

## PHARMACY COVERAGE GUIDELINE

### OXERVATE™ (cenegermin-bkbj) ophthalmic topical 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](http://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](mailto:Pharmacyprecert@azblue.com).

#### **Criteria:**

- **Criteria for therapy:** Oxervate (cenegermin-bkbj) 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 2 years of age or older
3. Individual has a confirmed diagnosis of Stage 2 or Stage 3 neurotrophic keratitis
4. Individual has documented failure, contraindication per FDA label, intolerance, or is not a candidate for **TWO** of the following, when or where clinically appropriate:

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- a. Preservative-free artificial tears used every 2-4 hours **and** ocular lubricant ointment at bedtime
  - b. Topical antibiotics for symptomatic **and** asymptomatic individuals
  - c. Use of corneal or scleral contact lens therapy
  - d. Autologous serum eye drops or punctal (silicone) plugs
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](#))

#### **Approval duration:**

8 weeks per affected eye

Requests for additional course for recurrence will follow the above criteria

- 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

### **Description:**

Oxervate (cenegermin-bkbj) is indicated for the treatment of neurotrophic keratitis. Oxervate (cenegermin-bkbj) is a recombinant human nerve growth factor (NGF) that is structurally identical to the NGF protein made in the human body, including in the ocular tissues. NGF receptors are expressed in the anterior segment of the eye (cornea, conjunctiva, iris, ciliary body, and lens), by the lacrimal gland, and by the posterior segment ocular tissues. NGF acts directly on corneal epithelial cells to stimulate growth and survival; it binds to receptors on lacrimal glands to promote tear production, and may support corneal innervation, which is lost in NK.

Cenegermin-bkbj is a topical solution instilled in the affected eye(s) 6 times a day at 2-hour intervals for 8 weeks. An alarm should be used to assure every 2-hour dosing. Administration of the drug requires 19 steps including connecting a vial adapter to the vial, inserting a pipette into the vial adapter, withdrawing the solution into the pipette, removing the pipette from the adapter, instilling the drug into the affected eye, and tracking each dose on the provided recording card.

Neurotrophic keratitis (NK) is a rare degenerative corneal disease resulting from impaired function of corneal nerves, which can be caused by infections, ocular surface injuries, ocular or neurologic surgeries, and some systemic conditions that can impair corneal sensation. NK is caused by an impairment in the trigeminal nerve (cranial nerve V1) which leads to a decrease (hypoesthesia) in or absence (anesthesia) of corneal sensitivity. The loss of corneal sensation causes progressive damage to the top layer of the cornea, resulting in corneal thinning, ulceration, and perforation in severe cases.

Damage to the cranial nerve may be caused by herpetic keratitis, ophthalmic and neurosurgical procedures, chemical burns, physical injuries, long-term use of contact lenses, chronic use of topical medications, aneurysm, and neoplasm. NK is also associated with diabetes mellitus, multiple sclerosis, and congenital syndromes (e.g.,

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Riley-Day syndrome, Goldenhar-Gorlin syndrome, Möbius syndrome). The most common causes of NK are herpetic corneal infections, surgery for trigeminal neuralgia, and surgery for acoustic neuroma.

The diagnosis of NK is based on the clinical history that may identify conditions associated with trigeminal impairment, presence of persistent epithelial defect (PED) or ulcers and decreased corneal sensitivity. Symptoms during the early stage of the disease may include dryness, photophobia, impaired quality of vision, and reduced blinking.

There is no formal clinical guideline available that addresses treatment. Diagnosis, prognosis, and treatment are based on disease severity. NK is classified into three stages. Stage 1 (mild) is characterized by ocular surface irregularity and reduced vision; stage 2 (moderate) is characterized by a non-healing PED; and stage 3 (severe) exhibits corneal ulceration involving sub-epithelial (stromal) tissue, which may progress to corneal melting and perforation. Early diagnosis and treatment may prevent progression of corneal damage.

Therapy for stage 1 (mild) disease is to prevent epithelial breakdown by administering preservative-free artificial tears and discontinuing all topical and systemic medications associated with ocular surface toxicity. Use of punctal (silicone) plugs may also help increase tear volume.

The goal of treatment for stage 2 (moderate) NK is to promote healing of the epithelial defect and to avoid the development of corneal ulcers. In addition to preservative-free artificial tears and punctal plugs, topical antibiotics are recommended to prevent infections. Autologous serum eye drops, which contain components of natural tears (e.g., growth factors, vitamins, cytokines, and neuromediators) are used.

