of age or older

3. Individual has a confirmed diagnosis (by the presence of *Demodex* mites on microscopic examination) of *Demodex* blepharitis

4. Individual has the presence of **ALL** of the following in at least one eye:

a. *Demodex* infestation with more than 10 lashes with collarettes present on the upper lid (collarette scale grade 2 or worse)
b. At least mild erythema of the upper eyelid margin
c. Average mite density of ≥1.5 mites per lash (upper and lower eyelids combined)

5. **If available:** Individual has failure after adequate trial, contraindication per FDA label, intolerance, or is not a candidate for a **generic equivalent** [Note: Failure, contraindication or intolerance to the generic should be reported to the FDA] (see Definitions section)

6. Individual has documented failure, contraindication per FDA label, intolerance, or is not a candidate for **ONE** the following:
   a. Ivermectin (oral or topical)
   b. Metronidazole (oral or topical)
   c. Ivermectin with metronidazole (oral or topical)

Initial approval duration: 6 months

- **Criteria for continuation of coverage (renewal request):** Xdemvy (lotilaner) and/or generic equivalent (if available) is considered ***medically necessary*** and will be approved when **ALL** the following criteria are met **(samples are not considered for continuation of therapy)**:

1. Individual continues to be seen by a physician specializing in the patient's diagnosis or is in consultation with an Ophthalmologist or Optometrist

2. Individual's condition has responded while on therapy with response defined as **TWO** of the following:
   a. Documented improvement in lids showing a reduction of collarettes to no more than 2 collarettes per upper lid
   b. Documented mite eradication showing a mite density of 0 mites/lash
   c. Documented erythema cure showing as Grade 0
   d. Documentation of no more than 2 collarettes **and** absence of erythema of upper lid

3. Individual has been adherent with the medication

4. **If available:** Individual has failure after adequate trial, contraindication per FDA label, intolerance, or is not a candidate for a **generic equivalent** [Note: Failure, contraindication or intolerance to the generic should be reported to the FDA] (see Definitions section)

Renewal duration: 12 months

- Criteria for a request for non-FDA use or indication, treatment with dosing, frequency, or duration outside the FDA-approved dosing, frequency, and duration, refer to one of the following Pharmacy Coverage Guideline:

1. **Off-Label Use of Non-Cancer Medications**

2. **Off-Label Use of Cancer Medications**

PHARMACY COVERAGE GUIDELINE

XDEMVY™ (lotilaner) ophthalmic solution Generic Equivalent (if available)

Description:

Xdemvy (lotilaner) is an ectoparasiticide (anti-parasitic) indicated for the treatment of *Demodex* blepharitis. Lotilaner ophthalmic solution, 0.25% (TP-03), is an acaricide of the isoxazoline parasiticide class. Lotilaner is a veterinary medication for the treatment of ticks and fleas in pets is now approved for human use.

Xdemvy (lotilaner) is a gamma-aminobutyric acid (GABA)-gated chloride channel inhibitor selective for mites. Inhibition of these GABA chloride channels causes a paralytic action in the target organism leading to its death. Lotilaner is not an inhibitor of mammalian GABA mediated chloride channels.

Demodex mites are a common microscopic ectoparasite found on the human skin. *Demodex* blepharitis is a common disease of the eyelid. Two species have been identified: *Demodex folliculorum* and *Demodex brevis*. In the eyelids, *D. folliculorum* can be found in the lash follicle, whereas *D. brevis* is found in sebaceous glands and meibomian glands. The presence of collarettes (waxy solidified exudative excretions that form a cylindrical collar around the base of the eyelash follicle) are said to be pathognomonic for Demodex blepharitis. The collarettes are also referred to in the literature as cylindrical dandruff (CD), sleeves, cuffs, crusting, or lash debris. The presence of collarettes is indicative of *Demodex* mites and a high number of collarettes has been associated with more severe mite infestation.

Blepharitis, rosacea, diabetes, and increasing age are risk factors for *Demodex* blepharitis. Other factors that may predispose people to *Demodex* blepharitis include local or systemic immunosuppression, stress, higher alcohol intake, greater sun exposure, and smoking. Dermatology literature suggests that *Demodex* may also be associated with a multitude of skin conditions beyond rosacea, including acne vulgaris, seborrheic dermatitis, and basal cell and sebaceous carcinoma.

Ocular itching is the symptom most commonly associated with *Demodex* blepharitis and evidence suggests that patients consider ocular itching to be one of the most bothersome symptoms associated with the disease. *Demodex*-related itching occurs at night or early morning after periods of mite activity. In addition to itching, often present with a range of other symptoms, including dryness, discharge, eye redness, burning, tearing, foreign body sensation, pain, and blurred (or fluctuating) vision.

