cenegermin-bkbi (Oxervate™)

EOCCO POLICY

Policy Type: PA Pharmacy Coverage Policy: EOCCO013

Description

Cenegermin-bkbj (Oxervate) is a recombinant human eye growth factor ophthalmic solution indicated for the treatment of neurotrophic keratitis.

Length of Authorization

- Initial: Eight weeks
- Renewal: Not approvable

Quantity limits

Product Name	Indication	Dosage Form	Quantity Limit*
cenegermin-bkbj (Oxervate)	Neurotrophic keratitis	0.002% (20 mcg/mL) vial	56mL per 56 days, per eye

**Quantity limit of 56 mL per 56 days (28 mL/28 days) is sufficient to treat one eye. If both eyes are affected/require treatment, allowance of 112 mL per 56 days (56 mL/28 days) can occur. Treatment is once per lifetime.*

Initial Evaluation

I. Cenegermin-bkbj (Oxervate) may be considered medically necessary when the following criteria are met:
   A. Prescribed by, or in consultation with, an ophthalmologist; **AND**
   B. A diagnosis of Neurotropic Keratitis; **AND**
   C. Antibiotic drops in combination with preservative-free artificial tears has been ineffective, contraindicated, or not tolerated; **AND**
   D. Member has Stage 2 (persistent epithelial defect) or Stage 3 (corneal ulceration, corneal perforation, or corneal stromal melting) disease; **AND**
      1. For Stage 2 disease: Therapeutic contact lens (scleral lens) have been ineffective, contraindicated, or are not tolerated; **AND**
   E. Member has NOT received prior therapy with cenegermin-bkbj (Oxervate) in the requested eye in their lifetime.

II. Cenegermin-bkbj (Oxervate) is considered investigational when used for all other conditions, including but not limited to:
   A. Treatment duration longer than 8 weeks

Renewal Evaluation

I. Treatment beyond the initial eight-week duration is considered experimental and investigational.

Supporting Evidence

I. Neurotrophic keratitis (NK) is a rare, degenerative disease of the cornea caused by damage to the trigeminal nerve, which results in reduction/loss of corneal sensitivity, epithelium breakdown, decreased corneal healing, ulceration, melting, and perforation. NK severity is divided into three stages.
   - Stage 1: characterized by epithelial irregularity most commonly in the form of punctate keratopathy without epithelial defect.
   - Stage 2: defined by recurrent or persistent epithelial defects (PED) usually oval in shape and its margins are characteristically smooth and rolled due to impaired epithelial healing. Descemet's membrane folds and stromal edema may be observed.
   - Stage 3: characterized by stromal involvement that appears as a stromal corneal ulcer and stromal edema and infiltrates; this may result in perforation and/or corneal thinning due to stromal melting.

II. The goal of therapy is to prevent progression of corneal damage and promote healing of the corneal epithelium. Treatment of NK is based on disease severity; however, use of preservative-free artificial tears may help improve the corneal surface at all stages of disease severity. Topical antibiotic eye drops are recommended in eyes with NK at stages 2 and 3 to prevent infection. Nonpharmacological treatments for NK include therapeutic corneal or scleral contact lenses in the event of PED to promote corneal epithelial healing. Surgical treatments are reserved for refractory cases.

III. Cenegermin-bkbj (Oxervate) was studied in two 8-week, phase II multi-center, randomized, double blind, placebo controlled clinical trials (Study NGF0212 (REPARO) and Study NGF0214) in adult patients with Stage 2 or Stage 3 NK who were refractory to 1 or more conventional nonsurgical treatments. In NGF0212 72% of patients treated with cenegermin-bkbj (Oxervate) achieved complete corneal healing at week 8, as well as 65.2% of patients in Study NGF0214. In patients who were healed after 8 weeks of treatment, recurrences occurred in approximately 20% of patients in Study NGF0212 and 14% of patients in Study NGF0214. Retreatment following recurrence was not assessed in either study.

IV. Efficacy of cenegermin-bkbj (Oxervate) beyond a single 8-week course of treatment or repeat treatment has not been evaluated.

V. Cenegermin-bkbj (Oxervate) is packaged in a box of #7 x 1 mL vials and is dosed to a maximum of 1 vial (1 mL) per day for 8 weeks (56 days) per treated eye. If both eyes are being treated, the patient will require two vials (2 mL) each day.

Investigational or Not Medically Necessary Uses

I. Neurotrophic Keratitis
   A. Treatment beyond the initial 8 week duration is considered experimental and investigational due to lack of studies to demonstrate efficacy beyond a single eight week course of treatment.

References

1. Oxervate [Prescribing Information]. Boston, MA: Dompé US, Inc. October 2019.
2. Bonini S, Lambiase A, Rama P, et al. Phase II randomized, double-masked, vehicle-controlled trial of recombinant human nerve growth factor for neutrophic keratitis. *Opthalmology.* 2018;125(9):1332-1343.
3. Shaheen B, Bakir M, Jain S. Corneal nerves in health and disease. *Surv Opthalmol.* 2014;59(3):263-285.
4. Mantelli F, Nardella C, Tiberi E, et al. Congenital corneal anesthesia and neurotrophic keratitis: diagnosis and management. *Biomed Res Int.* 2015;2015:805876. Epub Sept. 16, 2015.
5. Semeraro F, Forbice E, Romano V, et al. Neurotrophic keratitis. *Opthalmologica*. 2014;231(4):191-197.
6. Sacchetti M, Lambiase A. Diagnosis and management of neurotrophic keratitis. *Clin Opthalmol.* 2014;8:571-579.
7. An Evidence based Approach to the Diagnosis and Treatment of Neurotrophic Keratopathy. CME monograph. Johns Hopkins School of Medicine. March 2020. Available at: https://hopkinscme.cloud-cme.com/assets/hopkinscme/Presentations/28879/28879.pdf

Policy Implementation/Update:

Action and Summary of Changes	Date
Clarification of QL differences when treating one versus both eyes.	11/2022
Removal of requirement "lack of active ocular infection (bacterial, viral, fungal, or protozoal) and lack of current severe blepharitis and/or severe meibomian gland disease". Removal of "documentation of cause not due to infective or autoimmune keratitis". Removal of required history of use of a topical collagenase inhibitor as this is specific to the management of stromal melting. Broke down requirement of therapeutic contact lens to be specific to Stage 2 NK. Additional requirement assuring member has not received treatment with Oxervate in their lifetime. Updates to supporting evidence.	04/2021
Policy created	01/2019