The aim of treatment at stage 3 (severe) disease is to prevent corneal thinning and perforation. Various surgeries and procedures are available to treat ulcers not responding to medical treatment. Tarsorrhaphy is the most commonly used procedure to promote corneal healing. Alternatives include botulinum-induced ptosis, amniotic membrane transplantation, eyelid closure with tape, patching, and use of the conjunctival flap to cover the corneal surface.

The safety and efficacy of Oxervate (cenegermin-bkbj) compared to vehicle was established in two, 8-week clinical studies in 151 patients with NK. All eye drops in both studies were given six times daily in the affected eye(s). In the first study, 72.0% of individuals with disease in one eye experienced complete corneal healing with Oxervate (cenegermin-bkbj) vs. 33.3% with vehicle (difference: 38.7% [95% CI: 20.7%, 56.6%];  $p < 0.01$ ). In the second study, 65.2% of individuals with disease in both eyes experienced complete corneal healing with Oxervate (cenegermin-bkbj) vs 16.7% with vehicle (difference: 48.6% [95% CI: 24%, 73.1%];  $p < 0.01$ ). According to the package label, individuals who were healed after 8 weeks of treatment with Oxervate (cenegermin-bkbj), recurrences occurred in approximately 20% in study 1 and 14% in study 2.

In 2021, an expert panel using a validated methodology (a RAND/UCLA modified Delphi panel) developed consensus on when to screen for and how best to diagnose and treat NK. For all stages of NK, the panel agreed that optimal care should include discontinuing preservative-containing topical medications, when possible. For topical medications that do not have preservative-free alternatives, the panel recommended decreasing the dose if possible. The panel also concluded that for all patients with NK (regardless of stage), optimal treatments (alone or in combination) may include preservative-free artificial tears or ocular lubricants (gels and ointments), punctal occlusion, and autologous serum tears/umbilical cord serum drops/platelet rich plasma drops. For patients with Stage 2 disease, the panel considered cenegermin-bkbj, prophylactic topical preservative-free antibiotics, matrix metalloproteinases inhibitors such as oral tetracyclines (e.g., doxycycline), corneal therapeutic contact lenses,

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and fresh-frozen self-retained amniotic membrane as additional optimal treatments. For Stage 3 disease, in addition to the treatments recommended in Stage 2, the panel agreed that synthetic tissue adhesive, tarsorrhaphy, amniotic membrane transplant, and corneal neurotization were optimal treatments. The authors also concluded that these recommendations need to be validated with studies that include patient outcomes, as the consensus statements were derived from studies with small sample sizes, observational studies, and experience of clinicians.

In 2022 data from a retrospective, observational case series was published from a single-center setting of 18 patients with diagnosis of stage 2 or 3 NK, who were treated with Oxervate (cenegermin-bkbj) and followed for up to 48 months. In case of recurrence, retreatment with Oxervate (cenegermin-bkbj) was not permitted and patients were treated with conventional management based on clinical findings. At the end of 8-weeks of treatment, all patients had corneal healing. Recurrence of lesion during follow-up was evaluated at 12, 24, 36, and 48 months. Three patients experienced recurrence of persistent epithelial defects (PEDs) within 12 months and one patient experienced recurrence of a corneal ulcer within 36 months. All patients with recurrence of NK were treated with therapeutic contact lens application and topical lubricants and all showed complete corneal healing. Corneal sensitivity, Schirmer tear test, and visual acuity (VA) were recorded at baseline, end of treatment, and at 12, 24, 36, and 48 months. Corneal sensitivity was significantly improved at all timepoints. Significant improvements in visual acuity and tear production were seen at the completion of treatment and at 12, 24, and 36 months when compared to baseline. The authors concluded that a single 8-week treatment regimen of Oxervate (cenegermin-bkbj) eye drops had clinical efficacy that can persist for up to 48 months. The long-term clinical utility of treatment with Oxervate (cenegermin-bkbj) for NK was demonstrated through the low rate of lesion recurrence (4/18 or 22%) along with improvements in corneal sensitivity and tear production.

#### Definitions:

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

Stages of NK:	
<b>Stage 1</b>	Punctate epithelial staining Decreased tear breakup test Rose bengal staining of inferior palpebral conjunctiva Dellen Gaule spots Stromal scarring
<b>Stage 2</b>	Persistent epithelial defect (PED) Stromal swelling Surrounding rim of loose epithelium Rare anterior chamber reaction
<b>Stage 3</b>	Corneal ulcer Stromal lysis Perforation

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#### **Resources:**

Oxervate (cenegermin-bkbj) product information, revised by Dompe Farmaceutici S.p.A. 02-2025. Available at DailyMed <http://dailymed.nlm.nih.gov>. Accessed February 18, 2025.

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