cenegermin-bkbj (Oxervate™)

Policy # 00665
Original Effective Date: 03/20/2019
Current Effective Date: 04/12/2021

Applies to all products administered or underwritten by Blue Cross and Blue Shield of Louisiana and its subsidiary, HMO Louisiana, Inc.(collectively referred to as the "Company"), unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

When Services May Be Eligible for Coverage

Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:

- *Benefits are available in the member's contract/certificate, and*
- *Medical necessity criteria and guidelines are met.*

Based on review of available data, the Company may consider cenegermin-bkbj (Oxervate™)‡ for the treatment of neurotrophic keratitis to be **eligible for coverage.****

Patient Selection Criteria

Coverage eligibility for cenegermin-bkbj (Oxervate) will be considered when the following criteria are met:

- Patient has a diagnosis of neurotrophic keratitis confirmed by decreased corneal sensitivity as measured by a corneal esthesiometer; AND
- Patient's neurotrophic keratitis is classified as Stage 2 or Stage 3 as determined by slit-lamp examination; AND
  *(Note: This specific patient criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met).*
- Patient is 2 years of age or older; AND
- Patient has persistent epithelial defect or corneal ulceration refractory to treatment with non-surgical therapy (e.g., preservative free artificial tears, ophthalmic antibiotics, etc.); AND
  *(Note: This specific patient criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met).*
- Patient has NOT received prior therapy with the requested drug in the requested eye in their lifetime.

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When Services Are Considered Not Medically Necessary

Based on review of available data, the Company considers the use of cenegermin-bkbj (Oxervate) for Stage 1 neurotrophic keratitis to be **not medically necessary.****

Based on review of available data, the Company considers the use of cenegermin-bkbj (Oxervate) when the patient's condition is NOT refractory to treatment with non-surgical therapy to be **not medically necessary.****

When Services Are Considered Investigational

Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Company considers the use of cenegermin-bkbj (Oxervate) for non-FDA approved indications OR for patients under 2 years of age OR for repeat therapy in a lifetime to be **investigational.***

Background/Overview

Oxervate is a recombinant human nerve growth factor indicated for the treatment of neurotrophic keratitis. 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. Overvate is supplied as an ophthalmic solution with a 0.002% (20 mcg/mL) concentration in a multi-dose vial. The dose of Oxervate is one drop in the affected eye(s), 6 times per day at 2 hour intervals, for eight weeks.

Neurotrophic keratitis is a degenerative disease of the corneal epithelium which results from impaired corneal innervation. The hallmark of the disease, reduction in corneal sensitivity or complete corneal anesthesia, is responsible for causing ulceration and perforation. The common underlying insult for this condition is a lesion of the trigeminal nerve (cranial nerve V) or its branches. This insult could be caused by infections (herpes simplex and herpes zoster), trigeminal neuralgia surgery, acoustic neuroma, toxicity from topical ocular medications, and diabetes mellitus.

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The Mackie classification for neurotrophic keratitis can be divided into 3 stages:

- Stage 1: Characterized by mild, nonspecific signs and symptoms, including rose bengal staining of the inferior palpebral conjunctiva.
- Stage 2: Characterized by a nonhealing corneal epithelial defect.
- Stage 3: Characterized by stromal melting leading to perforation.

Corneal sensitivity is a vital piece of information and may be measured qualitatively with a piece of twisted cotton or quantitatively with a Cochet-Bonnet esthesiometer. This device quantifies corneal sensitivity by the length of a nylon filament required to initiate a blink or patient response. The nylon filament may be extended to as long as 6 cm. One study reported that only those patients with values of 2 cm or less developed epithelial sloughing and ulceration. It is important to remember that in some cases, such as herpes simplex and herpes zoster keratitis, the anesthesia of the cornea may be sectoral and therefore different quadrants of the cornea should be tested separately. Slit-lamp and dilated funduscopic examinations must be performed in every patient and may give insight into the etiology. Corneal stromal scarring may indicate prior infection.

Treatment for neurotrophic keratitis needs to be initiated immediately to prevent progression. Early treatment should include the use of preservative free artificial tears and ointments. Prophylactic antibiotic drops are often added as the disease progresses. Oxervate is the first FDA approved drug for this condition. There are currently no defined treatment guidelines for this condition.

