GIG CYMRU NHS WALES

Pwyllgor Gwasanaethau Iechyd Arbenigol Cymru (PGIAC)

Welsh Health Specialised Services Committee (WHSSC)

Specialised Services Policy Position PP196

Voretigene Neparvovec for treating inherited retinal dystrophies caused by RPE65 gene mutations (Adults and children)

March 2020

Version 1.0

Document information	
Document purpose	Policy Position
Document name	Voretigene Neparvovec for treating inherited retinal dystrophies caused by RPE65 gene mutations
Author	Welsh Health Specialised Services Committee
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Commissioning Team	Cardiac
Target audience	Chief Executives, Medical Directors, Directors of Finance, Pharmacists, Ophthalmologists.
Description	NHS Wales will routinely commission this specialised service in accordance with the criteria described in this policy
Document No	PP196
Review Date	2026

Contents

Policy Statement

Welsh Health Specialised Services Committee (WHSSC) will commission Voretigene Neparvovec for treating inherited retinal dystrophies caused by RPE65 gene mutations in accordance with the criteria outlined in this document.

In creating this document WHSSC has reviewed the relevant guidance issued by National Institute of Health and Care Excellence[1] (NICE) and has concluded that Voretigene Neparvovec should be made available.

Disclaimer

WHSSC assumes that healthcare professionals will use their clinical judgment, knowledge and expertise when deciding whether it is appropriate to apply this policy position statement.

This policy may not be clinically appropriate for use in all situations and does not override the responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or their carer or guardian.

WHSSC disclaims any responsibility for damages arising out of the use or non-use of this policy position statement.

[1] Overview | Voretigene neparvovec for treating inherited retinal dystrophies caused by RPE65 gene mutations | Guidance | NICE

1. Introduction

This Policy Position has been developed for the planning and delivery of Voretigene neparvovec for treating inherited retinal dystrophies caused by RPE65 gene mutations for people resident in Wales. This service will only be commissioned by the Welsh Health Specialised Services Committee (WHSSC) and applies to residents of all seven Health Boards in Wales.

1.1 Plain language summary

Inherited retinal dystrophies (IRDs) are a group of rare genetic eye diseases. They are caused by germline mutations in more than 260 genes, including that for the enzyme RPE65. This enzyme is critical for the visual cycle. It is involved in a multistep process that converts light entering the eye into electrical signals, which are transmitted to the brain. Lack of RPE65 causes severe deficiency in functional rhodopsin (a sensory protein that converts light into an electrical signal) and death of photoreceptor cells on the retina through accumulation of toxic chemical compounds. People with RPE65-mediated IRD have progressive vision loss that ultimately leads to near-total blindness. There is variation in the presentation and time of diagnosis of the condition. Loss of vision can begin as early as the first few months of life, or during childhood or adolescence. Initially, people have problems with peripheral vision and seeing in dim light or night blindness. These symptoms are followed by progressive deterioration in visual field (range of vision) and visual acuity (clarity of vision), and reduced sensitivity to light. Ultimately, the deterioration leads to near-total blindness.

1.2 Aims and Objectives

This Policy Position aims to define the commissioning position of WHSSC on the use of Voretigene Neparvovec for treating inherited retinal dystrophies caused by RPE65 gene mutations.

The objectives of this policy are to:

- ensure commissioning for the use of Voretigene Neparvovec is evidence based
- ensure equitable access to Voretigene Neparvovec
- define criteria for people with Voretigene Neparvovec to access treatment
- improve outcomes for people with Inherited Retinal Dystrophies caused by RPE gene mutations

1.3 Epidemiology

Lack of RPE65 presents as the clinical conditions such as classically termed retinitis pigmentosa (RP) and Leber's congenital amaurosis (LCA). LCA is used to describe a group of severe early infantile onset rod–cone dystrophies. It is considered to have a worse prognosis than other clinical diagnoses. RP accounts for around half of IRDs, with a prevalence of around

20 to 30 people per 100,000. LCA is less common, affecting 2 to 3 people per 100,000. Mutations in the RPE65 gene account for 2% of RP and 6% to 16% LCA diagnoses. The exact prevalence and incidence of RPE65-mediated IRD is uncertain. The company estimated that 86 people would be eligible for treatment with voretigene neparvovec in England.

