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**Title:** Cenegermin-bkbj (Oxervate™)

**Policy #:** Rx.01.217

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***Application of pharmacy policy is determined by benefits and contracts. Benefits may vary based on product line, group, or contract. Some medications may be subject to precertification, age, quantity, or formulary restrictions (ie limits on non-preferred drugs). Individual member benefits must be verified.***

***This pharmacy policy document describes the status of pharmaceutical information and/or technology at the time the document was developed. Since that time, new information relating to drug efficacy, interactions, contraindications, dosage, administration routes, safety, or FDA approval may have changed. This Pharmacy Policy will be regularly updated as scientific and medical literature becomes available. This information may include new FDA-approved indications, withdrawals, or other FDA alerts. This type of information is relevant not only when considering whether this policy should be updated, but also when applying it to current requests for coverage.***

***Members are advised to use participating pharmacies in order to receive the highest level of benefits.***

**Intent:**

The intent of this policy is to communicate the medical necessity criteria for **cenegermin-bkbj (Oxervate™)** as provided under the member's prescription drug benefit.

**Description:**

Neurotrophic keratitis (NK) is a rare degenerative corneal disease caused by impairment in the first branch of the trigeminal nerve which leads to a decrease in or absence of corneal sensitivity. Loss of sensitivity impairs wound healing, leading to corneal epithelial breakdown, development of ulcerations, melting of the stroma, and corneal perforation. Diagnosis, prognosis, and treatment are based on disease severity, which is classified into 3 stages. Stage 1 (mild) NK is characterized by ocular surface irregularity and reduced vision; stage 2 (moderate) is characterized by a non-healing persistent epithelial defect (PED); and stage 3 (severe) exhibits corneal ulceration involving subepithelial (stromal) tissue, which may progress to corneal melting and perforation.

Therapy for stage 1 disease aims to prevent epithelial breakdown, generally by administering preservative-free artificial tears and discontinuing all topical and systemic medications associated with ocular surface toxicity. The use of punctal plugs may also help increase tear volume. The goal of treatment for stage 2 NK is to promote healing of the epithelial defect and to avoid the development of a corneal ulcer. In addition to the therapies in the previous stage, topical antibiotics are recommended to prevent infections. Therapeutic corneal or scleral contact lenses may be used to promote healing; however, there may be an increased risk of secondary infections. Autologous serum eye drops, which contain components of natural tears, have increasingly been used to treat ocular surface disorders including NK. The main goal of treatment at stage 3 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. Alternative treatments include botulinum-induced ptosis, amniotic membrane transplantation, eyelid closure with tape, patching, and use of the conjunctival flap to cover the corneal surface.

Cenegermin-bkbj (Oxervate™) is a novel recombinant human nerve growth factor (rhNGF) produced in *Escherichia coli* that is structurally identical to human NGF. NGF is an endogenous protein involved in the differentiation and maintenance of neurons, which acts through specific high-affinity and low affinity NGF receptors in the anterior segment of the eye to support corneal innervation and integrity. Cenegermin-bkbj (Oxervate™) is the first FDA-approved pharmacologic therapy indicated for the treatment of neurotropic keratitis (NK). Oxervate™ is an 8-week treatment cycle per affected eye(s).

**Policy:**

**INITIAL CRITERIA** Cenegermin-bkbj (Oxervate™) is approved when ALL of the following are met:

1. Diagnosis of Stage 2 or 3 neurotrophic keratitis; and
2. Documentation of an inadequate response or inability to tolerate at least one over-the-counter ocular lubricant used at an optimal dose and frequency for at least two weeks (e.g., artificial tears, lubricating gels/ointments, etc.); and
3. Prescribed by or in consultation with an ophthalmologist; and
4. Submission of chart documentation indicating treatment of left eye, right eye, or both; and

