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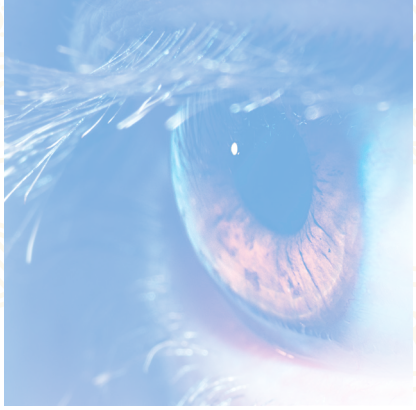
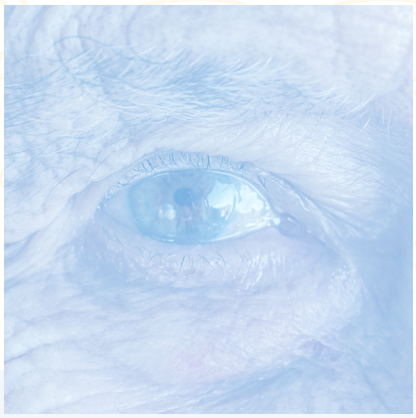




Neurotrophic Keratitis: Early Treatment and Co-management

Sumitra Khandelwal, MD (Moderator)

Brandon Ayres, MD

Neel Desai, MD

Matt Feng, MD

W. Barry Lee, MD, FACS

Five expert cornea specialists discuss early intervention for NK.

Neurotrophic Keratitis: Early Treatment and Co-management

Five expert cornea specialists discuss early intervention for NK.

Approval of OXERVATE® (cenegermin-bkbj) ophthalmic solution 0.002% (20 mcg/mL) (Dompé U.S. Inc. ["Dompé"]) by the US FDA for the treatment of neurotrophic keratitis (NK)[1] was welcomed by the ophthalmology community. For many years, treatments for NK were primarily palliative in nature and did not target the root cause. Untreated patients might have experienced corneal ulcers, corneal melts, corneal perforation[2]—and, potentially, vision loss.[3] OXERVATE, a biologic eye drop administered for 8 weeks, targets the root pathogenesis of NK resulting in complete corneal healing in a majority of patients.

In April 2021, Sumitra Khandelwal, MD, moderated a roundtable discussion with Brandon Ayres, MD; Neel Desai, MD; Matt Feng, MD; and W. Barry Lee, MD, FACS, to review the value of early diagnosis, the adoption of OXERVATE as a treatment for NK, and practical tips for managing this disease in patients.

EARLY DETECTION AND DIAGNOSIS OF NK

Sumitra Khandelwal, MD: The prevalence of NK in the United States has been estimated to be 65,000.[2] *Dr. Desai, how commonly are you seeing NK in your practice?*

Neel Desai, MD: My experience suggests that it is more common than initially thought. Dr. Khandelwal and I share the observation that underdiagnosis and misdiagnosis may obscure the actual numbers. I see many patients with NK—particularly those with stage 1 NK—who were diagnosed with dry eye disease (DED).[4] If they aren't diagnosed accurately, then routes to proper treatment may not be available. Ever since I've adopted more frequent use of corneal sensitivity testing (CST), I've detected NK at greater rates. Our ability to detect the disease has improved.

Brandon Ayres, MD: I see a lot of patients who are referred for a cataract or refractive surgery evaluation who have diagnosed and undiagnosed NK. I am wary that surgery could worsen neurotrophy in such patients, and I think that proper detection could be key to ensuring that NK doesn't worsen under our watch.

W. Barry Lee, MD, FACS: I recently saw two patients who underwent cataract surgery at a nearby practice, and both had autoimmune conditions.[2,3] They developed perforated corneal ulcers within 2 weeks of surgery. In general, we need to be aware of patients with risk factors for NK when performing cataract surgery.

Matt Feng, MD: These surgical concerns are legitimate ones. Postoperative complications are common referrals to my practice. I estimate that they constitute the third most common reason I see patients with NK, behind herpetic infections and diabetes.

