Complete, durable healing for most patients with neurotrophic keratitis

Please see inside this brochure for study design details and assessments.

Please see Important Safety Information, including patient information, throughout and at https://OXERVATE.com/prescribing-information.
Proven corneal healing for neurotrophic keratitis (NK)\textsuperscript{1-3}

In clinical trials, with a single 8-week course of therapy:

- Up to 72% of patients achieved complete corneal healing at week 8.\textsuperscript{1,11}
- 80% of patients in the REPARO trial who achieved complete corneal healing remained completely healed at 1 year.\textsuperscript{2,3}

\begin{itemize}
  \item \textbf{OXERVATE} is generally well tolerated, and the most common adverse reaction reported in clinical trials (16%) was eye pain following instillation.\textsuperscript{1,2}
\end{itemize}

**Important Safety Information**

Contact lenses should be removed before applying OXERVATE because the presence of a contact lens (either therapeutic or corrective) could theoretically limit the distribution of cenergermin-bkbj onto the area of the corneal lesion. Lenses may be reinserted 15 minutes after administration.

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OXERVATE is the only pharmacologic therapy that targets the root pathogenesis of NK

**Important Safety Information (continued)**

OXERVATE may cause mild to moderate eye discomfort such as eye pain during treatment. The patient should be advised to contact their doctor if a more serious eye reaction occurs.

The most common adverse reaction in clinical trials that occurred more frequently with OXERVATE was eye pain (16% of patients). Adverse reactions included corneal deposits, foreign body sensation in the eye, ocular hyperemia (enlarged blood vessels in the white of the eye), swelling (inflammation) of the eye, and increase of tears (1-10% of patients).

**INDICATION**

OXERVATE™ (cenergermin-bkbj) ophthalmic solution 0.002% is indicated for the treatment of neurotrophic keratitis.

**DOSAGE FORMS AND STRENGTHS**

Ophthalmic solution for topical use in the eye: cenergermin-bkbj 0.002% (20 mcg/mL) is a clear, colorless solution in a multiple-dose vial.

**CONTRAINdications**

None.

**WARNINGS AND PRECAUTIONS**

Use With Contact Lenses

Contact lenses should be removed before applying OXERVATE because the presence of a contact lens (either therapeutic or corrective) could theoretically limit the distribution of cenergermin-bkbj onto the area of the corneal lesion. Lenses may be reinserted 15 minutes after administration.

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As of April 2020, more than 3,200 patients have been treated with OXERVATE in the US.

OXERVATE is indicated for mild, moderate, and severe NK and is an important treatment option that provides complete and durable corneal healing.

Sources:

Important Safety Information (continued)

WARNINGS AND PRECAUTIONS (continued)

Eye Discomfort
OXERVATE may cause mild to moderate eye discomfort such as eye pain during treatment. The patient should be advised to contact their doctor if a more serious eye reaction occurs.

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Important Safety Information (continued)

ADVERSE REACTIONS

Clinical Studies Experience
Because clinical studies are conducted under widely varying conditions, adverse reaction rates observed in the clinical studies of a drug cannot be compared directly to rates in the clinical studies of another drug and may not reflect the rates observed in practice.

In 2 clinical trials of patients with neurotrophic keratitis, a total of 101 patients received cenegermin-bkbj eye drops at 20 mcg/mL at a frequency of 6 times daily in the affected eye(s) for a duration of 8 weeks. The mean age of the population was 61 to 65 years of age (18 to 95).

The most common adverse reaction in clinical trials that occurred more frequently with OXERVATE was eye pain (16% of patients). Other adverse reactions included corneal deposits, foreign body sensation in the eye, ocular hyperemia (enlarged blood vessels in the white of the eye), swelling (inflammation) of the eye, and increase in tears (1%-10% of patients).

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Important Safety Information (continued)

USE IN SPECIFIC POPULATIONS

PREGNANCY
Risk Summary
There are no data from the use of OXERVATE in pregnant women to inform any drug-associated risks. Administration of cenegermin-bkbj to pregnant rats or rabbits during the period of organogenesis did not produce adverse fetal effects at clinically relevant doses. In a pre- and postnatal development study, administration of cenegermin-bkbj to pregnant rats throughout gestation and lactation did not produce adverse effects in offspring at clinically relevant doses.

Data
Animal Data
In embryofetal development studies, daily subcutaneous administration of cenegermin-bkbj to pregnant rats and rabbits throughout the period of organogenesis produced a slight increase in postimplantation loss at doses greater than or equal to 42 mcg/kg/day (267 times the maximum recommended human ophthalmic dose [MRHOD]). A no-observed-adverse-effect level (NOAEL) was not established for postimplantation loss in either species. In rats, hydrocephaly and ureter anomalies were observed once each in fetuses at 267 mcg/kg/day (1709 times the MRHOD). In rabbits, cardiovascular malformations, including ventricular and atrial septal defects, enlarged heart, and aortic arch dilation, were observed once each in fetuses at 83 mcg/kg/day (534 times the MRHOD). No fetal malformations were observed in rats and rabbits at doses of 133 mcg/kg/day and 42 mcg/kg/day, respectively.

In a pre- and postnatal development study, daily subcutaneous administration of cenegermin-bkbj to pregnant rats during the period of organogenesis and lactation did not affect parturition and was not associated with adverse toxicity in offspring at doses up to 267 mcg/kg/day.

In parental rats and rabbits, an immunogenic response to cenegermin-bkbj was observed. Given that cenegermin-bkbj is a heterologous protein in animals, this response may not be relevant to humans.

LACTATION
Risk Summary
There are no data on the presence of OXERVATE in human milk, the effects on breastfed infants, or the effects on milk production. The developmental and health benefits of breastfeeding should be considered along with the mother’s clinical need for OXERVATE and with any potential adverse effects on the breastfed infant.

PEDIATRIC USE
The safety and effectiveness of OXERVATE have been established in the pediatric population. Use of OXERVATE in pediatric patients 2 years of age and older is supported by evidence from adequate and well-controlled trials of OXERVATE in adults with additional safety data in children.

GERIATRIC USE
Of the total number of subjects in clinical studies of OXERVATE, 43.5% were 65 years old and older. No overall differences in safety or effectiveness were observed between elderly and younger adult patients.

The FDA-approved product labeling can be found at https://OXERVATE.com/prescribing-information. You may report side effects to FDA at 1-800-FDA-1088 or www.fda.gov/medwatch. You may also report side effects to Dompé at 1-833-366-7387 or Usmedinfo@dompe.com.

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