BlueCross BlueShield of Arizona
An Independent Licensee of the Blue Cross and Blue Shield Association

PHARMACY COVERAGE GUIDELINES	**ORIGINAL EFFECTIVE DATE: 5/16/19**
SECTION: DRUGS	**LAST REVIEW DATE: 5/16/19**
	LAST CRITERIA REVISION DATE:
	ARCHIVE DATE:

OXERVATE™ (cenegermin-bkbj) ophthalmic topical solution

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Pharmacy Coverage Guideline must be read in its entirety to determine coverage eligibility, if any.

This Pharmacy Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide BCBSAZ complete medical rationale when requesting any exceptions to these guidelines.

The section identified as "Description" defines or describes a service, procedure, medical device or drug and is in no way intended as a statement of medical necessity and/or coverage.

The section identified as "Criteria" defines criteria to determine whether a service, procedure, medical device or drug is considered medically necessary or experimental or investigational.

State or federal mandates, e.g., FEP program, may dictate that any drug, device or biological product approved by the U.S. Food and Drug Administration (FDA) may not be considered experimental or investigational and thus the drug, device or biological product may be assessed only on the basis of medical necessity.

Pharmacy Coverage Guidelines are subject to change as new information becomes available.

For purposes of this Pharmacy Coverage Guideline, the terms "experimental" and "investigational" are considered to be interchangeable.

This Pharmacy Coverage Guideline does not apply to FEP or other states' Blues Plans.

Information about medications that require precertification is available at www.azblue.com/pharmacy.

Some large (100+) benefit plan groups may customize certain benefits, including adding or deleting precertification requirements.

All applicable benefit plan provisions apply, e.g., waiting periods, limitations, exclusions, waivers and benefit maximums.

Precertification for medication(s) or product(s) indicated in this guideline requires completion of the request form in its entirety with the chart notes as documentation. All requested data must be provided. Once completed the form must be signed by the prescribing provider and faxed back to BCBSAZ Pharmacy Management at (602) 864-3126 or emailed to Pharmacyprecert@azblue.com. **Incomplete forms or forms without the chart notes will be returned.**

OXERVATE™ (cenegermin-bkbj) ophthalmic topical solution (cont.)

Criteria:

- **Criteria for initial therapy:** Oxervate (cenegermin-bkbj) is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

  1. Prescriber is a physician specializing in eye disorders or is in consultation with an Ophthalmologist or Optometrist

  2. Individual is 2 years of age or older

  3. A confirmed diagnosis of Stage 2 or Stage 3 neurotrophic keratitis

  4. Individual has failed, or is intolerant to, or has a contraindication such that the individual is unable to use **ALL** the following preferred step therapy agents:
     - Preservative-free artificial tears used every 2-4 hours **and** ocular lubricant ointment at bedtime
     - Topical antibiotics for symptomatic **and** asymptomatic individuals
     - Use of corneal or scleral contact lens therapy
     - Autologous serum eye drops or punctal (silicone) plugs

  Initial approval duration: 8 weeks

- **Criteria for continuation of coverage (renewal request):** Oxervate (cenegermin-bkbj) is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

  1. Individual continues to be seen by a physician specializing in eye disorders or is in consultation with an Ophthalmologist or Optometrist

  2. Individual's condition has not responded or has worsened while on therapy
     - Worsening is defined as **either** of the following:
       - There is residual corneal fluorescein staining of the PED or corneal ulcer
       - There is persistent fluorescein staining elsewhere in the cornea

  3. Individual has been adherent with the medication, documentation of adherence is required

  4. Individual has not developed any significant level 4 adverse drug effects that may exclude continued use
     - Significant adverse effect such as:
       - Severe eye pain

  Renewal duration: 8 weeks

OXERVATE™ (cenegermin-bkbj) ophthalmic topical solution (cont.)

- Oxervate (cenegermin-bkbj) for all other indications not previously listed or if above criteria not met is considered ***experimental or investigational*** based upon:
  1. Lack of final approval from the Food and Drug Administration, and
  2. Insufficient scientific evidence to permit conclusions concerning the effect on health outcomes, and
  3. Insufficient evidence to support improvement of the net health outcome, and
  4. Insufficient evidence to support improvement of the net health outcome as much as, or more than, established alternatives, and
  5. Insufficient evidence to support improvement outside the investigational setting.

  These indications include, *but are not limited to:*
  - Treatment with dosing or frequency outside the FDA-approved dosing and frequency

Description:

Oxerbate (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., 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.

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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.

Definitions:

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

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Resources:

Oxervate (cenegermin-bkbj) product information accessed 04-15-19 at DailyMed: https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=89e4bfec-d710-40ed-8885-5d13ba46b1cd

Semeraro F, Forbice E, Romano V, et al. Neurotrophic keratitis. Ophthalmologica. 2014; 231(4):191-197

Technology appraisal guidance: Cenegermin for treating neurotophic keratitis. National Institute for Heath and Care Excellence (NICE) July 16 2018 nice.org.uk/guidance/ta532

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Fax completed prior authorization request form to 602-864-3126 or email to pharmacyprecert@azblue.com.
Call 866-325-1794 to check the status of a request.
All requested data must be provided. **Incomplete forms or forms without the chart notes will be returned.**
Pharmacy Coverage Guidelines are available at www.azblue.com/pharmacy.

Pharmacy Prior Authorization Request Form

Do not copy for future use. Forms are updated frequently.
REQUIRED: Office notes, labs, and medical testing relevant to the request that show medical justification are required.

Member Information

Member Name (first & last):	Date of Birth:	Gender:	BCBSAZ ID#:
Address:	City:	State:	Zip Code:

Prescribing Provider Information

Provider Name (first & last):	Specialty:	NPI#:	DEA#:
Office Address:	City:	State:	Zip Code:
Office Contact:	Office Phone:	Office Fax:	

Dispensing Pharmacy Information

Pharmacy Name:	Pharmacy Phone:	Pharmacy Fax:

Requested Medication Information

Medication Name:	Strength:		Dosage Form:
Directions for Use:	Quantity:	Refills:	Duration of Therapy/Use:

☐ Check if requesting **brand** only ☐ Check if requesting **generic**

☐ Check if requesting continuation of therapy (prior authorization approved by BCBSAZ expired)

Turn-Around Time For Review

☐ Standard ☐ Urgent. Sign here: _____ ☐ Exigent (requires prescriber to include a written statement)

Clinical Information

1. **What is the diagnosis? Please specify below.**

   ICD-10 Code: _____ **Diagnosis Description:** _____

2. ☐ Yes ☐ No **Was this medication started on a recent hospital discharge or emergency room visit?**

3. ☐ Yes ☐ No **There is absence of ALL contraindications.**

4. **What medication(s) has the individual tried and failed for this diagnosis? Please specify below.**
Important note: Samples provided by the provider are not accepted as continuation of therapy or as an adequate trial and failure.

Medication Name, Strength, Frequency	Dates started and stopped or Approximate Duration	Describe response, reason for failure, or allergy

5. **Are there any supporting labs or test results? Please specify below.**

Date	Test	Value

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6. Is there any additional information the prescribing provider feels is important to this review? Please specify below.
For example, explain the negative impact on medical condition, safety issue, reason formulary agent is not suitable to a specific medical condition, expected adverse clinical outcome from use of formulary agent, or reason different dosage form or dose is needed.

Signature affirms that information given on this form is true and accurate and reflects office notes

Prescribing Provider's Signature: Date:

Please note: Some medications may require completion of a drug-specific request form.

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