Dr. Khandelwal: This brings us to the question of comorbidities and underlying conditions in patients with NK. Dr. Feng points out that herpetic infections and diabetes are leading causes of NK in his practice, which aligns with what has been reported in the literature.[5] We also know that topical drug use and chronic contact lens use can lead to NK.[5] *Dr. Desai, which comorbidities encourage you to consider NK as a possible diagnosis?*

Dr. Desai: Identifying patients with chronic ocular surface disease (OSD) is very important. OSD and NK often coexist. I find that OSD and NK share some risk factors,[5] such as those listed by Dr. Khandelwal. I look for patients that complain of visual symptoms of ocular surface disease but lack some of the physical complaints.

Dr. Khandelwal: I find it useful to think of etiologies and comorbidities as a Venn diagram. Some patients have two, three, or more etiologies and/or comorbidities. I see patients who fit into those overlap zones. They often have stage 2 or stage 3 disease,[2] and it becomes clear that they should have been caught sooner. Gathering patient history is key to understanding whether patients are at risk for NK, and it could allow us to catch stage 1 disease early.

KEY INSIGHT

W. Barry Lee, MD, FACS
Atlanta

Any comorbidity that could affect nerve function (eg, diabetes, autoimmune disorders) raises my suspicion that a patient may have NK. Patients who report sudden changes in symptoms could be NK patients, too. In these patient types, I remind myself that what I'm detecting during my examination may not be just ocular surface disease, but could be something with a different root cause altogether.

Please see Important Safety Information on OXERVATE on page 8.

KEY INSIGHT

Matt Feng, MD
Indianapolis

Delayed diagnosis may confer high risk of progression in some patients. In my opinion, the greater the number of ocular surface comorbidities, the greater the risk. These comorbidities may mask NK and accelerate corneal injury until an NK diagnosis is made. I suspect NK early when evaluating patients with fluctuating blurry vision without other dry eye symptoms.

Dr. Lee: Patient history can raise a lot of red flags, which is helpful especially in identifying patients with NK earlier in their disease. Whenever a patient presents with recalcitrant OSD or DED with chronic punctate keratitis, I begin to suspect NK. I seek to uncover if the patient's history may reveal diabetes, autoimmune diseases, retinal detachment, and other surgeries. If any of those appear in the patient's history, I perform CST to confirm. The value to diagnosing stage 1 NK cannot be understated, as we are able to help patients before their condition worsens.

Dr. Khandelwal: I think the glaucoma framework or diabetic retinopathy staging is useful when thinking of NK intervention. We want to treat patients before their disease progresses. In my experience, after a patient has stage 2 NK, there is no promise that the cornea will be the same again.

RISK STRATIFICATION

Dr. Khandelwal: How might we best assess risk of disease progression in patients with stage 1 NK?

Dr. Lee: Once again, history is key. Patients with a history of infections, such as herpes zoster and herpes simplex, or neuropathic complications such as stroke, I would consider high-risk. Poorly controlled diabetes is also a serious problem, and I would consider these patients at high risk of progression.

Dr. Desai: Gathering even more from their history, I consider the rate of disease onset or an acute change in their symptoms. If their symptoms have changed quickly–either acutely worsened or nearly disappeared—then I am concerned that the patient is at high risk.

Dr. Khandelwal: We've touched on the various stages of NK a few times in our discussion, so let's take a moment to go more in-depth on disease staging. The Mackie Classification stratifies disease into mild, moderate, and severe classes, or stages 1, 2, and 3, respectively.[2] (See Table on page 4 for more details). I'm curious how the panel employs the Mackie Classification in the diagnosis, documentation, and treatment of NK.

Dr. Desai: The Mackie Classification is a great reminder that NK exists on a spectrum and is not only the severe cases with corneal ulcers. However, a clinician must remember that not all patients will fit neatly into one of the Mackie Classification stages. Risk of progression is often more informative about the state of their disease than stage classification alone. In other words, not all stage 1 patients have the same disease.