1.4 Current Treatment

There are no licensed treatments currently available in the UK for RPE65-mediated IRD. Current management focuses on strategies to improve the use of remaining vision. This includes using low-vision aids, social and educational support, and specialised genetic counselling for people with the condition and their families. Care is provided as part of a specialised multidisciplinary service.

1.5 Proposed Treatment

Voretigene neparvovec (Luxturna®) is an adeno-associated virus vector-based gene therapy. It introduces a healthy copy of the defective RPE65 gene into the retinal cells of people with RPE65-mediated inherited retinal dystrophy (IRD), enabling patients to produce functional RPE65 protein.

The aim is to improve visual function (performance of the eyes) and functional vision (the ability to carry out activities of daily living dependent on vision).

Voretigene neparvovec is administered as a sub-retinal injection using a one-off dose of 1.5×10^{11} vector genomes to each eye on separate days (no fewer than 6 days apart). Before administration, patients have an immunomodulatory regimen that is continued for 18 to 30 days.

The adverse reactions listed as common in the summary of product characteristics include: eye inflammation (including endophthalmitis), retinal disorder, an increase in intraocular pressure and temporary visual disturbances. For full details of adverse reactions see the summary of product characteristics[2].

1.6 What NHS Wales has decided

WHSSC has carefully reviewed the relevant guidance issued by National Institute of Health and Care Excellence (NICE) who have concluded that the use of Voretigene Neparvovec should be made available within the criteria set out in section 2.1.

[2] https://www.ema.europa.eu/en/documents/product-information/luxturna-epar-product-information_en.pdf

2. Criteria for Commissioning

The Welsh Health Specialised Services Committee approve funding of Voretigene Neparvovec for Welsh patients (adults and Children) with inherited retinal dystrophies caused by RPE65 gene mutations in-line with the criteria identified in the policy.

2.1 Access to Treatment

Voretigene neparvovec is recommended, within its marketing authorisation, as an option for treating RPE65-mediated inherited retinal dystrophies in people with vision loss caused by inherited retinal dystrophy from confirmed biallelic RPE65 mutations and who have sufficient viable retinal cells. It is recommended only if the company provides voretigene neparvovec according to the commercial arrangement[3].

Sufficient viable retinal cells is defined as:

- an optical coherence tomography showing more than a 100-micrometre thickness in an area of retina within the posterior pole;
- 3 or more disc areas without atrophy or pigmentary degeneration within the posterior pole or
- a remaining visual field (VF) within 30º of fixation.

In practice functional and structural assessments might also be used. Functional assessment would review the patient's visual function and functional vision. If patients still have visual function, their eyes have the potential to respond to treatment. The NICE committee concluded that clinical judgement incorporating both structural and functional assessment would be used in clinical practice to identify patients eligible for treatment.

Access to treatment will require completion of a Prior Approval Form (annex iii)

2.2 Acceptance Criteria

The service outlined in this specification is for patients ordinarily resident in Wales, or otherwise the commissioning responsibility of the NHS in Wales. This excludes patients who whilst resident in Wales, are registered with a GP practice in England, but includes patients resident in England who are registered with a GP Practice in Wales.

[3] Overview | Voretigene neparvovec for treating inherited retinal dystrophies caused by RPE65 gene mutations | Guidance | NICE

2.3 Patient Pathway (Annex i)

Following confirmation of presence of RPE65 Gene Mutation, all adult patients should be referred to:

Manchester Eye Hospital
Oxford Rd
Manchester
M13 9WL

All Paediatric patients should be referred to:

Great Ormond Street Hospital
Great Ormond Street
London
WC1N 3JH

2.4 Exceptions

If the patient does not meet the criteria for treatment as outlined in this policy, an Individual Patient Funding Request (IPFR) can be submitted for consideration in line with the All Wales Policy: Making Decisions on Individual Patient Funding Requests. The request will then be considered by the All Wales IPFR Panel.

If the patient wishes to be referred to a provider outside of the agreed pathway, and IPFR should be submitted.

Further information on making IPFR requests can be found at: Welsh Health Specialised Services Committee (WHSSC) | Individual Patient Funding Requests

2.5 Clinical Outcome and Quality Measures

The Provider must work to written quality standards and provide monitoring information to the lead commissioner.

The centre must enable the patient's, carer's and advocate's informed participation and to be able to demonstrate this. Provision should be made for patients with communication difficulties and for children, teenagers and young adults.

2.6 Responsibilities

Referrers should:

- inform the patient that this treatment is not routinely funded outside the criteria in this policy, and
- refer via the agreed pathway.

