Pharmacy Manual for

the Dose Preparation of LUXTURNA® (voretigene neparvovec)

IMPORTANT

The purpose of this Pharmacy Manual is to provide information to pharmacy personnel on the preparation of voretigene neparvovec in accordance with the Summary of Product Characteristics or product information approved in your country.

The information in this manual is correct as of November 2020. If you have questions about the preparation of voretigene neparvovec, please contact your Novartis representative.

RMP Code: Luxturna EU RMP V1.5 Feb 2022

NOVARTIS

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

Contents

Purpose of the Pharmacy Manual

The purpose of this Pharmacy Manual is to provide information to pharmacy personnel on the dose preparation of voretigene neparvovec in accordance with the Summary of Product Characteristics.

Voretigene neparvovec should be prepared by pharmacists who have received training on the preparation of this gene therapy product.

RMP Code: Luxturna EU RMP V1.5 Feb 2022

Dosage

Dosage
forms and strengths

Each mL of concentrate contains 5 x 10^{12} vector genomes (vg). Each single-dose 2 mL vial of voretigene neparvovec contains 0.5 extractable mL of concentrate solution for subretinal injection, which requires a 1:10 dilution prior to administration. Each dose of voretigene neparvovec contains 1.5 x 10^{11} vg in a deliverable volume of 0.3 mL.

RMP Code: Luxturna EU RMP V1.5 Feb 2022

Dose Preparation

Required materials

The following materials are required for dilution and administration syringe preparation:

- One single-use vial of voretigene neparvovec
- Two 2-mL vials of solvent
- One 3-mL sterile syringe
- One 20G, 1-in sterile needle
- Three 1-mL sterile syringes
- Three 27G ½-in sterile needles
- Two sterile syringe caps
- One 10-mL sterile empty glass vial
- One sterile utility drape
- One sterile plastic bag
- Two sterile labels for administration syringes
- One sterile plain label
- Two sterile skin markers

The storage temperature of the concentrate and solvent is ≤-65°C. Following thawing of the vials, leave at room temperature.

Table 1 lists a commercially available syringe that has been tested in biocompatibility experiments for use with voretigene neparvovec. Figure 1 shows this syringe.

Table 1. Sterile biocompatible syringe

Product description	Manufacturer	Reference number
BD Luer-Lok™ 1-mL disposable syringe Has 1/100 mL graduations	Becton, Dickinson & Company Franklin Lakes, NJ	309628

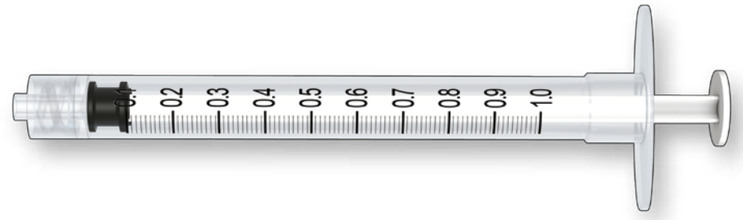

Figure 1. Representative syringe (model shown: BD Luer-Lok™ 1-mL disposable syringe, Franklin Lakes, NJ; reference number 309628)
Image copyrights Spark Therapeutics

RMP Code: Luxturna EU RMP V1.5 Feb 2022

Dilution

Dose preparation of voretigene neparvovec should be performed within 4 hours of beginning the administration procedure in accordance with the following recommended procedures, performed under aseptic conditions in a Class II vertical laminar flow biological safety cabinet (BSC).

IMPORTANT

Always use sterile technique under aseptic conditions in a Class II vertical laminar flow BSC to prepare voretigene neparvovec for administration.

1 Thaw the contents of the carton, 1 single-dose vial of voretigene neparvovec and 2 vials of solvent, at room temperature. Inspect the vials for damage. Ensure the voretigene neparvovec and solvent vials are within expiry. Mix the contents of the thawed solvent vials by gently inverting them approximately 5 times and inspect the solvent vials for particulates, cloudiness, or discoloration. Any anomalies or appearance of visual particulates should be reported to the Marketing Authorisation Holder and product should not be used.

IMPORTANT

Inspect the vials for any particulates, cloudiness, or discoloration after thawing. If particulates, cloudiness, or discoloration are visible, do not use the vial or vials.

2 Obtain a 3-mL sterile syringe, a 20G 1-in sterile needle, and a 10-mL sterile empty glass vial.

3 Transfer 2.7 mL of the solvent to the 10-mL glass vial using the 3-mL sterile syringe with the 20G 1-in sterile needle by sequential transfer of 1.4 mL and 1.3 mL volumes from the two vials of solvent, respectively. Dispose of the needle and syringe in an appropriate sharps container.

IMPORTANT

If particulates, cloudiness, or discoloration are visible, do not use the vial. A new single dose vial of voretigene neparvovec should be used. Any anomalies or appearance of visual particulates should be reported to the Marketing Authorisation Holder.