Dr. Ayres: Catching stage 1 patients early—particularly if they're considered high-risk—is key to addressing the disease before it progresses. Early treatment prevents future complications. If we wait for the disease to progress to the point that a patient has a corneal ulcer or a nonhealing defect, then they're going to have a scarred cornea even if therapy successfully treats their condition.

Dr. Khandelwal: Early treatment in patients at risk of progression is very important. Progression from stage 1 NK to stage 2 NK can happen in a few days, for example with a simple incision from cataract surgery. Only a few years ago, detection of stage 1 patients was less of a focus for some clinicians, as some did not know to differentiate NK from diseases such as OSD and DED. Detection and treatment of early stage NK is very important.

CORNEAL SENSITIVITY TESTING

Dr. Khandelwal: Preventing a stage 1 NK patient from progression to stage 2 should be one of our goals. What pearls does the panel have for diagnosis of stage 1 patients?

Dr. Ayres: Corneal sensitivity testing is essential to confirm diagnosis of NK, and it is easy to integrate CST

KEY INSIGHT

Brandon Ayres, MD
Philadelphia

When communicating with a referring comprehensive ophthalmologist or optometrist, I offer a stepwise description of corneal sensitivity testing that I perform. By explaining that the test is inexpensive, easy to perform, and highly useful in detection of NK, I hope that these clinicians will begin to adopt CST as a practice pattern.

into your clinical examination.[4] Personally, I perform CST with a sterile swab. I place it on the supernasal, infranasal, supertemporal, infratemporal, and center areas of the cornea to check for sensation. I diagnose patients with NK who have reduced or lack of corneal sensation. This test is inexpensive and does not require specialized equipment, and I encourage my referral base to perform it before considering sending patients to a corneal specialist.

Dr. Feng: Performing CST in our clinics must be prioritized before anesthetizing their eyes to check staining and IOP. This is especially true for patients who traveled far to the clinic.

Dr. Khandelwal: How do you identify potential NK patients before they receive an exam?

Dr. Feng: To reduce in-office time for patients during the COVID-19 pandemic, I began aquiring histories over the phone before patients set foot in the office. As we've said, history is key to identifying potential NK. I can flag possible NK patients in this way and order a targeted workup including CST before any anesthetic drops are administered.

Dr. Desai: I have a general rule that patients are not to receive drops before they receive CST from one of our technicians. This allows patients to still receive topography and refraction, which do not require drops. After my team performs CST with a 2-inch piece of dental floss and documents results in the patient's record, any further elements of the exam that require drops can proceed. In this way, we have integrated CST into our workflow without disrupting it.

TABLE. STAGING IN NK*[1-3]

Stage 1 (Mild)	• Punctate epithelial keratopathy (PEK)
Stage 2 (Moderate)	• Persistent epithelial defect (PED)
Stage 3 (Severe)	• Corneal ulcer

1. Versura P, Giannaccare G, Pellegrini, et al. Neurotrophic keratitis: current challenges and future prospects. *Eye Brain.* 2018;10:37-45.
2. Sacchetti M, Lambiase A. Diagnosis and management of neurotrophic keratitis. *Clin Ophthalmol.* 2014;8:571-579.
3. Dua HS, Said DG, Messmer EM, et al. Neurotrophic keratopathy. *Prog Retin Eye Res.* 2018;66:107-31.

