



HSE Guidelines for the Treatment of Inherited Retinal Dystrophy with Voretigene Neparvovec (Luxturna®)

This document is intended for use by healthcare professionals only.

While the guidance is intended to strengthen clinical management of these patients it does not replace clinical judgment or specialist consultation.

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Voretigene Neparvovec Guidelines

The voretigene neparvovec guidelines have been reviewed by prescribing physicians and healthcare professionals working in the treatment centres of excellence in Ireland. The guidelines are designed to standardise practice and support the implementation of treatment pathways for these patients in Ireland. This guideline should be used in conjunction with the full prescribing and administration details in the Voretigene neparvovec (Luxturna®) Summary of Product Characteristics (SmPC) https://www.ema.europa.eu/en/documents/product-information/luxturna-epar-product-information_en.pdf¹

The approved treatment centres at The Mater Misericordiae University Hospital (MMUH) and the Royal Victoria Eye and Ear Hospital (RVEEH) should use this guideline in conjunction with the Medicines Management Programme Managed Access Protocol and the Full-Field Light Sensitivity Threshold (FST) Protocol For Luxturna® and the FST Results Form agreed with Novartis in accordance with the Supply Agreement between MMUH/REEVH and Novartis.

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1.0 Indication

Voretigene neparvovec (Luxturna®) is indicated for the treatment of adult and paediatric patients with vision loss due to inherited retinal dystrophy (IRD) caused by confirmed biallelic RPE65 mutations and who have sufficient viable retinal cells¹.

The gene transfer treatments outlined in this guideline should be performed in an appropriate setting for the management of IRDs with voretigene neparvovec. Paediatricians will undertake to refer patients to the adult centre on reaching the age of 16-18 years. Adult and paediatric centres undertake to ensure as much as possible a seamless transfer of care.

2.0 IRD Diagnosis and confirmation of biallelic RPE65 mutations

IRD diagnosis involves assessment of medical history and clinical symptoms, and an analysis of previous family history. A molecular diagnosis via genetic testing is required to confirm eligibility for treatment. The patient must have confirmed biallelic RPE65 mutations with two alleles (V and/or IV) to be considered for treatment with voretigene neparvovec². A patient pathway for selection of treatment with voretigene neparvovec is illustrated in appendix 1.

Table 1: Classification of RPE65 mutations

Allele Class	Mutation	Action
Class V	Pathogenic Mutation	Actionable
Class IV	Likely Pathogenic	Actionable
Class III	Variant of unknown significance	Not actionable

3.0 Treatment:

The licensed voretigene neparvovec product in Ireland is Luxturna® 5x10¹² vector genomes/ml concentrate and solvent for solution for injection. Treatment should be initiated and administered by a retinal surgeon experienced in performing macular surgery¹.

Patients will receive a single dose of 1.5 x 10¹¹ vg voretigene neparvovec in each eye. (Please see Voretigene neparvovec (Luxturna®) SmPC for dilution and administration details

https://www.ema.europa.eu/en/documents/product-information/luxturna-epar-product-information_en.pdf¹). 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.

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Table 2: Pre-and Post-operative immunomodulatory regimen for each eye

Pre-Operative	3 days prior to Voretigene neparvovec 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)

*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.

Patients will also be discharged with an anti-microbial eye drop, anti-inflammatory eye drop and cycloplegic eye drop.

4.0 Eligibility Criteria for starting voretigene neparvovec treatment

- Subjects ≥ 4 years old with a confirmed genetic diagnosis of biallelic *RPE65* gene mutations
- Visual Acuity (VA) worse than 20/60 and/or Visual Field <20 degrees in any meridian
- Sufficient viable retinal cells as determined by non-invasive means, such as Optical Coherence Tomography (OCT) and/or ophthalmoscopy. Must have either:
 - an area of retina within the posterior pole of > 100 µm thickness shown on OCT
 - ≥ 3 disc areas of retina without atrophy or pigmentary degeneration within the posterior pole; or
 - remaining visual field within 30° of fixation as measured by III4e isopter or equivalent

5.0 Exclusion Criteria for starting voretigene neparvovec treatment

- Hypersensitivity to the active substance(s) or to any of the excipients listed in section 6.1 of the SPC
- Ocular or periocular infection.
- Active intraocular inflammation.

6.0 Monitoring following voretigene neparvovec treatment

- Visual Function:
 - FST
 - Visual Field
- Visual Acuity:

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- Best Corrected Visual Acuity (BCVA) measured by Snellen and/or LogMar visual acuity by the team
- Structure:
 - Photography (colour and autofluorescence).
 - OCT
 - Optional: Adaptive Optics.

7.0 Follow up

Day case patients will be discharged home with supportive medications (see treatment section 3.0 above) and follow up will be arranged in outpatient clinic. High risk patients may be observed overnight as an inpatient following surgery.

