Package leaflet:
Information for the patient

RMP Code: Luxturna EU RMP V1.5 Feb 2022

This document has been reviewed and approved by The Saudi Food and Drug Authority (SFDA)

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Package leaflet:
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Luxturna *5 x 10^{12} vector genomes/mL concentrate and solvent for solution for injection voretigene neparvovec*

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.

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Read all of this leaflet carefully before you are given 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 nurse.
- If you get any side effects, talk to your doctor or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet:

1. What Luxturna is and what it is used for

Luxturna is a gene therapy product that contains the active substance voretigene neparvovec.

Luxturna is used for the treatment of adults and children with vision loss due to inherited retinal dystrophy caused by mutations in the *RPE65* gene. These mutations prevent the body from producing a protein needed for vision and so lead to loss of sight and eventual blindness.

The active substance in Luxturna, voretigene neparvovec is a modified virus that contains a working copy of the *RPE65* gene. After injection it delivers this gene into the cells of the retina, the layer at the back of the eye that detects light. This enables the retina to produce the proteins needed for vision. The virus used to deliver the gene does not cause disease in humans.

Luxturna will be given to you only if genetic testing shows that your vision loss is caused by mutations in the *RPE65* gene.

2. What you need to know before you are given Luxturna

You will not be given Luxturna

- if you are allergic to voretigene neparvovec or any of the other ingredients of this medicine (listed in section 6)
- if you have an eye infection
- if you have eye inflammation

If any of the above applies to you, or if you are unsure of any of the above, please talk to your doctor before you receive Luxturna.

Warnings and precautions

Before receiving treatment with Luxturna:

- Tell your doctor if you have signs of an eye infection or eye inflammation, for example if you have eye redness, sensitivity to light, eye swelling or eye pain.
- Tell your doctor if you have an active infection of any sort. Your doctor may delay your treatment until your infection is gone because this medicine may make it more difficult for you to fight an infection. See also section 3.

After receiving Luxturna

- Get immediate care from your doctor if your eye or eyes become red, painful, sensitive to light, you see flashes or floaters in your vision, or if you notice any worsening or blurred vision.
- You should avoid air travel or other travel to high elevations until advised by your doctor. During treatment with this medicine, the doctor inserts an air bubble in the eye, which is slowly absorbed by your body. Until the bubble is fully absorbed, air travel or other travel to high elevations may make the bubble expand and lead to eye damage, including vision loss. Please talk to your doctor before travelling.
- You should avoid swimming because of an increased risk of infection in the eye. Please talk to your doctor before going to swim after receiving treatment with Luxturna.
- You should avoid strenuous physical activity because of an increased risk of injury to the eye. Please talk to your doctor before beginning to engage in strenuous physical activity after receiving Luxturna
- Some people develop cataracts. A cataract is clouding of the natural lens inside the eye that can make it harder to see clearly. The development or worsening of cataracts is a known complication of the eye surgery that will be required before you receive Luxturna.There is an additional risk of cataract if the lens inside the eye is damaged by the needle used to inject the medicine into the back of the eye.
- You may have temporary visual disturbances, such as light sensitivity and blurred vision. Tell your doctor about any visual disturbances that you experience. Your doctor may be able to help reduce any discomfort caused by these temporary disturbances.
- Some medicine may be present in your tears. You and your caregiver should place any used dressings and waste material with tears and nasal secretions in s bags before disposing of them. You should follow these precautions for 14 days.
- You and your caregiver, especially if pregnant, breast-feeding or with a suppressed immune system, should wear gloves during dressing changes and when disposing of the dressings and other waste material. Follow these precautions for 14 days after the treatment.
- You will not be able to donate blood, organs, tissues and cells for transplantation after you have been treated with Luxturna.

Children and adolescents

Luxturna has not been studied in children under four years of age.

Other medicines and Luxturna

Please tell your doctor if you are taking, have recently taken or might take any other medicines.

