Policy and Procedure	
PHARMACY PRIOR AUTHORIZATION POLICY AND CRITERIA ORPTCTOP028.0625	**TOPICAL PRODUCTS** **OXERVATE®** (cenegermin-bkbj ophthalmic solution 0.002%)
Effective Date: 8/1/2025	**Review/Revised Date**: 03/19, 10/19, 09/20, 05/21, 05/22, 05/23, 04/24, 04/25 (MTW)
Original Effective Date: 06/19	**P&T Committee Meeting Date**: 04/19, 12/19, 12/20, 06/21, 06/22, 06/23, 06/24, 06/25
Approved by: Oregon Region Pharmacy and Therapeutics Committee	

SCOPE:
Providence Health Plan and Providence Health Assurance as applicable (referred to individually as "Company" and collectively as "Companies").

APPLIES TO:
Commercial
Medicaid

POLICY CRITERIA:

COVERED USES:
All Food and Drug Administration (FDA) approved indications not otherwise excluded from the benefit.

REQUIRED MEDICAL INFORMATION:
1. Patient has a diagnosis of stage 2 (recurrent/persistent epithelial defect) or stage 3 (corneal ulcer) neurotrophic keratitis in the affected eye(s) with diagnosis supported by chart notes
2. For Commercial only: Patient is refractory to at least one conventional treatment for neurotrophic keratitis (such as preservative-free artificial tears/gels/ointment, topical antibiotic eye drops, autologous serum tears/umbilical cord serum drops/platelet rich plasma drops, therapeutic contact lenses, amniotic membrane transplant, tarsorrhaphy)
3. The request specifies the affected eye(s) intended for treatment

EXCLUSION CRITERIA:
Retreatment of the same eye

AGE RESTRICTIONS: N/A

PRESCRIBER RESTRICTIONS:
Must be prescribed by or in consultation with an ophthalmologist or optometrist

COVERAGE DURATION:

Initial authorization will be approved for eight weeks, an additional eight weeks will be covered for treatment of the second eye when appropriate. Reauthorization will not be renewed for retreatment of the same eye.

QUANTITY LIMIT:
Cenegermin-bkbj ophthalmic solution 0.002% (Oxervate®): 1 mL (one vial) per day (If both eyes are being treated a quantity of 2 mL (two vials) a day will be allowed)

Requests for indications that were approved by the FDA within the previous six (6) months may not have been reviewed by the health plan for safety and effectiveness and inclusion on this policy document. These requests will be reviewed using the New Drug and or Indication Awaiting P&T Review; Prior Authorization Request ORPTCOPS047.

Requests for a non-FDA approved (off-label) indication requires the proposed indication be listed in either the American Hospital Formulary System (AHFS), Drugdex, or the National Comprehensive Cancer Network (NCCN) and is considered subject to evaluation of the prescriber's medical rationale, formulary alternatives, the available published evidence-based research and whether the proposed use is determined to be experimental/investigational.

Coverage for Medicaid is limited to a condition that has been designated a covered line item number by the Oregon Health Services Commission listed on the Prioritized List of Health Care Services.

Coverage decisions are made on the basis of individualized determinations of medical necessity and the experimental or investigational character of the treatment in the individual case.

INTRODUCTION:
Cenegermin-bkbj ophthalmic solution (Oxervate®) is a recombinant form of human nerve growth factor. Nerve growth factor is an endogenous protein involved in the differentiation and maintenance of neurons, which acts through specific high-affinity and low-affinity nerve growth factor receptors in the anterior segment of the eye to support corneal innervation and integrity.

FDA APPROVED INDICATIONS:
Treatment of neurotrophic keratitis

POSITION STATEMENT:

- Neurotrophic keratitis is a rare degenerative disease resulting from corneal anesthesia, which causes progressive damage to the top layer of the cornea. Corneal impairment due to loss of corneal sensation includes corneal thinning, ulceration, and perforation in severe cases. Patients may develop bacterial infections. If neurotrophic keratitis is not treated, it will progress in severity which can lead to vision loss. Neurotrophic keratitis can be caused by any condition affecting the trigeminal nerve or its branches that lead to a loss of corneal sensation. The most common causes are herpes simplex and herpes zoster viral

infections, followed by trigeminal neuralgia surgery and acoustic neuroma. Toxicity from chronic use of topical ocular medications also may cause nerve damage and corneal anesthesia. Patients with diabetes can also develop neurotrophic keratitis.