*Adapted from Mackie Classification

Treating the Root Pathogenesis of NK with OXERVATE®

ADOPTION & EARLY INTERVENTION WITH OXERVATE

Dr. Khandelwal: OXERVATE® (cenegermin-bkbj) ophthalmic solution 0.002% (20 mcg/mL) is FDA-approved for the treatment of all stages of neurotrophic keratitis in patients 2 years of age and older.[1] Cenegermin-bkbj, the active ingredient in OXERVATE, is structurally identical to the human nerve growth factor (NGF) protein made in ocular tissues.[1] Endogenous NGF is a protein involved in the differentiation and maintenance of neurons and is believed to support corneal integrity through three mechanisms (in preclinical models): corneal innervation, tear secretion, and epithelial cell growth.[1]

A pair of randomized controlled clinical trials enrolled the largest ever combined population of NK patients.[1] In the REPARO (European) trial, 72% of patients receiving OXERVATE were completely healed at week 8 compared with 33.3% of patients receiving vehicle.[6] In the NGF0214 (US) trial, 65% of patients receiving OXERVATE had complete corneal healing compared to 16.7% of vehicle-treated patients.[7] Complete corneal healing was defined as 0 mm staining in the lesion area and no persistent staining in the rest of the cornea.[7]

Approximately 80% of patients who achieved complete corneal healing in the REPARO (European) trial remained completely healed 48 weeks after one 8-week course of OXERVATE.[8]

The most common side effect was eye pain following instillation (16%).[1] Other adverse reactions, occurring in 1% to 10% of patients, were corneal deposits, foreign body sensation, ocular hyperemia, ocular inflammation, and tearing.[1] There was no evidence of systemic absorption or immunogenicity in clinical trials.[1]

KEY INSIGHT

Neel Desai, MD
Tampa, FL

OXERVATE is approved for the treatment of NK regardless of stage, which is important to remember for a clinician like me who is more concerned with risk of progression than disease stage. I remind myself that I am able to achieve complete corneal healing with OXERVATE, which I prefer to the palliative options I used to employ. This makes us more effective when treating disease.

Please see Important Safety Information on OXERVATE on page 8.

Dr. Khandelwal: OXERVATE® (cenegermin-bkbj) ophthalmic solution 0.002% (20 mcg/mL) has been one of my most used interventions for NK since I started orienting part of my practice around NK detection and treatment. *Dr. Ayres, how is OXERVATE incorporated in your NK treatment approach and practice?*

Dr. Ayres: OXERVATE quickly became my clinic's primary treatment for any patients with NK. Our early positive experiences with OXERVATE pushed us in this direction.

Dr. Desai: My clinic experienced success with OXERVATE. Stage 1 patients who are at high risk of progression receive OXERVATE therapy at my practice. Rather than go through alternative treatment courses that forgo targeting the root cause of NK, I think that OXERVATE should be considered for any patient at high risk of NK progression.

Dr. Feng: Setting expectations with patients is an important factor in ensuring successful treatment. I make sure I take the time to counsel my patients—they may experience eye pain given the side effect profile, adherence is important, and the role of the CONNECT to Care team.

Dr. Khandelwal: Before we move to our real-world cases, let's discuss the role of Dompe CONNECT to Care, as Dr. Feng mentions. Are there any insights we can provide to help ensure a smooth process for our office and patients to access this medication?

Dr. Feng: It's important to know about the support available when prescribing OXERVATE. Dompé CONNECT to Care (DC2C) is the team that helps clinicians and patients access OXERVATE. I have found this service to be very effective. Additionally, I recommend having a point person in your practice who can interact with DC2C and prepare the necessary paperwork to augment workflow when prescribing this treatment.

Dr. Lee: One of the benefits of OXERVATE is that there are few barriers to treatment for patients thanks to the DC2C program's facilitation with benefits verification, prior authorization, and financial resources. I agree with Dr. Feng that having a designated staff member who manages submissions will streamline your practice.

Dr. Desai: I tell my patients that after I prescribe OXERVATE, a representative from the DC2C program will contact them. This prepares them for next steps and hopefully prevents any delays in the approval process.

Collaboration With Other Eye Care Providers

Dr. Khandelwal: Treatment of NK is a collaborative endeavor, and many of the cases I see are referred to me by other eye care providers. Who is referring patients to your practices? And do all of these cases need to be referred?

