

## Early Access to Medicines Scheme – Treatment protocol – Information for patients

### Introduction

The aim of the Early Access to Medicines Scheme (EAMS) is to provide earlier availability of promising new unlicensed medicines (medicines that do not have a marketing authorisation) to UK patients that have a high unmet clinical need. The medicines included in the scheme are those that are intended to treat, diagnose or prevent seriously debilitating or life threatening conditions where there are no adequate treatment options. More information about the scheme can be found

here: <http://www.mhra.gov.uk/Howweregulate/Innovation/EarlyaccesstomedicinesschemeEAMS/index.htm>

The information below is intended for you, the patient, and is provided by the pharmaceutical company that manufactures the medicine. This medicine does not yet have a drug licence (also called a marketing authorisation). More information about medicines licensing can be found here:

<http://www.mhra.gov.uk/Safetyinformation/Generalsafetyinformationandadvice/Adviceandinformationforconsumers/MymedicineFromlaboratorytopharmacyshelf/Licensingmarketingauthorisation/index.htm>

This medicine can be prescribed for individual patients to meet specific needs provided they are given sufficient information about the medicine to make an informed decision. Informed consent should be obtained from you prior to treatment.

This information is provided to help you decide with your doctor on whether to use the medicine and helps explain how to use the medicine in accordance with the pharmaceutical company's instructions for safe and proper use. Whilst you are using this medicine, data will be collected on the use and safety profile of the medicine, to ensure that the benefits of taking the medicine outweigh any potential risks.

## Information for the patient:

### **OXERVATE 20 micrograms/ml eye drops solution** cenegermin

▼ This medicine is subject to additional monitoring. This will allow quick identification of new safety information. You can help by reporting any side effects you may get. See the end of section 4 for how to report side effects.

#### **Read all of this leaflet carefully before you start using this medicine because it contains important information for you.**

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

#### **What is in this leaflet**

1. What OXERVATE is and what it is used for
2. What you need to know before you use OXERVATE
3. How to use OXERVATE
4. Possible side effects
5. How to store OXERVATE
6. Contents of the pack and other information

#### **1. What OXERVATE is and what it is used for**

OXERVATE contains the active ingredient cenegermin. Cenegermin is a type of nerve growth factor (a human protein) which is naturally present on the eye surface.

OXERVATE is used to treat adults with moderate or severe 'neurotrophic keratitis'. This is a disease affecting the cornea (the transparent layer in the front part of the eye) which causes defects on the outer surface of the cornea that do not heal naturally or corneal ulcers.

OXERVATE is intended to allow the healing of the cornea.

#### **2. What you need to know before you use OXERVATE**

##### **Do not use OXERVATE:**

- if you are allergic to cenegermin or any of the other ingredients of this medicine (listed in section 6).

### Warnings and precautions

Only use this medicine in your affected eye(s).

Talk to your doctor **before** using this medicine:

- if you have an infection in your eye, as the infection should be treated first. If you get an eye infection **whilst** using OXERVATE, you should stop your treatment and consult your doctor for advice straightaway.
- if you have an eye cancer, because this medicine might worsen your cancer.
- if you are taking any eye drops containing corticosteroids (e.g. to treat an ocular inflammation) or preservatives (e.g. benzalkonium chloride, polyquaternium-1, benzododecinium bromide, cetrimide). Eye drops containing these substances could slow down or interfere with the healing of your eye and should therefore be avoided during treatment with this medicine.

Treatment with OXERVATE may cause you mild to moderate eye discomfort such as eye pain. If you experience a severe eye reaction seek medical advice from your doctor.

Contact lenses could interfere with the correct use of this medicine. If you wear contact lenses remove them before using this medicine and **wait 15 minutes after** using this medicine before reinserting them.

### Children and adolescents

This medicine should not be used in children and adolescents below 18 years of age, as there is not enough information about its use in this age group.

### Other medicines and OXERVATE

Tell your doctor or pharmacist if you are using, have recently used or might use any other medicines.

