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Coverage Policy Number **IP0302**

Cenegermin Ophthalmic Solution

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Related Coverage Resources

INSTRUCTIONS FOR USE
The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

Overview

This policy supports medical necessity review for **Oxervate™** (cenegermin-bkbj) ophthalmic solution.

Receipt of sample product does not satisfy any criteria requirements for coverage.

Medical Necessity Criteria

Cenegermin-bkbj ophthalmic solution (Oxervate) is considered medically necessary for Neurotrophic Keratitis when the individual meets ALL of the following criteria:

1. Stage 2 (moderate) or stage 3 (severe) neurotrophic keratitis
2. Has not yet received a total of 8 weeks of treatment in the affected eye(s)
3. Medication is being prescribed by, or in consultation with, an ophthalmologist

When coverage is available and medically necessary, the dosage, frequency, duration of therapy, and site of care should be reasonable, clinically appropriate, and supported by evidence-based literature and adjusted based upon severity, alternative available treatments, and previous response to therapy.

Reauthorization Criteria

Cenegermin-bkbj ophthalmic solution (Oxervate) is considered medically necessary for continued use when initial criteria are met AND there is documentation of beneficial response, including the following:

1. Individual has previously received at least 8 weeks but less than 16 weeks of treatment per affected eye(s)
2. Attestation of need for additional course of therapy based upon partial response or recurrence

Authorization Duration

Initial approval duration is up to 2 months.

Reauthorization approval duration is up to 2 months.

Conditions Not Covered

Cenegermin-bkbj ophthalmic solution (Oxervate) is considered experimental, investigational or unproven for **ANY** other use including the following (this list may not be all inclusive):

1. **Treatment duration of greater than 16 weeks per affected eye(s).** Available data does not support use of Oxervate beyond 16 weeks for each eye.[2,7]

Background

OVERVIEW
Oxervate, a recombinant human nerve growth factor, is indicated for the treatment of **neurotrophic keratitis**.[1]

Duration of Treatment
The recommended dosing regimen is one drop six times a day (at 2 hour intervals) for 8 weeks.[1] In one of the pivotal studies, five patients who experienced a recurrence of neurotrophic keratitis after an 8-week course of Oxervate were re-treated with another 8 weeks of Oxervate.[2] Four of these patients achieved corneal healing, which was maintained through the end of the follow-up period.

Disease Overview
Neurotrophic keratitis, a rare degenerative disease, is characterized by corneal epithelium breakdown, impairment of corneal healing, and development of corneal ulceration, melting, and perforation.[3-6] Corneal epithelial cells release various neurotrophic growth factors, including nerve growth factors, which are important in maintaining the integrity and function of the ocular surface and in stimulating both epithelial and nerve fiber proliferation and survival.[7,8] When corneal sensory innervation is impaired, reduction of both protective reflexes and trophic neuromodulators essential for the vitality, metabolism, and wound healing of the ocular surface tissues results. *In vivo* studies have shown that increasing nerve growth factor concentration after injury can accelerate healing.[4,8]

Guidelines/Recommendations
Neurotrophic keratosis is classified into three stages: Stage 1 (mild), corneal epithelial changes; Stage 2 (moderate), corneal epithelial defect; Stage 3 (severe), corneal ulcer, perforation, melting.[6] Prior to the approval of Oxervate, there were no approved pharmacologic therapies for the treatment of neurotrophic keratitis.[3] If neurotrophic keratitis is left untreated, the condition can progress to anatomical loss of the eye; even with treatment, loss of vision is common.[6,7] Treatment should target corneal sensory innervation impairment to restore corneal integrity; treatment goals are to stop progression and promote epithelial healing.

There are no formal clinical guidelines, although there are expert opinion on the diagnosis and treatment of neurotrophic keratitis.[6] Optimal care requires identifying and treating the underlying causes of neurotrophic keratitis; for example, using antiviral medications for herpetic disease, correcting eyelid abnormalities, controlling hemoglobin A1c levels in patients with diabetes, and providing supportive therapy for limbal stem cell deficiency. For all stages, optimal care includes discontinuation of all preservative-containing ophthalmic medications to the extent possible and use of preservative-free tear substitutes or lubricants is recommended. For patients with Stage 2 disease, Oxervate, prophylactic ophthalmic preservative-free antibiotics, oral tetracyclines (e.g., doxycycline), corneal therapeutic contact lenses, and fresh-frozen self-retained amniotic membrane may be considered. For patients with Stage 3 disease, all of the listed options for Stage 2 disease as well as synthetic tissue adhesive, tarsorrhaphy, amniotic membrane transplant, and corneal neurotization are optimal treatments.

References

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4. Mastropasqua L, Massaro-Giordano G, Nubile M, Sacchetti M. Understanding the pathogenesis of neurotrophic keratitis: the role of the corneal nerve. *J Cell Physiol*. 2017;232:717-724.
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8. Vesura P, Giannaccare G, Pellegrini M, et al. Neurotrophic keratitis: current challenges and future prospects. *Eye and Brain*. 2018;10:37-45.