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)

Oxervate is a recombinant human nerve growth factor indicated for the treatment of neurotrophic keratitis. The safety and effectiveness of Oxervate have been established in the pediatric population. Use of Oxervate in this population is supported by evidence from adequate and well controlled trials of Oxervate in adults with additional safety data in pediatric patients from 2 years of age and older.

Rationale/Source

This medical policy was developed through consideration of peer-reviewed medical literature generally recognized by the relevant medical community, U.S. Food and Drug Administration approval status, nationally accepted standards of medical practice and accepted standards of medical practice in this community, Blue Cross and Blue Shield Association technology assessment program

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(TEC) and other non-affiliated technology evaluation centers, reference to federal regulations, other plan medical policies, and accredited national guidelines.

The efficacy and safety of Oxervate for the treatment of neurotropic keratitis was studied in a total of 151 patients, evaluated in two 8-week, randomized, multi-center, double-masked, vehicle-controlled studies. Patients were randomized to Oxervate, cenegermin-bkbj 10 mcg/mL, or vehicle in Study 1, and Oxervate or vehicle in Study 2 dosed 6 times daily in the affected eye(s) for 8 weeks. In study 1, only patients with unilateral disease were enrolled, while in study 2 patients with bilateral disease were treated bilaterally. In Study 1, 65.2% (15/23) of patients treated with Oxervate achieved complete corneal healing at week 8 versus 16.7% (4/24) in the vehicle group ($p<0.01$). In Study 2, 72% (36/50) of patients treated with Oxervate achieved complete corneal healing at week 8 versus 33.3% (17/51) in the vehicle group ($p<0.01$). In patients who were healed after 8 weeks of treatment with Oxervate, recurrences occurred in approximately 20% of patients in Study 1 and 14% of patients in Study 2. Mean changes in corneal sensitivity were not clinically significant in either study.

References

1. Oxervate [package insert]. Dompe farmaceutici S.P.A. Italy. Updated August 2018.
2. Wells JR, Michelson Marc. Diagnosing and Treating Neurotrophic Keratopathy. American Academy of Ophthalmology. 2008.

Policy History

Original Effective Date: 03/20/2019
Current Effective Date: 04/12/2021
03/07/2019 Medical Policy Committee review
03/20/2019 Medical Policy Implementation Committee approval. New policy.
03/05/2020 Medical Policy Committee review
03/11/2020 Medical Policy Implementation Committee approval. New policy.
03/04/2021 Medical Policy Committee review
03/10/2021 Medical Policy Implementation Committee approval. No change to coverage.
Next Scheduled Review Date: 03/2022

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*Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

A. Whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. Food and Drug Administration (FDA) and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or
B. Whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:
    1. Consultation with the Blue Cross and Blue Shield Association technology assessment program (TEC) or other nonaffiliated technology evaluation center(s);
    2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
    3. Reference to federal regulations.

**Medically Necessary (or "Medical Necessity") - Health care services, treatment, procedures, equipment, drugs, devices, items or supplies that a Provider, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury, disease or its symptoms, and that are:

A. In accordance with nationally accepted standards of medical practice;
B. Clinically appropriate, in terms of type, frequency, extent, level of care, site and duration, and considered effective for the patient's illness, injury or disease; and
C. Not primarily for the personal comfort or convenience of the patient, physician or other health care provider, and not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.

For these purposes, "nationally accepted standards of medical practice" means standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, Physician Specialty Society recommendations and the views of Physicians practicing in relevant clinical areas and any other relevant factors.

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‡ Indicated trademarks are the registered trademarks of their respective owners.

NOTICE: If the Patient's health insurance contract contains language that differs from the BCBSLA Medical Policy definition noted above, the definition in the health insurance contract will be relied upon for specific coverage determinations.

NOTICE: Medical Policies are scientific based opinions, provided solely for coverage and informational purposes. Medical Policies should not be construed to suggest that the Company recommends, advocates, requires, encourages, or discourages any particular treatment, procedure, or service, or any particular course of treatment, procedure, or service.