Special warnings: Viral Shedding:

Transient and low-level vector shedding may occur in patient tears (see SmPC <https://www.ema.europa.eu/en/medicines/human/EPAR/luxturna>). 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 voretigene neparvovec should be counselled not to donate blood, organs, tissues and cells for transplantation.

8.0 Stopping Criteria

Course completion: One intravitreal injection in each eye.

Application for Treatment

Medicine Management Programme (MMP) Managed Access Protocol (MAP) available:

<https://www.hse.ie/eng/about/who/cspd/ncps/medicines-management/managed-access-protocols/>

Reimbursement

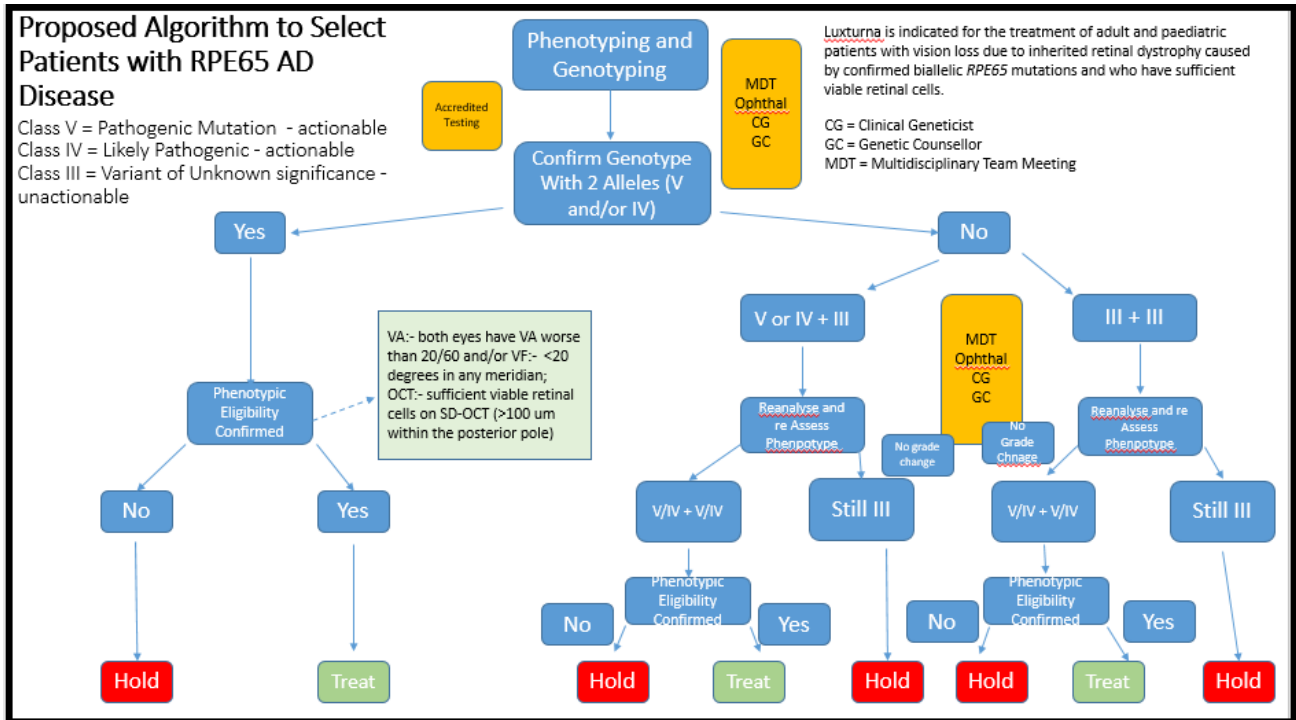
Acute Hospital Drug Management Programme

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Appendices

Appendix 1.0 Algorithm to Select Patients with RPE65 AD Disease



Algorithm shared by ophthalmologic clinical experts in Mater Misericordiae University Hospital, Dublin

Appendix 2.0 Revision History

Revision number	Revision date	Summary of changes

References:

1. Summary of Product Characteristics Luxturna 5 x 1012 vector genomes/mL concentrate and solvent for solution for injection. Available From: https://www.ema.europa.eu/en/documents/product-information/luxturna-epar-product-information_en.pdf Accessed on: 27/06/2023
2. National Institute for Health and Care Excellence. Voretigene neparvovec for treating inherited retinal dystrophies caused by RPE65 gene mutations. Highly specialised technologies guidance Reference number: HST11 Published: 09 October 2019. <https://www.nice.org.uk/guidance/hst11/chapter/4-Consideration-of-the-evidence> Accessed on: 27/06/2023
3. Cost-effectiveness of voretigene neparvovec (Luxturna®) 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. National Centre for Pharmacoeconomics. September 2020

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