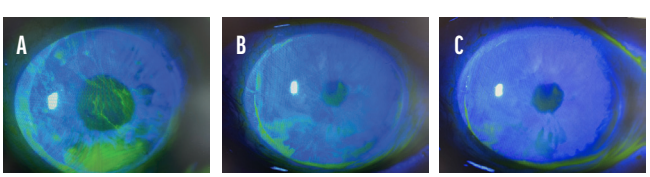
Dr. Feng: Comprehensive ophthalmologists and optometrists are well suited to manage the disease and keep patients with NK in their care. Given the tools now at their disposal and increased experience, these clinicians are best positioned to identify early and manage a patient's disease.

Dr. Desai: It is my impression that a vast majority of NK can be detected and diagnosed in solo practices by comprehensive ophthalmologists and optometrists. Such practices are well equipped to detect and diagnose NK through patient history and CST, and they should also consider themselves prepared to treat NK now that OXERVATE is available.

Dr. Lee: As important as it is to educate eye care providers who can diagnose and treat NK, we cannot overlook the importance of educating our colleagues in the retina and glaucoma spaces. I send these providers notes about how we managed their patients' NK, and we can use the same approach to educate other subspecialists to be aware of the disease and risks.

CASE 1: STAGE 1 NK

Dr. Khandelwal: An 85-year-old woman was referred to my clinic after undergoing pars plana vitrectomy (PPV) several weeks prior. A corneal abrasion was present after surgery, which had started to heal over several weeks under a bandaged contact lens. When she presented to my clinic, irregular epithelium, epithelial hyperplasia, and subepithelial haze were all detected, and visualization of the retina was difficult.



Photos courtesy of Sumitra Khandelwal, MD.

Figure 1. This patient was determined to have stage 2 NK by the time OXERVATE therapy was initiated (A). Four weeks after starting OXERVATE therapy, the patient showed moderate signs of improvement (B). After 8 weeks of OXERVATE therapy, significant healing was observed in this patient (C).

Please see Important Safety Information on OXERVATE on page 8.

KEY INSIGHT

Sumitra Khandelwal, MD
Houston

The Dompé CONNECT to Care program works hard to ensure that patients can access this biologic. In fact, most patients with commercial insurance pay less than $100 out-of-pocket for an 8-week course of OXERVATE® (cenegermin-bkbj) ophthalmic solution 0.002% (20 mcg/mL) therapy.

This patient had a history of glaucoma that was managed long-term with topical brimonidine/timolol ophthalmic solution. Surgical history included Descemet's Stripping Endothelial Keratoplasty, cataract surgery, and her recent PPV. She had multiple factors that led me to suspect possible NK. I then performed CST with a cotton swab, which showed complete anesthesia of the cornea.

Dr. Feng: Were you able to classify this patient's disease based on your clinical findings?

Dr. Khandelwal: I was worried about progression. I believed that the patient had stage 2 NK that had improved slightly during the period in which she wore a bandaged contact lens, and I diagnosed her with stage 1 NK with a risk of reverting back to stage 2 if intervention was not initiated. The bandaged contact lens, while protective, did not address the underlying cause of this patient's disease, and I knew that a therapy that addressed the root cause of NK was needed.

When we began OXERVATE therapy, the patient had reverted to stage 2 NK (Figure 1A). We prescribed a regimen of 1 drop 6 times daily for 8 weeks at 2-hour intervals. At week 4, evidence of healing was detected (Figure 1B). At week 8, the patient's condition had improved significantly (Figure 1C).

Dr. Lee: Starting this patient on therapy quickly was key to preventing scarring that could result in long-term vision loss. Did you observe any changes to the subepithelial haze first detected upon presentation?

Dr. Khandelwal: Subepithelial haze had resolved by week 8, which was noted by the retina specialist with whom I co-managed this patient. In this case, prompt intervention likely halted disease progression.