You should wait **at least 15 minutes before or after** using OXERVATE if you use any other eye drops. This will help to avoid one eye drop diluting the other eye drop. If you also use an eye ointment or gel or an eye drop with a thick consistency, you should use OXERVATE **first**, and then wait **at least 15 minutes before** using the other medicine.

### Pregnancy and breast-feeding

If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before using this medicine.

The use of this medicine should be avoided during pregnancy. Talk to your doctor if you are pregnant or think you may be pregnant.

It is not known if this medicine passes into breast milk. Talk to your doctor before breast-feeding your baby, as a decision must be made whether to stop breast-feeding or to avoid or stop OXERVATE therapy.

### Driving and using machines

Your vision may be temporarily blurred immediately after using this medicine. If this happens, wait until your vision clears before you drive or use machines.

### 3. How to use OXERVATE

Always use this medicine exactly as your doctor or pharmacist has told you. Check with your doctor or pharmacist if you are not sure.

**The recommended dose** is 1 drop in the affected eye 6 times a day at 2-hourly intervals, starting in the morning (i.e. 6 drops per day within 12 hours). You should continue your treatment for 8 weeks.

#### Instructions for use

Follow these instructions carefully and ask your doctor or pharmacist if there is anything you do not understand.

Ocular use.

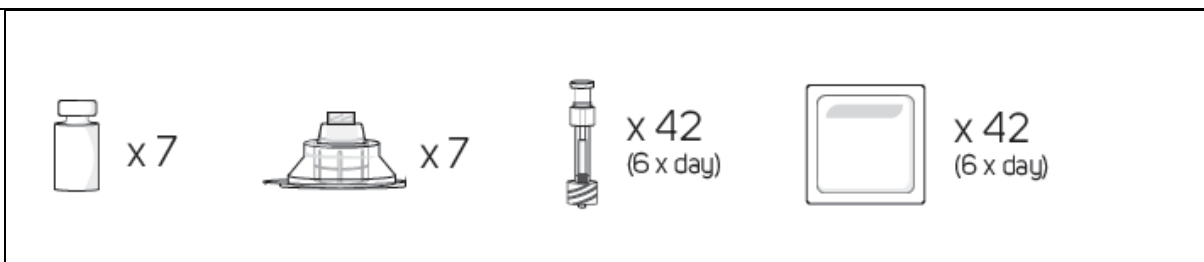
At the beginning of your treatment (day 0) and at the end of first 4 weeks of treatment, you will receive:

- a carton box containing 4 weekly cartons containing cenegermin eye drops solution
  - You should bring cenegermin eye drops solution, one box containing 4 weekly kits, at home as soon as possible and immediately store it in a freezer below -20 °C.
  - Once removed from the box, the weekly kit in use containing 7 vials of cenegermin eye drops solution must be kept at 2-8°C for a maximum of 7 days.
  - Once taken out from the weekly kit, the individual daily vial can be kept at room temperature before you use it for each instillation in the affected eye (s) as far as 12 hours from vial opening are not exceeded.
- a carton box containing:
  - 30 vial adapters (i.e. 1 per day + 2 spare ones).
  - 175 pipettes (i.e. 6 per day + 7 spare ones).Pipettes and adapters will be provided separately in single sterile PE packages and may be kept at room temperature (please do not freeze them).
- 2 carton boxes containing 100 disinfectant wipes each (i.e. 6 per day + 32 spare ones). Disinfectant wipes are included to clean the surface of the valve on the luer lock connector of the vial adapter as described in the instructions.

These quantities are sufficient to administer the product for four weeks.

Vial adapters, pipettes and wipes can be stored at room temperature, but should not be frozen.

