Medicines Management Programme

Managed Access Protocol – 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.

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Table of contents

1. Voretigene neparvovec 1
1.1 Licensed indication 1
1.2 Licensed dose 1
1.3 Reimbursement 2
1.3.1 Approval Process 2
1.4 Reimbursement price 2
2. Reimbursement criteria - Initiation 3
2.1 Prescribers 3
2.2 Diagnosis 3
2.2.1 Genetic testing 3
2.3 Age 3
2.4 Patient's clinical history 3
2.5 Reimbursement exclusion criteria 4
2.6 Full Field Stimulus Threshold 4
3. Reimbursement criteria – Requirement for Outcome Data 4
4. Reimbursement criteria – Medicines Management 5
5. Prescribing of voretigene neparvovec (Luxturna®) 5

List of Tables

Table 1: Price to wholesaler of the presentation of voretigene neparvovec (Luxturna®) available for reimbursement under hospital pricing approval 2

List of Abbreviations

cDNA	Complimentary deoxyribonucleic acid
DNA	Deoxyribonucleic acid
FST	Full field stimulus threshold
HSE-MMP	Health Service Executive-Medicines Management Programme
IRD	Inherited retinal dystrophy
kDa	Kilodalton
mL	Millilitre
SmPC	Summary of Product Characteristics
MAP	Managed Access Protocol
OCT	Optical Coherence Tomography
Vg	Vector genomes

1. Voretigene neparvovec

Voretigene neparvovec is a gene transfer vector that employs an adeno-associated viral vector serotype 2 capsid as a delivery vehicle for the human retinal pigment epithelium 65 kDa protein (hRPE65) complementary deoxyribonucleic acid (cDNA) to the retina. Voretigene neparvovec is derived from wild-type adeno-associated viral vector serotype 2 using recombinant deoxyribonucleic acid (DNA) techniques.

From August 2023, voretigene neparvovec (Luxturna®) is available for reimbursement under hospital pricing approval as:

- Luxturna® 5 x 10^{12} vector genomes/mL concentrate and solvent for solution for injection ▼

Each mL of concentrate contains 5 x 10^{12} vector genomes (vg).

Each vial of voretigene neparvovec (Luxturna®) contains 0.5 extractable mL of concentrate which requires a 1:10 dilution prior to administration.

After dilution of 0.3 mL of concentrate with 2.7 mL of solvent, each mL contains 5 x 10^{11} vg. Each dose of 0.3 mL voretigene neparvovec (Luxturna®) contains 1.5 x 10^{11} vg.

1.1 Licensed 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 cells. This managed access protocol (MAP) relates to its use for this indication.

1.2 Licensed dose

Patients will receive a single dose of 1.5 x 10^{11} vg voretigene neparvovec (Luxturna®) 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.

It is recommended that an immunomodulatory regimen is started three days prior to the administration of voretigene neparvovec (Luxturna®). 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. Please refer to the Summary of Product Characteristics (SmPC) for voretigene neparvovec (Luxturna®) for full prescribing information on the immunomodulatory regimen.

▼ This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions.

1.3 Reimbursement

Approved prescribers are required to apply for reimbursement approval on an individual patient basis. Applications for the individual reimbursement of voretigene neparvovec (Luxturna®) should be sent by secure email to the Health Service Executive-Medicines Management Programme (HSE-MMP) at mmp@hse.ie. *See Section 2 for further details on reimbursement criteria.*

1.3.1 Approval Process

The following outlines the process for individual treatment approvals:

1. An individual application is submitted by the prescribing clinician to the HSE-MMP.

2. The HSE-MMP review the application with two possible outcomes:

    a. HSE-MMP make a positive recommendation for reimbursement

    b. HSE-MMP do not recommend reimbursement and notifies applicant of same.

3. HSE-MMP notifies the Office of the Assistant National Director for Acute Operations of their recommendation after a positive recommendation for reimbursement is made.

4. The Office of the Assistant National Director for Acute Operations notifies the prescribing consultant, the Hospital Group CEO and the HSE-MMP of the final reimbursement decision.

If a patient is recommended and approved for reimbursement of voretigene neparvovec (Luxturna®), reimbursement will be supported for a maximum of one single dose of 1.5 x 10^{11} vg voretigene neparvovec (Luxturna®) in each eye, in line with the licensed dose as per SmPC. *See Section 2 for further details on reimbursement criteria.*

1.4 Reimbursement price

The price to wholesaler of the presentation of voretigene neparvovec (Luxturna®), available for reimbursement under hospital pricing approval as of August 2023, is as follows:

Table 1: Price to wholesaler of the presentation of voretigene neparvovec (Luxturna®) available for reimbursement under hospital pricing approval

Strength (pack size)	Price to wholesaler
Luxturna® 5 x 10^{12} vg/mL concentrate and solvent for solution for injection (pack x 2)	€666,524.00

mL: millilitre, vg: vector genomes

A commercial-in-confidence arrangement is in place with the marketing authorisation holder to reduce the net acquisition cost of voretigene neparvovec (Luxturna®) to the HSE.