Clinician considering treatment should:

- advise the patient of any side effects and risks of the potential treatment
- inform the patient that treatment is not routinely funded outside of the criteria in the policy, and
- confirm that there is contractual agreement with WHSSC for the treatment.

In all other circumstances an IPFR must be submitted.

3. Documents which have informed this policy

The following documents have been used to inform this policy:

- **National Institute of Health and Care Excellence (NICE) guidance**
  - Voretigene neparvovec for treating inherited retinal dystrophies caused by RPE65 gene mutations, NICE Highly Specialised Technologies Guidance (HST11), October 2019.

This document should be read in conjunction with the following documents:

- **NHS Wales**
  - All Wales Policy: Making Decisions in Individual Patient Funding requests (IPFR).

4. Date of Review

This document will be reviewed in line with the NICE review period of 3 years.

5. Putting Things Right:

5.1 Raising a Concern

Whilst every effort has been made to ensure that decisions made under this policy are robust and appropriate for the patient group, it is acknowledged that there may be occasions when the patient or their representative are not happy with decisions made or the treatment provided.

The patient or their representative should be guided by the clinician, or the member of NHS staff with whom the concern is raised, to the appropriate arrangements for management of their concern.

If a patient or their representative is unhappy with the care provided during the treatment or the clinical decision to withdraw treatment provided under this policy, the patient and/or their representative should be guided to the LHB for NHS Putting Things Right. For services provided outside NHS Wales the patient or their representative should be guided to the NHS Trust Concerns Procedure, with a copy of the concern being sent to WHSSC.

5.2 Individual Patient Funding Request (IPFR)

If the patient does not meet the criteria for treatment as outlined in this policy, an Individual Patient Funding Request (IPFR) can be submitted for consideration in line with the All Wales Policy: Making Decisions on Individual Patient Funding Requests. The request will then be considered by the All Wales IPFR Panel.

If an IPFR is declined by the Panel, a patient and/or their NHS clinician has the right to request information about how the decision was reached. If the patient and their NHS clinician feel the process has not been followed in accordance with this policy, arrangements can be made for an independent review of the process to be undertaken by the patient's Local Health Board. The ground for the review, which are detailed in the All Wales Policy: Making Decisions on Individual Patient Funding Requests (IPFR), must be clearly stated

If the patient wishes to be referred to a provider outside of the agreed pathway, an IPFR should be submitted.

Further information on making IPFR requests can be found at: Welsh Health Specialised Services Committee (WHSSC) | Individual Patient Funding Requests

6. Equality Impact and Assessment

The Equality Impact Assessment (EQIA) process has been developed to help promote fair and equal treatment in the delivery of health services. It aims to enable Welsh Health Specialised Services Committee to identify and eliminate detrimental treatment caused by the adverse impact of health service policies upon groups and individuals for reasons of race, gender re-assignment, disability, sex, sexual orientation, age, religion and belief, marriage and civil partnership, pregnancy and maternity and language (Welsh).