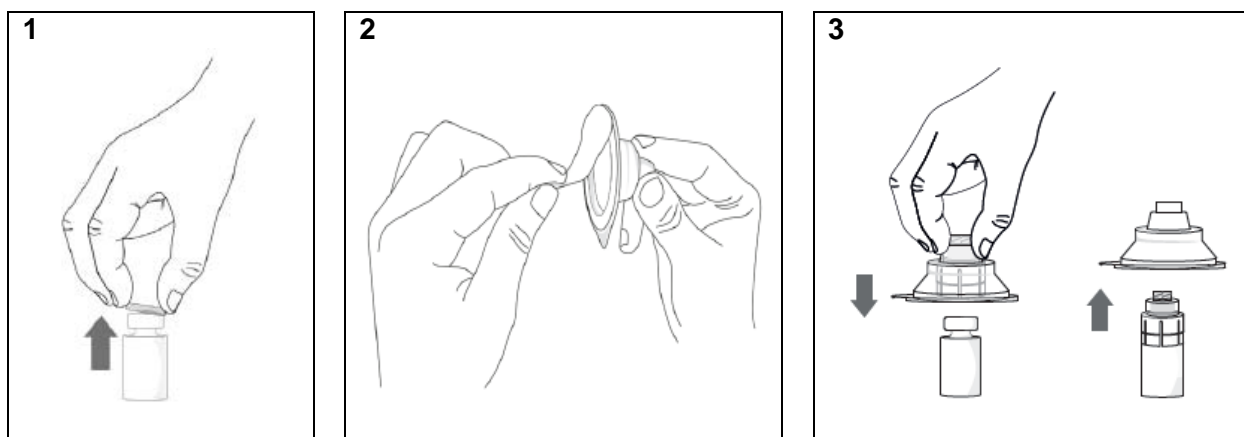
#### Items provided for a week of treatment



The weekly carton contains 7 vials of OXERVATE (1 vial per day of the week). Remove the weekly carton of OXERVATE from the insulated container and store it in a fridge as soon as you can (and in any case no later than 5 hours from when you receive the medicine from your pharmacist). Since at the pharmacy this medicine is stored in a freezer, in case treatment is started right away after receiving the weekly carton, you will have to wait until the first vial is thawed (this could take up to 30 minutes).

Take an individual vial of this medicine from the fridge in the morning (always at the same time each morning), and prepare it in the following way:

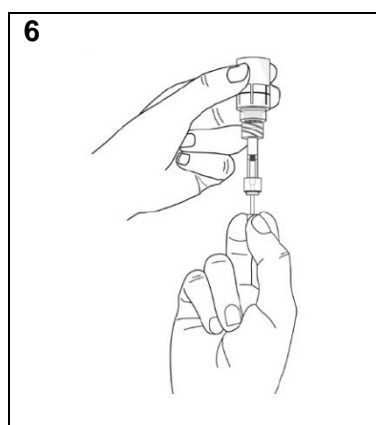
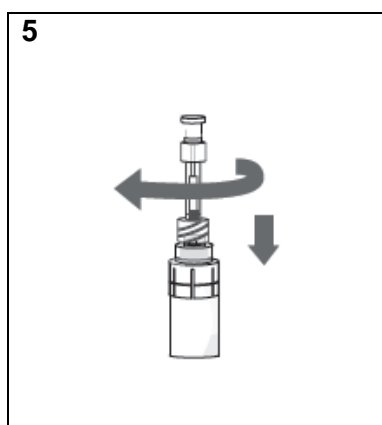
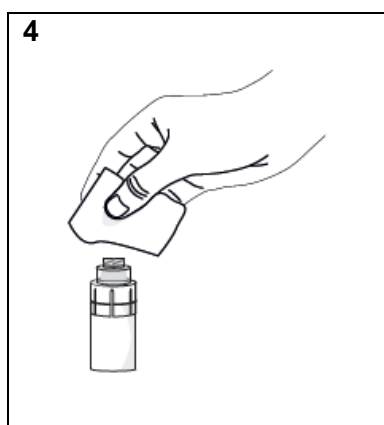
- Wash your hands.
- If you wear contact lenses, take them out before using the drops.
- Remove the plastic flip-off cap from the vial (**picture 1**).
- Peel-off the back of the vial adapter blister pack (**picture 2**).
- Without removing the vial adapter from its blister pack, connect it to the vial by firmly pushing it down until it snaps into place over the neck of the vial. The spike of the vial adapter should pierce through the vial's rubber stopper. Once the vial adapter has been connected correctly, it should not be removed from the vial (**picture 3**).
- Remove and discard the packaging of the vial adapter.