4 Mix the contents of the thawed voretigene neparvovec single-dose vial by inverting gently approximately 5 times.

5 Inspect the voretigene neparvovec single-dose vial for particulates, cloudiness, or discoloration. The diluted solution should be clear to slightly opalescent.

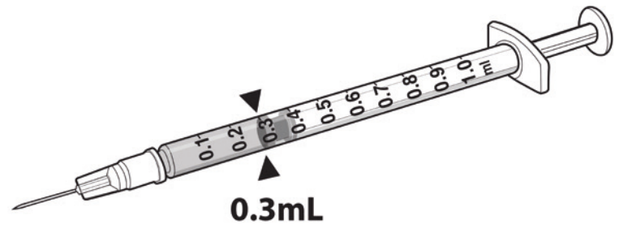

Figure 2. Syringe with 0.3 mL voretigene neparvovec.
Image copyrights Spark Therapeutics

6 Draw 0.3 mL of voretigene neparvovec into a 1-mL sterile syringe with a 27G ½-inch sterile needle (Figure 2).

IMPORTANT

Mix the contents of the vial containing voretigene neparvovec and solvent by gently inverting the vial approximately 5 times.

7 Transfer 0.3 mL of voretigene neparvovec to the 10-mL sterile glass vial containing 2.7 mL of solvent from Step 3. Dispose of the needle and syringe in an appropriate sharps container. Gently invert the 10-mL glass vial approximately 5 times to mix the contents.

8 Using the sterile plain label and sterile skin marker, label the 10-mL glass vial containing the diluted voretigene neparvovec as follows: “Diluted voretigene neparvovec”.

9 Remove all items from the BSC except the glass vial labelled “Diluted voretigene neparvovec”. Resanitize the BSC prior to the next steps and place the glass vial to the left side in the BSC.

RMP Code: Luxturna EU RMP V1.5 Feb 202

Preparation of voretigene neparvovec
for subretinal injection

Two operators are required for transfer of 0.8 mL of voretigene neparvovec from the 10-mL glass vial labelled “Diluted voretigene neparvovec” into each of the two 1-mL sterile syringes. The objective is to ensure that the syringes remain sterile, including the external surfaces of the syringes that will be handled by the surgeon.

The Primary Operator will withdraw 0.8 mL of diluted voretigene neparvovec into each of two sterile 1-mL syringes and then place both syringes in a sterile plastic bag. The Primary Operator will touch only sterile surfaces, and his or her hands will stay within the BSC throughout the preparation and packaging of the two 1-mL sterile syringes containing voretigene neparvovec. The Secondary Operator will unwrap the required materials in a manner that prevents a breach of the sterility of the packaged contents.

1 Place a sterile utility drape, a sterile plastic bag, a sterile skin marker, and 2 sterile labels into the BSC. The Primary Operator changes to a new pair of sterile gloves. Place the sterile utility drape near the Primary Operator on the right side of the sanitized BSC surface, away from the diluted voretigene neparvovec. The Secondary Operator unwraps the items in the BSC, including the two 1-mL sterile syringes, two 27G ½-in sterile needles, and 2 sterile syringe caps, ensuring that the Primary Operator touches only sterile surfaces while transferring the items onto the sterile utility drape.

IMPORTANT

Maintain sterility at all times and follow aseptic techniques.

2 Prior to the next step, the Secondary Operator changes to a new pair of sterile gloves and positions himself or herself to the left of the Primary Operator. The Secondary Operator holds the 10-mL glass vial labelled “Diluted voretigene neparvovec” during step 3 as shown on the right (Figure 3a.).

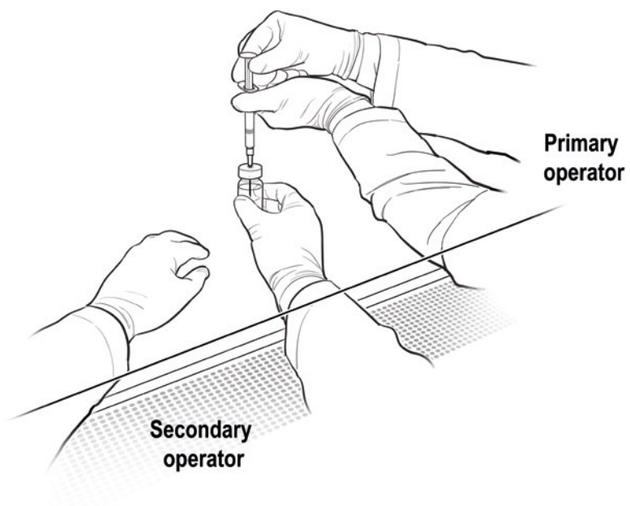

Figure 3a. First position of the operators during preparation of voretigene neparvovec administration syringes.
Image copyrights Spark Therapeutics

3 The Primary Operator withdraws 0.8 mL of the diluted voretigene neparvovec into a 1-mL sterile syringe using a 27G ½-in sterile needle while the Secondary Operator holds the 10-mL glass vial. After insertion of the needle (Figure 3a), the Secondary Operator inverts the 10-mL glass vial enabling the Primary Operator to withdraw 0.8 mL without touching the surfaces of 10-mL glass vial (Figure 3b).