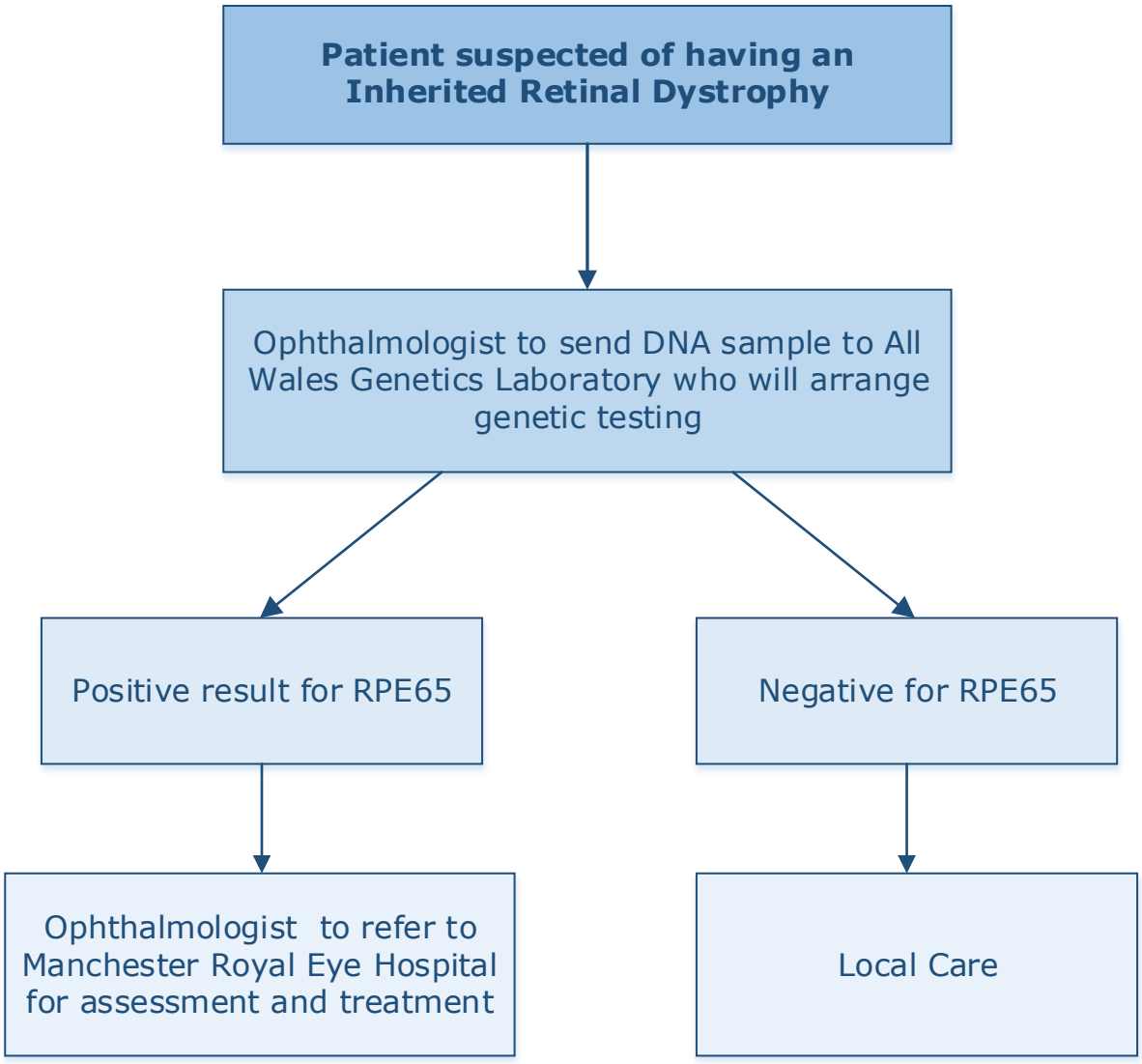
This policy has been subjected to an Equality Impact Assessment.

The Assessment demonstrates the policy is robust and there is no potential for discrimination or adverse impact. All opportunities to promote equality have been taken.