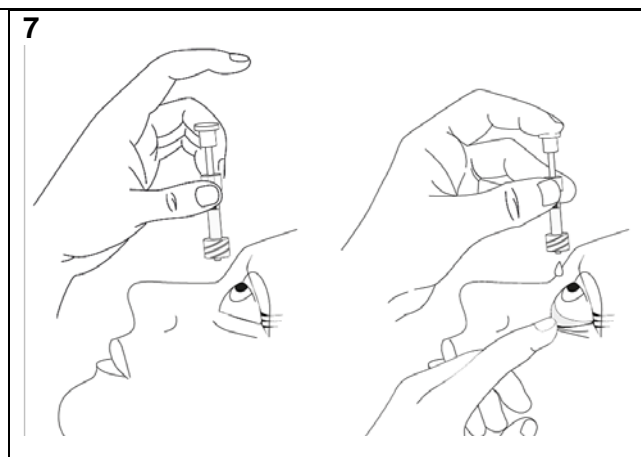
The multi-dose vial of OXERVATE is now ready for use (1 drop in the affected eye every 2 hours six times a day). The vial can be stored in the fridge or below 25 °C throughout the day, but should not be frozen.

To withdraw and administer each dose of this medicine, follow the steps below:

- Take a single disinfectant wipe and gently clean the surface of the valve on the connector part of the vial adapter (**picture 4**). After cleaning, wait for approximately 1 minute to allow the valve to dry.
- Take a pipette (dropper) and remove it from its protective packaging.
- Screw the pipette (clockwise) into the connector part of the vial adapter (**picture 5**).
- Ensure that the pipette plunger is pushed all the way down.
- Turn the vial upside-down (with the pipette still connected) and gently pull the plunger until it stops, to draw the solution into the pipette. Ensure the plunger has reached the stop point (**picture 6**).



- Check the pipette to ensure it contains the eye drops solution. Air bubbles may cause blockage and prevent the pipette from filling properly (especially at first withdrawal). If the pipette is empty, keep the vial with the connected pipette upside-down, push the plunger all the way in and pull it out again.
- Once it has been correctly filled, unscrew the pipette from the connector part of the vial adapter.
- Holding the pipette, pointing down, between your middle finger and thumb, tilt your head back and position the pipette above your affected eye. Pull down your lower eyelid, folding between the inner eyelid and the eyeball. Gently push the plunger in until a single drop is dropped into the conjunctival fornix (**picture 7**). Make sure you do not touch your eye with the tip of the pipette.
- With your head still tilted back, blink a few times so that the medicine covers the surface of your eye.
- Immediately discard the used pipette after use, even if there is still some liquid left in it.
- If a drop misses your eye, try again, using a new pipette and wipe.
- After each use throughout the day, place the vial back in the fridge (or keep it below 25 °C) for the rest of the day, with the vial adapter still connected.



Repeat the above process (from picture 4 onwards) every 2 hours 6 times a day. Use a new disinfectant wipe and a new pipette each time.

If you use drops in both eyes, repeat the above instructions for your other eye using a new pipette (in this case, you will need to use 2 vials per day).

Discard the used vial at the end of each day (even if there is still some liquid left in it), and in any case no later than 12 hours from the time you connected the vial adapter to it.

You will receive a new supply of OXERVATE after the first 4 weeks of treatment.

To ensure accurate dosing every 2 hours, you could set an alarm as a reminder for dosing.

To control that six doses have been taken at the end of each treatment day, you should use the weekly dose recording card provided with the delivery system. On that card you should write down the date of the first use of the weekly supply, the time of the vial opening (i.e. when you connect the vial adapter to the vial) and track each time you use an eye drop of this medicine, over the week.