Pregnancy and breast-feeding and fertility

If you are pregnant or breast-feeding, think you might be pregnant, or are planning to have a baby, ask your doctor or nurse for advice before being treated with Luxturna.

The effects of this medicine on pregnancy and the unborn child are not known.
As a precaution, you should not receive Luxturna while you are pregnant.
Luxturna has not been studied in breast-feeding women. It is not known whether it passes into breast milk. Ask your doctor whether you should stop breast-feeding after receiving Luxturna.
There is no information on the effect of Luxturna on male or female fertility.

Driving and using machines

You may have temporary visual disturbances after receiving Luxturna. Do not drive or use heavy machines until your vision has recovered. Talk to your doctor before resuming these activities.

Important information about some of the ingredients of Luxturna

Luxturna contains less than 1 mmol sodium (23 mg) per dose, i.e. essentially 'sodium-free'.

3. How Luxturna is given to you

VLuxturna will be given to you in an operating room by surgeons experienced in performing eye surgery.

Luxturna is given under anaesthesia. Your doctor will talk to you about the anaesthesia and how it will be given to you.

Your doctor will carry out eye surgery to remove the clear gel inside the eye, and then inject Luxturna directly under your retina, the thin light-sensing layer at the back of that eye. This will be repeated on your other eye at least 6 days afterwards. You will need to stay for post-operative observation for a few hours after each procedure to monitor your recovery and watch for any side effects from the surgery or the anaesthesia.

Before Luxturna treatment is started, your doctor may prescribe a medicine that will suppress your immune system (the body's natural defences) so that it will not try to fight the Luxturna when it is given. It is important that you take this medicine according to the instructions given. Do not stop taking the medicine without first talking to your doctor.

If you are given more Luxturna than you should be
As this medicine is given to you by a doctor, it is unlikely that you will be given too much. If it does occur, your doctor will treat the symptoms as necessary. Tell your doctor or nurse if you have any visual problems.
If you have any further questions on the use of this medicine, ask your doctor or nurse.

4. Possible side effects

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

The following side effects may happen with Luxturna:

Common (may affect up to 1 in 10 people)

- Deposits under the retina

The following side effects may happen with the injection procedure:

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

- Redness of the eye
- Cataract (clouding of the lens)
- Increased pressure in the eye

Common (may affect up to 1 in 10 people)

- Break in the retina
- Eye pain
- Eye swelling
- Detachment of the retina
- Nausea (feeling sick), vomiting, abdominal (belly) pain, lip pain
- Change of the electrical activity of the heart
- Headache, dizziness
- Rash, facial swelling
- Anxiety
- Problems associated with the placement of a breathing tube in the windpipe
- Breakdown of the surgical wound

Not known (frequency cannot be estimated from the available data)

- Clouding in the gel-like substance inside the eye (vitreous opacities)
- Atrophy of the (chorio)retina

Damage to the tissues of the eye may be accompanied by bleeding and swelling and an increased risk of infection. There is reduced vision in the days after surgery that usually improves; tell your doctor if vision does not return.

Reporting of side effects

If you get any side effects, talk to your doctor or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via www.report.novartis.com. By reporting side effects, you can help provide more information on the safety of this medicine.

You can report any problem or adverse events or request additional copies of the materials through:

Patient Safety Department Novartis Pharma AG - Saudi Arabia -.
Toll Free Number: 8001240078
Phone: +966112658100
Fax: +966112658107
Email: adverse.events@novartis.com
Or by online: https://report.novartis.com/

Saudi Food and Drug Authority National Pharmacovigilance Center
Unified Contact Center: 19999
Fax: +966112057662
Email: npc.drug@sfda.gov.sa
Or by online: https://ade.sfda.gov.sa

Other sources of information

This leaflet is available as an audio file and in a large print from the web site: www.voretigeneneparvovec.support.