CASE 2: STAGE 1 NK

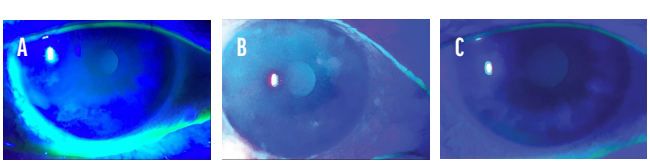
Dr. Desai: A 66-year-old monocular woman was referred to my clinic for a dry eye consultation. She came in complaining of blurry, fluctuating vision and was not having dry eye symptoms. Upon interviewing the patient, she explained that she previously had dry eye symptoms, but that she had not experienced them for several months. She expressed frustration with her referring providers, who pursued dry eye treatments despite her insistence that she was symptom free.

She was monocular due to childhood retinoblastoma, which resulted in a prosthesis in her left eye. Her right eye had undergone LASIK approximately 25 years ago, with 2 subsequent PRK touchups. She had seasonal allergies managed with over-the-counter therapy, as well as long-standing dry eye and meibomian gland dysfunction.

Dr. Lee: Listening to our patients is key to understanding their diagnosis. For a patient with dry eye experience to articulate that they do not have dry eye is meaningful. I would be concerned that her exposure to multiple surgeries had resulted in damage to her corneal nerves.

Dr. Desai: One of my mentors told me that we should listen to our patients and they will tell us their diagnosis. I agree that listening is important. Dr. Lee highlighted her multiple ocular surgeries; her history also led me to suspect NK. I used dental floss to check her corneal sensitivity to confirm NK. This test revealed anesthesia in 3 of the 5 corneal zones (ie, inferonasal, inferotemporal, and central cornea). Mild punctate staining was also observed, which corresponded with the areas of anesthesia observed on CST (Figure 2A).

Dr. Ayres: The risk factors for NK in this patient include multiple ocular surgeries, experience with dry eye, and seasonal allergies managed with over-the-counter drugs that



Photos courtesy of Neel Desai, MD.

Figure 2. At baseline, mild punctate staining was observed (A). After 4 weeks, corneal staining showed evidence of improvement (B). At week 8, corneal staining demonstrated significant improvement (C). This corresponded with improved corneal sensation.

Please see Important Safety Information on OXERVATE on page 8.

may have a drying effect. I would consider a patient with this many risk factors to be at high risk of NK progression, and I would recommend prompt therapy.

Dr. Desai: I diagnosed this patient with stage 1 NK and prescribed OXERVATE® (cenegermin-bkbj) ophthalmic solution 0.002% (20 mcg/mL) therapy at 1 drop every 2 hours 6 times per day for 8 weeks. Corneal staining improvement was observed at week 4 (Figure 2B) and was resolved by week 8 (Figure 2C). We monitored this patient closely given her history and monocular status. At month 5, she had not experienced recurrence of NK symptoms. She has resumed dry eye therapies.

Dr. Khandelwal: I want to thank my colleagues for joining me at this roundtable discussion. I trust that the wisdom, insights, and real-world experience they offered may be useful to clinicians who are increasingly identifying, diagnosing, and treating NK in their practices. ■

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2. Sacchetti M, Lambiase A. Diagnosis and management of neurotrophic keratitis. *Clin Ophthalmol*. 2014;8:571-579.
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4. Semeraro F, Forbice E, Romano V, et al. Neurotrophic keratitis. *Ophthalmologica*. 2014;231(4):191-197.
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8. Data on file. NGF0212.

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Please see Important Safety Information on OXERVATE on page 8.

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 cenegermin-bkbj onto the area of the corneal lesion. Lenses may be reinserted 15 minutes after administration.

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 sensations in the eye, ocular hyperemia (enlarged blood vessels in the white of the eyes), swelling (inflammation) of the eye, and increase of tears (1-10% of patients).

WHAT IS OXERVATE™?

OXERVATE® (cenegermin-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: cenegermin-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 cenegermin-bkbj onto the area of the corneal lesion. Lenses may be reinserted 15 minutes after administration.

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.

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).

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 risk information provided here is not comprehensive. To learn more, talk about OXERVATE® with your health care provider or pharmacist.