**If you use more OXERVATE than you should**

If you use more than you should, flush the affected eye with lukewarm water. Do not put in any more drops until it is time for your next regular dose. Using more OXERVATE than is recommended is not likely to be harmful. Continue with your next dose as scheduled.

**If you forget to use OXERVATE**

Continue with your next dose as scheduled. Do not use a double dose to make up for the forgotten dose. You can give the missed dose 2 hours after your last scheduled dose of the day, provided this is still within 12 hours from first opening the daily vial. Do not use more than 6 drops each day in the affected eye(s).

**If you stop using OXERVATE**

The lesion or ulcer in your eye will worsen and could lead to infections or impaired vision. Speak to your doctor first if you intend to stop using OXERVATE.



If you have any further questions on the use of this medicine, ask your doctor or pharmacist.

#### **4. Possible side effects**

Like all medicines, this medicine can cause side effects, although not everybody gets them.

The majority of side effects occur generally in and around the eyes.

The following side effects have been reported:

##### **Very common (may affect more than 1 in 10 people)**

- eye pain.

##### **Common (may affect up to 1 in 10 people)**

- inflammation of the eye;
- pain in the eyelid;
- abnormal sensation and discomfort in the eye, including feeling that there is something in the eye;
- increase of tears (this could include symptoms such as discharge in the eye);
- inflammation of the eyelid with itching and redness;
- redness of the conjunctiva (mucous membrane that covers the front of the eye and lines the inside of the eyelids);
- sensitivity to light;
- irritation in or around the eye;
- headache.

##### **Uncommon (may affect up to 1 in 100 people)**

- excessive ingrowth of blood vessels into the cornea;
- infection of the cornea with pus and swelling.

##### **Reporting of side effects**

If you get any side effects, talk to your prescribing doctor. This includes any possible side effects not listed in this leaflet. By reporting side effects you can help provide more information on the safety of this medicine.

#### **5. How to store OXERVATE**

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the outer carton and vial label after "EXP". The expiry date refers to the last day of that month.



Store the 4 week treatment carton in the freezer below -20 °C.

Store only the weekly carton in use (containing 7 vials of OXERVATE) in the fridge (2-8 °C).

Once a weekly carton is used, another one should be moved from freezer to refrigerator.

After the vial adapter is connected to the vial, it can be stored in the fridge or below 25 °C. Discard the used vial at the end of the day (even if there is still some liquid left in it), and in any case no later than 12 hours from the time you connected the vial adapter to it.

The pipettes included in the delivery system are single-use only. Each pipette should be discarded immediately after using, even if there is still some liquid left in it.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

If you have any further questions on the use of this medicine, ask your doctor.

You will receive a new supply of cenegermin eye drops after 4 weeks.

Any used/unused medicinal product should be put again in its weekly carton and brought back to the study site for accountability and treatment compliance verification.

Waste materials should be disposed of in accordance with local requirements.

## 6. Contents of the pack and other information

### What OXERVATE contains

- The active substance is cenegermin. 1 ml of OXERVATE contains 20 micrograms of cenegermin.
- The other ingredients are trehalose dihydrate, mannitol, disodium hydrogen phosphate anhydrous, sodium dihydrogen phosphate dihydrate, hydroxypropylmethyl cellulose, polyethylene glycol 6000, L-methionine and water for injections, hydrochloric acid and sodium hydroxide and nitrogen.

### What OXERVATE looks like and contents of the pack

OXERVATE is a clear, colourless eye drops solution.

It is supplied in multi-dose glass vials.

Each vial contains 1 ml eye drops solution.

The vials are contained in a weekly cardboard carton containing 7 vials.

A 4 week treatment cardboard will be delivered in a box, containing 4 weekly cartons.

For each weekly treatment, you will receive 7 vial adapters, 42 pipettes, 42 disinfectant wipes and a dose recording card are provided separately from the vials. Extra adapter (1), pipettes (3) and wipes (3) are included as spares.

7. Scientific Opinion Holder

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Berks. SL1 4DX

8. EAMS number

EAMS 32162/0001

9. Date of Scientific Opinion

01/06/2017

**Additional information:**

N.A.

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