- Cenegermin-BKBJ (Oxervate®) is now the first FDA approved treatment for neurotrophic keratitis. Prior to the approval of Oxervate® treatment consisted of supportive care, off-label pharmacologic treatment, and surgical intervention. Treatment typically varies by severity/stage and surgical care may be necessary in stage 2 or 3 neurotrophic keratitis.
    - **Stage 1 disease:**
        - Discontinue any topical ocular therapies, especially those that can decrease corneal sensitivity (for example, timolol, betaxolol, sulfacetamide, diclofenac, ketorolac) or that contain preservatives.
        - Optimal treatments may include: preservative-free artificial tears, gels, and ointments, punctal occlusion, and autologous serum tears/umbilical cord serum drops/platelet rich plasma drops
    - **Stage 2 disease:**
        - Stage 1 treatment options
        - Prophylactic antibiotic drops (for example, topical tetracycline)
        - Oral tetracycline (250 mg PO bid) or doxycycline (100 mg PO every other day) may be used and has shown reduce the amount of mucus produced
        - Topical cycloplegia with atropine 1% or scopolamine 0.25% once daily in the presence of anterior chamber inflammation
        - Topical cenegermin (Oxervate®) 6 drops daily
        - Corneal therapeutic contact lenses, fresh-frozen self-retained amniotic membrane
        - Patients are more likely to require surgical intervention
    - **Stage 3 disease:**
        - Stage 1 and 2 treatment options
        - Most patients will need surgical intervention
        - Synthetic tissue adhesive, tarsorrhaphy, amniotic membrane transplant, and corneal neurotization
        - In cases of stromal melting, topical collagenase inhibitors such as N-acetylcysteine, tetracycline or medroxyprogesterone may be administered
- The safety and efficacy of cenegermin was based on two randomized vehicle controlled eight-week clinical studies of 151 patients with stage 2 and 3 neurotrophic keratitis.
    - Study NGF0212 looked at patients with disease in one eye; 72.0% of patients experienced complete corneal healing with cenegermin vs. 33.3% with vehicle (difference: 38.7% [95% CI: 20.7%, 56.6%]; $p < 0.01$).

  - Study NGF0214 looked at patients with disease in both eyes; 65.2% of patients experienced complete corneal healing with cenegermin vs 16.7% with vehicle (difference: 48.6% [95% CI: 24%, 73.1%]; p < 0.01).
- Cenegermin (Oxervate®) represents a new treatment option for patients with Stage 2 and Stage 3 neurotrophic keratitis. However, given high cost of therapy it is reasonable for patients to try lower cost alternatives first before approval of cenegermin. Even in the clinical trials, a portion of patients were able to achieve complete corneal healing with vehicle alone.
- The recommended dose of cenegermin (Oxervate®) is one drop instilled in the affected eye(s), six times a day at 2-hour intervals for eight weeks. Oxervate® comes in 1 mL vials that are used daily and should be discharged each day. If patient is treating both eyes they will need two vials per day.

REFERENCE/RESOURCES:

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3. [Cenegermin:] In: Lexi-Drugs Online [Internet database]. Hudson, OH: Lexi-Comp, Inc. Updated periodically. Accessed [May 7, 2023].
4. Wells, JR, Michelson MA. Ophthalmic Pearls: Diagnosing and Treating Neurotrophic Keratopathy. https://www.aao.org/eyenet/article/diagnosing-treating-neurotrophic-keratopathy?JulyAugust-2008 Accessed [March 8, 2019]
5. Neurotrophic Keratitis Treatment & Management https://emedicine.medscape.com/article/1194889-treatment#showall Updated: Mar 12, 2023 Robert H Graham, MD
6. European Medicines Agency, Science Medicines Health/Assessment Report. https://www.ema.europa.eu/en/documents/assessment-report/oxervate-epar-public-assessment-report_en.pdf Updated May 18, 2017. Accessed April 10, 2025.
7. Bonini S, Lambiase A, Rama P et al. Phase 2 Randomized, Double-Masked, Vehicle-Controlled Trial of Recombinant Human Nerve Growth Factor for Neurotrophic Keratitis. Ophthalmology 2018.
8. Dompé Farmaceutici. An 8-week phase II, multicenter, randomized, double-masked, vehicle controlled, parallel group study with a 24 or 32 week follow-up period to evaluate the efficacy of a formulation containing anti-oxidant of recombinant human nerve growth factor (rhNGF) in 20 µg/ml, eye drops solution versus vehicle containing anti-oxidant in patients with Stage 2 and 3

Neurotrophic Keratitis. Clinical Study Report.: Dompé Farmaceutici, Data on File; 2016.

9. Dana R, Farid M, Gupta PK, et al. Expert consensus on the identification, diagnosis, and treatment of neurotrophic keratopathy. BMC Ophthalmol. 2021 Sep 8;21(1):327. doi: 10.1186/s12886-021-02092-1. PMID: 34493256; PMCID: PMC8425140.