In the decades since *Demodex* blepharitis was first identified, many agents have been evaluated to better manage the disease, including selenium, antiparasitics, topical and oral antibiotics, and many naturally derived products.

Ivermectin and metronidazole have long been used safely to treat *Demodex*-related skin conditions. A recent meta-analysis reported that the combination of systemic and topical ivermectin and metronidazole had been shown to reduce mite counts in *Demodex* blepharitis. Both ivermectin (oral or topical) and metronidazole (oral or topical) are established treatments that improves signs and symptoms and reduces mite density. Ivermectin is known to have an acaricidal (destructive or fatal) effect on mites and ticks, and metronidazole has a broad anti-inflammatory effect through neutrophil-mediated reduction of reactive oxygen species and T lymphocytes.

In a recent study of lotilaner ophthalmic solution, 0.25%, for *Demodex* blepharitis, collarettes were graded separately for the upper and lower eyelids according to a quantitative scale. Grade 2 (>10 collarettes) or higher on this scale for the upper eyelid was required for inclusion in the study. Grade 0, or “collarette cure,” was considered the primary outcome measure, whereas a reduction in collarettes to 10 lashes or less (grade 0 or 1) was considered clinically meaningful because this level of change in collarettes had previously been associated with reduced mite density.

PHARMACY COVERAGE GUIDELINE

XDEMVY™ (lotilaner) ophthalmic solution
Generic Equivalent (if available)

Definitions:

U.S. Food and Drug Administration (FDA) MedWatch Forms for FDA Safety Reporting
MedWatch Forms for FDA Safety Reporting | FDA

Collarette Grading Scale	
0	0–2 lashes with collarettes
1	3–10 lashes with collarettes
2	>10 but less than one third of lashes with collarettes
3	One third of lashes or more but less than two thirds of lashes with collarettes
4	Two thirds or more of lashes with collarette
Grade 0 is considered “collarette cure” Reduction in collarettes to 10 lashes or less (Grade 0 or 1) is considered clinically meaningful due to a reduction in mite density	

Lid Margin Erythema Grading Scale	
0 = None	Normal age-related lid coloration
1 = Mild	Pink capillary involvement along the lid edge, no patches of confluent capillary redness throughout the lid edge
2 = Moderate	Deep pink or red confluent capillary redness present locally along the lid edge
3 = Severe	Deep red, diffuse confluent capillary redness present along the lid edge

Resources:

Xdemvy (lotilaner) product information, revised by Tarsus Pharmaceuticals 07-2023. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed August 14, 2024.

Shtein RM. Belphariris. In: UpToDate, Jacobs DS, Li H (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Literature current through August 2024. Topic last updated on August 20, 2024. Accessed September 30, 2024.

Liua J, Shehaa H,Tseng SCG. Pathogenic role of Demodex mites in blepharitis. Curr Opin Allergy Clin Immunol. 2010 October; 10(5): 505–510. doi:10.1097/ACI.0b013e32833df9f4. Accessed November 08, 2023. Re-evaluated September 30, 2024.

Navela V, Mulliezb A, d’Azya CB, et al.: Efficacy of treatments for Demodex blepharitis: A systematic review and meta-analysis. Ocular Surface 2019 Oct;17(4): 655-669. https://doi.org/10.1016/j.jtos.2019.06.004. Accessed November 09, 2023. Re-evaluated September 30, 2024.

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 Aug;49 (8): 311–318. doi:10.1097/ICL.0000000000001003. Accessed November 08, 2023. Re-evaluated September 30, 2024.

Yeu E, Wirta DL, Karpecki P, et al.: Lotilaner Ophthalmic Solution, 0.25% for the Treatment of Demodex Blepharitis: Results of a Prospective, Randomized, Vehicle-Controlled, Double-Masked, Pivotal Trial (Saturn-1). Cornea 2023;42(4):435–443 doi:10.1097/ICO.0000000000003097. Accessed November 08, 2023. Re-evaluated September 30, 2024.

Gaddie IB, Donnenfeld ED, Karpecki P, et al.: Lotilaner Ophthalmic Solution 0.25% for Demodex Blepharitis Randomized, Vehicle-Controlled, Multicenter, Phase 3 Trial (Saturn-2). Ophthalmology 2023 Oct; 130 (10):1015-1023. doi:10.1016/j.ophtha.2023.05.030. Accessed November 08, 2023. Re-evaluated September 30, 2024.