For any information about this medicine, please contact the local representative of the Marketing Authorisation Holder:

Patient Safety Department Novartis Pharma AG - Saudi Arabia -. Toll Free Number: 8001240078 Phone: +966112658100 Fax: +966112658107 Email: adverse.events@novartis.com Or by online: https://report.novartis.com/

RMP reference:
Luxturna EU RMP V1.5 Feb, 2022

Notes

Notes

Presentation:
Each mL of concentrate contains 5 x 1012 vector genomes (vg).
Each single dose 2 mL vial of Luxturna contains 0.5 extractable mL of concentrate which requires a 1:10 dilution prior to administration.
After dilution each dose of Luxturna contains 1.5 x 1011 vg in a deliverable volume of 0.3 mL
Indications: Luxturna is indicated for the treatment of adult and paediatric patients with vision loss due to inherited retinal dystrophy caused by confirmed biallelic RPE65 mutations and who have sufficient viable retinal cells.
Dosage and administration:
Treatment should be initiated and administered by a retinal surgeon experienced in performing macular surgery.
Posology: Patients will receive a single dose of 1.5 x 1011 vg voretigene neparvovec in each eye. Each dose will be delivered into the subretinal space in a total volume of 0.3 mL. The individual administration procedure to each eye is performed on separate days within a close interval, but no fewer than 6 days apart
Immunomodulatory regimen: Prior to initiation of the immunomodulatory regimen and prior to administration of Luxturna, the patient must be checked for symptoms of active infectious disease of any nature, and in case of such infection the start of treatment must be postponed until after the patient has recovered.
Starting 3 days prior to the administration of Luxturna to the first eye, it is recommended that an immunomodulatory regimen is initiated following the schedule below. Initiation of the immunomodulatory regimen for the second eye should follow the same schedule and supersede completion of the immunomodulatory regimen of the first eye.
Pre operative: 3 days prior to Luxturna administration, Prednisone (or equivalent)
1 mg/kg/day. (maximum of 40 mg/day)
Post operative:
- 4 days (including the day of administration), Prednisone (or equivalent)1 mg/kg/day
(maximum of 40 mg/day)
- Followed by 5 days, Prednisone (or equivalent) 0.5 mg/kg/day (maximum of 20 mg/day)
- Followed by 5 days of one dose every other day, Prednisone (or equivalent) 0.5 mg/kg every other day (maximum of 20 mg/day)
Elderly: The safety and efficacy of voretigene neparvovec in patients ≥65 years old have not been established. However, no adjustment in dosage is necessary for elderly patients
Hepatic and renal impairment: The safety and efficacy of voretigene neparvovec have not been established in patients with hepatic or renal impairment. No dose adjustment is required in these patients
Paediatric population: The safety and efficacy of voretigene neparvovec in children aged up to 4 years have not been established. No data are available. No adjustment in dosage is necessary for paediatric patients.
Method of administration: Subretinal use. Luxturna is a sterile concentrate solution for subretinal injection that requires thawing and dilution prior to administration
This medicinal product must not be administered by intravitreal injection. Luxturna is a single use vial for a single administration in one eye only. The product is administered as a subretinal injection after vitrectomy in each eye. It should not be administered in the immediate vicinity of the fovea to maintain foveal integrity.
The administration of voretigene neparvovec should be carried out in the surgical suite under controlled aseptic conditions. Adequate anaesthesia should be given to the patient prior to the procedure. The pupil of the eye to be injected must be dilated and a broad spectrum microbicide should be topically administered prior to the surgery according to standard medical practice.
Precaution to be taken before manipulating or administering the medicinal product
This medicinal product contains genetically modified organisms. Personal protective equipment (to include laboratory coat, safety glasses and gloves) should be worn while preparing or administering voretigene neparvovec
Contraindications: Hypersensitivity to the active substance(s) or to any of the excipients.
Ocular or periocular infection. Active intraocular inflammation.
Warnings and precautions:
Proper aseptic techniques should always be used for the preparation and administration of Luxturna.
The following adverse reactions have been observed with the administration procedure:
Eye inflammation (including endophthalmitis), retinal tear and retinal detachment. Patients should be instructed to report any symptoms suggestive of endophthalmitis or retinal detachment without delay and should be managed appropriately.
Retinal disorder (foveal thinning, loss of foveal function), macular hole, maculopathy (epiretinal membrane, macular pucker) and eye disorder (foveal dehiscence).
Increase in intraocular pressure. Intraocular pressure should be monitored prior to and following administration of the medicinal product and managed appropriately. Patients should be instructed to avoid air travel or other travel to high elevations until the air bubble formed as a result of administration of Luxturna has completely dissipated from the eye. A time period of up to one week or more following injection may be required before dissipation of the air bubble; this should be verified on ophthalmic examination. A rapid increase in altitude while the air bubble is still present can cause a rise in eye pressure and irreversible vision loss.
Temporary visual disturbances, such as blurred vision and photophobia, may occur during the weeks that follow the treatment. Patients should be instructed to contact their healthcare professional if visual disturbances persist. Patients should avoid swimming because of an increased risk of infection in the eye. Patients should avoid strenuous physical activity because of an increased risk of injury to the eye. Patients may resume swimming and strenuous activity, after a minimum of one to two weeks, on the advice of their healthcare professional.