2. Reimbursement criteria - Initiation

This section outlines the criteria that must be satisfied in order for a patient to be recommended for reimbursement of voretigene neparvovec (Luxturna®), for the treatment of adult and paediatric patients with vision loss due to IRD caused by confirmed biallelic *RPE65* mutations and who have sufficient viable retinal cells, for reimbursement under hospital pricing approval.

2.1 Prescribers

The prescribing of voretigene neparvovec (Luxturna®) for reimbursement under hospital pricing approval will be confined to consultant ophthalmologists with expertise in the care and treatment of patients with IRD, and the presence of or affiliation with a retinal surgeon experienced in sub-retinal surgery and capable of administering voretigene neparovoec (Luxturna®) in specialist centre(s), who have agreed to the terms of this MAP and have been approved by the HSE.

Applications for reimbursement approval will only be considered from these prescribers.

2.2 Diagnosis

For a positive reimbursement recommendation, clinicians will be required to provide documented evidence of a diagnosis of vision loss due to an IRD caused by confirmed biallelic *RPE65* mutations.

2.2.1 Genetic testing

A confirmed genetic diagnosis of biallelic *RPE65* mutations (with two alleles having mutations classifed as V and/or IV) is a condition of reimbursement.

2.3 Age

Individuals should be aged ≥ 4 years old. The safety and efficacy of voretigene neparvovec (Luxturna®) in children aged up to 4 years of age have not been established.

2.4 Patient's clinical history

Clinicians will be required to confirm and provide documented evidence that the patient satisfies the following eligibility criteria for both eyes at the time of the application:

- Visual Acuity 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.

2.5 Reimbursement exclusion criteria

In line with the SmPC, reimbursement will **not** be considered in patients with:

- Ocular or periocular infection
- Active intraocular inflammation

2.6 Full Field Stimulus Threshold

A baseline full field stimulus threshold (FST) measurement averaged over both eyes must be provided with the application*. This baseline FST measurement is valid for 90 days prior to treatment with voretigene neparvovec (Luxturna®). If treatment with voretigene neparvovec (Luxturna®) is beyond 90 days since the date of this measurement, then another baseline FST measurement must be provided [within 90 days prior to treatment with voretigene neparvovec (Luxturna®)].

Subsequent FST measurements must be provided as outlined in section 3*.

Outcomes must be measured using the approved FST Diagnosys system as is outlined in the hospital/company agreed FST protocol.

*There may be circumstances where a baseline FST measurement averaged over both eyes is not attainable. In such cases, an application may be submitted for consideration, however sufficient clinical justification for not attaining the baseline measurement must be clearly outlined. Alternative measurements should be provided in such cases.

3. Reimbursement criteria – Requirement for Outcome Data

Following approval of a patient for reimbursement of voretigene neparvovec (Luxturna®) under hospital pricing approval, the prescribing clinician will be required to submit outcome data and documented evidence using the approved FST Diagnosys System at specified intervals as requested. Outcome data for each patient should be submitted and sent by secure email to the HSE-MMP (mmp@hse.ie) when requested outlining:

- FST measurement averaged over both eyes compared to baseline within 30 – 90 days of treatment of second eye with voretigene neparvovec (Luxturna®), and
- FST measurement averaged over both eyes compared to baseline by 24 months post treatment of second eye with voretigene neparvovec (Luxturna®).

Provision of follow-up data when requested by the HSE-MMP is a condition of ongoing access to apply for reimbursement support of voretigene neparvovec (Luxturna®).

4. Reimbursement criteria – Medicines Management

Specialist site(s) must ensure a local policy is in place for appropriate medicines management, including protocols for preparation and administration of voretigene neparvovec (Luxturna®) taking into consideration information outlined in the SmPC and conditions of the marketing authorisation.

A condition of the marketing authorisation is that voretigene neparvovec (Luxturna®) will only be distributed by the marketing authorisation holder through specialist centres where the relevant personnel have completed mandatory training on the use of the product.

5. Prescribing of voretigene neparvovec (Luxturna®)

Please refer to the SmPC for voretigene neparvovec (Luxturna®) for full prescribing information including monitoring and patient counselling requirements. Only approved prescriber(s) will be able to apply for voretigene neparvovec (Luxturna®) reimbursement approval.

The following confirmations are required when prescribing voretigene neparvovec (Luxturna®):

- Confirmation that voretigene neparvovec (Luxturna®) is being prescribed for a MMP approved patient in accordance with the MAP established in line with the terms of reimbursement approval given by the HSE.
- Confirmation that the prescriber will provide outcome data as requested and provision of this outcome data within the time frame specified with the request, is a condition of ongoing access to apply for reimbursement support of voretigene neparvovec (Luxturna®).
- Confirmation that the prescriber will assist the HSE/MMP in their conduct of audits* through provision of information as requested, to provide assurance that the product is being prescribed in line with HSE reimbursement approval and the MAP.
- Confirmation that the patient or their representative/guardian is aware that the application for reimbursement approval is being made on behalf of the patient and that audits may occur during which their personal data will be reviewed.

* Follow-up data may be requested by the HSE/MMP for audit purposes and provision of same is a condition of ongoing reimbursement.