5. Member will not exceed 8 weeks of Oxervate therapy per affected eye(s)

Initial authorization duration: 3 months

**REAUTHORIZATION CRITERIA** Cenegermin-bkbj (Oxervate™) is re-approved when ALL of the following are met:

1. Submission of chart documentation indicating treatment of left eye, right eye, or both; and
2. Member has received less than or equal to 8 weeks of therapy (one course of therapy) per affected eye(s); and
3. Documentation of clinical rationale for treatment greater than 8 weeks (e.g., member has a recurrence of neurotropic keratitis in the same eye, or treatment of a different eye); and
4. Documentation of clinical response to prior Oxervate™ therapy; and
5. Member will not exceed a total of 16 weeks of Oxervate™ therapy per affected eye(s); and
6. Prescribed by or in consultation with an ophthalmologist

Reauthorization duration: 3 months

Lifetime limit: 16 weeks of therapy per affected eye

**Black Box Warning as shown in the drug Prescribing Information:**

None

**Guidelines:**

Refer to the specific manufacturer's prescribing information for administration and dosage details and any applicable Black Box warnings.

**BENEFIT APPLICATION**

Subject to the terms and conditions of the applicable benefit contract, the applicable drug(s) identified in this policy is (are) covered under the prescription drug benefits of the Company's products when the medical necessity criteria listed in this pharmacy policy are met. Any services that are experimental/investigational or cosmetic are benefit contract exclusions for all products of the Company.

**References:**

Bonini S, Lambiase A, Rama P, et al.; REPARO Study Group. Phase II randomized, double-masked, vehicle-controlled trial of recombinant human nerve growth factor for neurotrophic keratitis. *Ophthalmology*. 2018;125(9):1332-1343. Accessed January 26, 2022.

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Oxervate® (cenegermin-bkbj) [prescribing information]. Boston, MA: Dompe U.S. Inc. October 2019. Available at: <https://oxervate.com/pdf/PrescribingInformation.pdf>. Accessed January 26, 2022.

Pflugfelder SC, Massaro-Giordano M, Perez VL, Hamrah P, Deng SX, Espandar L, Foster CS, Affeldt J, Seedor JA, Afshari NA, Chao W, Allegretti M, Mantelli F, Dana R. Topical Recombinant Human Nerve Growth Factor (Cenegermin) for Neurotrophic Keratopathy: A Multicenter Randomized Vehicle-Controlled Pivotal Trial. *Ophthalmology*. 2020 Jan;127(1):14-26. Accessed January 26, 2022.

Pocobelli A, Komaiha C, De Carlo L, Pocobelli G, Boni N, Colabelli Gisoldi RAM. Role of Topical Cenegermin in Management of a Cornea Transplant in a Functionally Monocular Patient with Neurotrophic Keratitis and Facial Nerve Palsy: A Case Report. *Int Med Case Rep J*. 2020 Nov 11;13:617-621. Accessed January 26, 2022.

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Semeraro F, Forbice E, Romano V, et al. Neurotrophic keratitis. *Ophthalmologica*. 2014;231(4):191-197. Accessed January 26, 2022.

Versura P, Giannaccare G, Pellegrini M, Sebastiani S, Campos EC. Neurotrophic keratitis: current challenges and future prospects. Eye Brain. 2018; 10:37-45. Accessed January 26, 2022.

**Applicable Drugs:**

Inclusion of a drug in this table does not imply coverage. Eligibility, benefits, limitations, exclusions, precertification/referral requirements, provider contracts, and Company policies apply.

Brand Name	Generic Name
Oxervate™	cenegermin-bkbj

**Cross References:**

Rx.01.33 Off-Label Use

Rx.01.76 Quantity Level Limits for Pharmaceuticals Covered Under the Prescription Drug Benefit

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<b>Policy Version Number:</b>	6.00
<b>P&amp;T Approval Date:</b>	December 9, 2021
<b>Policy Effective Date:</b>	April 1, 2022
<b>Next Required Review Date:</b>	June 10, 2022

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The Policy Bulletins on this web site were developed to assist the Company in administering the provisions of the respective benefit programs, and do not constitute a contract. If you have coverage through the Company, please refer to your specific benefit program for the terms, conditions, limitations and exclusions of your coverage. Company does not provide health care services, medical advice or treatment, or guarantee the outcome or results of any medical services/treatments. The facility and professional providers are responsible for providing medical advice and treatment. Facility and professional providers are independent contractors and are not employees or agents of the Company. If you have a specific medical condition, please consult with your doctor. The Company reserves the right at any time to change or update its Policy Bulletins.

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