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LUXTURNA
voretigene neparvovec
for subretinal injection

Shedding

Transient and low-level vector shedding may occur in patient tears. Patients/caregivers should be advised to handle waste material generated from dressings, tears and nasal secretion appropriately, which may include storage of waste material in sealed bags prior to disposal. These handling precautions should be followed for 14 days after administration of voretigene neparvovec. It is recommended that patients/caregivers wear gloves for dressing changes and waste disposal, especially in case of underlying pregnancy, breast-feeding and immunodeficiency of caregivers.

Patients treated with Luxturna should not donate blood, organs, tissues and cells for transplantation.

Immunogenicity

To reduce the potential for immunogenicity patients should receive systemic corticosteroids before and after the subretinal injection of voretigene neparvovec to each eye. The corticosteroids may decrease the potential immune reaction to either vector capsid (adeno-associated virus serotype 2 [AAV2] vector) or transgene product (retinal pigment epithelial 65 kDa protein [RPE65]).

Sodium content

This medicinal product contains less than 1 mmol sodium (23 mg) per dose, i.e. essentially 'sodium-free'.

Fertility, Pregnancy and lactation:

Pregnancy: There are no or limited amount of data (less than 300 pregnancy outcomes) from the use of voretigene neparvovec in pregnant women. Animal studies do not indicate direct or indirect harmful effects with respect to reproductive toxicity. As a precautionary measure, it is preferable to avoid the use of voretigene neparvovec during pregnancy.

Breast-feeding: Luxturna has not been studied in breast-feeding women.

Fertility: No clinical data on the effect of the medicinal product on fertility are available. Effects on male and female fertility have not been evaluated in animal studies

Adverse drug reactions:

Very common (≥1/10): Conjunctival hyperaemia, cataract, Intraocular pressure increased,

Common (≥1/100 to <1/10): Retinal deposits, Anxiety, Headache, dizziness, Retinal tear, dellen, macular hole, eye inflammation, eye irritation, eye pain, maculopathy, choroidal haemorrhage, conjunctival cyst, eye disorder, eye swelling, foreign body sensation in eyes, macular degeneration, endophthalmitis, retinal detachment, retinal disorder, retinal haemorrhage, Nausea, vomiting, abdominal pain upper, lip pain, Rash, swelling face, Electrocardiogram T wave inversion, Endotracheal intubation complication, wound dehiscence.

Uncommon (≥1/1,000 to <1/100);

Not Known (cannot be estimated from the available data): Vitreous

Interactions:

♦ There are no known clinically significant interactions. No interaction studies have been performed.

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Patient Safety Department Novartis Pharma AG - Saudi Arabia

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LUXTURNA voretigene neparvovec for subretinal injection