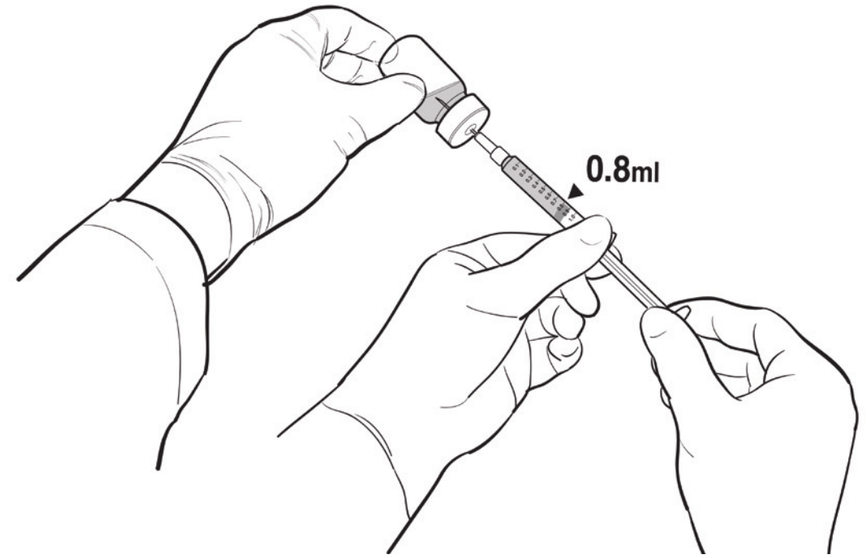

Figure 3b. Second position of the operators during preparation of voretigene neparvovec administration syringes.
Image copyrights Spark Therapeutics

4 The Primary Operator removes the needle and affixes a sterile syringe cap to the sterile syringe, disposes of the needle in an appropriate container, and attaches a sterile label to the administration syringe. Affix the label in a manner that the graduations on the syringe are not obscured and are clearly visible.

RMP Code: Luxturna EU RMP V1.5 Feb 2022

5 The Primary Operator repeats the previous 2 steps to prepare a total of 2 administration syringes. Label the first syringe “Diluted voretigene neparvovec” and label the second syringe “Back-up diluted voretigene neparvovec” using the sterile skin marker. The second syringe will serve as a back-up for the surgeon performing the subretinal administration procedure. Discard the back-up syringe after surgery if not used.

IMPORTANT

Prepare a total of 2 syringes, with one serving as a back-up for the surgeon. Discard the back-up syringe after surgery if not used. The first syringe and second back-up syringe must be available for the surgeon performing the subretinal administration.

6 Inspect both syringes.

7 The Primary Operator places the two 1-mL sterile syringes each containing 0.8 mL of the diluted voretigene neparvovec into a sterile plastic bag in an aseptic manner and seals the bag.

IMPORTANT

If particulates, cloudiness, or discoloration are visible, do not use the syringe. Do not proceed if a back-up syringe is not available for the surgeon performing the subretinal administration.

8 Place the sterile plastic bag with syringes each containing diluted voretigene neparvovec into an appropriate secondary container (e.g. hard plastic cooler) for delivery to the surgical suite at room temperature.

IMPORTANT

Dispose of all materials that may have come in contact with voretigene neparvovec in accordance with local biohazard waste disposal guidelines.

References

1. Novartis Saudi Limited LUXTURNA® Summary of Product Characteristics. Last updated 20.12.2019.
2. Data on File_1. 2019. Study report of a biocompatibility assessment for the 1mL syringe and glass vial used during voretigene neparvovec preparation and dilution.
3. Data on File_2. 2019. Study report of a biocompatibility assessment for the 1mL syringe and glass vial used during voretigene neparvovec preparation and dilution.
4. Data on File_3. 2019. Clinical protocol of a drug administration and dosing study, including naming the reference number for the 1mL syringe to be used and specifying handling procedure of voretigene neparvovec.

RMP Code: Luxturna EU RMP V1.5 Feb 2022

Please Refer to the Saudi SPC for more information

For reporting of adverse events:

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 Toll free phone: 8002490000 Fax:+966112057662 E-mail: npc.drug@sfda.gov.saOr by online: https://ade.sfda.gov.sa

RMP Code: Luxturna EU RMP V1.5 Feb 2022

SA2109074459

NOVARTIS

LUXTURNA
voretigene neparvovec
for subretinal injection