Annex i Patient Pathway

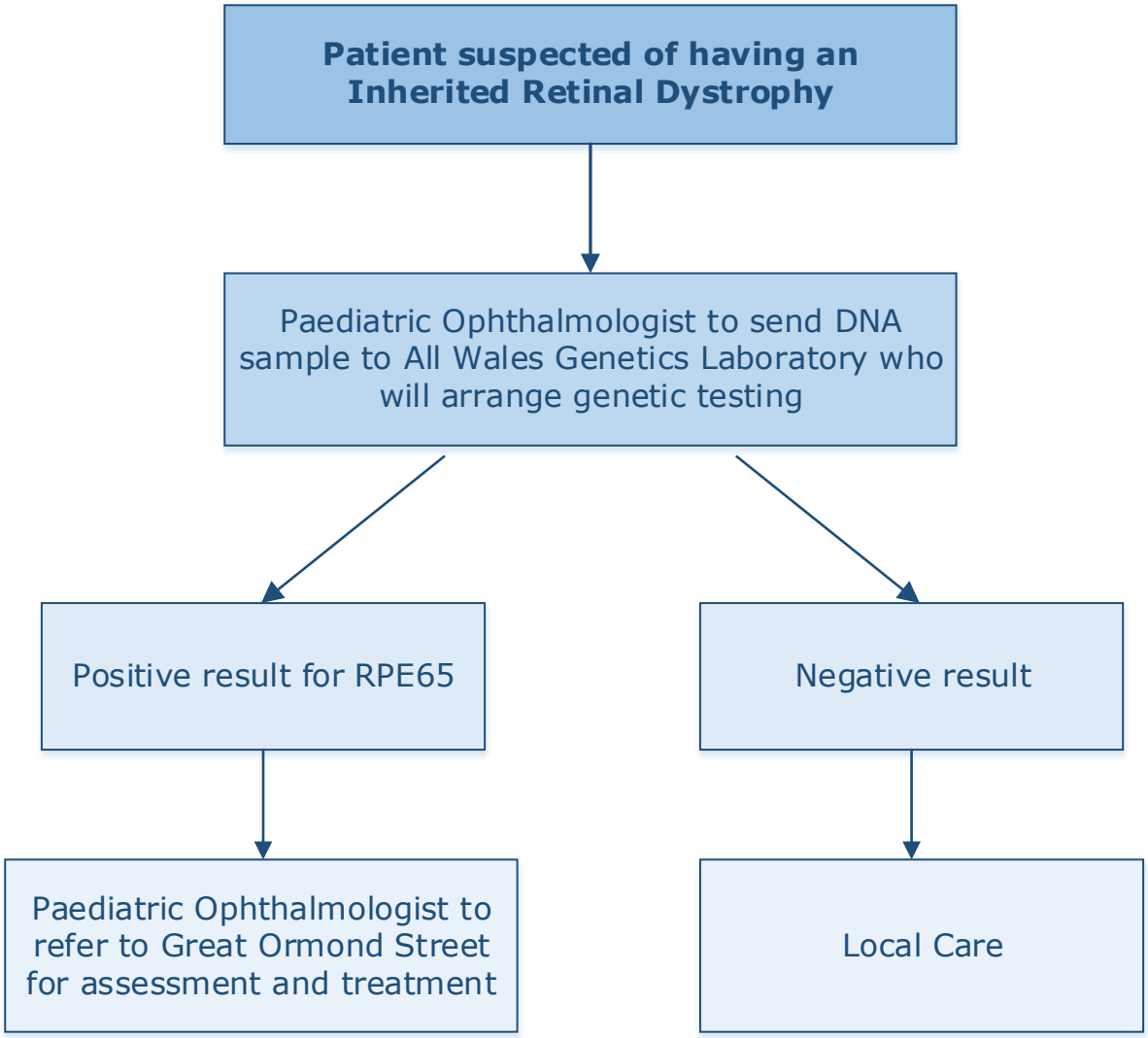
Adult Pathway

The following pathway should be followed for adult patients suspected of having inherited retinal dystrophies.



Paediatric Pathway

The following pathway should be followed for children suspected of having inherited retinal dystrophies.



Annex ii Abbreviations and Glossary

Abbreviations

IPFR Individual Patient Funding Request

WHSSC Welsh Health Specialised Services

Glossary

Individual Patient Funding Request (IPFR)

An IPFR is a request to Welsh Health Specialised Services Committee (WHSSC) to fund an intervention, device or treatment for patients that fall outside the range of services and treatments routinely provided across Wales.

Welsh Health Specialised Services Committee (WHSSC)

WHSSC is a joint committee of the seven local health boards in Wales. The purpose of WHSSC is to ensure that the population of Wales has fair and equitable access to the full range of Specialised Services and Tertiary Services. WHSSC ensures that specialised services are commissioned from providers that have the appropriate experience and expertise. They ensure that these providers are able to provide a robust, high quality and sustainable services, which are safe for patients and are cost effective for NHS Wales.

Annex iii –Prior Approval Form

PRIOR APPROVAL REQUEST FORM

Details of clinician making the referral:	
Name:	
Designation:	
Address:	
Postcode:	
Telephone number:	
Email:	
Secretary name:	
Telephone	Email:

Patient Details	
First Name:	Last Name:
Address:	Date of birth:
	NHS number:
Postcode:	Hospital number:

Urgency			
How urgent is the request? (tick as applicable)	**Urgent:** 24-48 hours	**Soon:** Within 3 weeks	**Non-urgent:** 4-6 weeks

Please note: If a decision is required urgently, clinical reasons must be provided. Administrative reasons will not be considered.

Reason for request
☐ NICE Approved Drugs ☐ NICE Technology Appraisals and Highly Specialised Technology Appraisals ☐ AWMSG Health Technology Appraisals (including the orphan and ultra-orphan status)

Clinical details
Details of treatment requested (including weight of patient, dosage and duration)
Medical history and current clinical status: (**Please provide a copy of the latest clinical report**)
Additional information to support the referral: (e.g. relevant clinical letters/reports)
Recommendation as per NICE or AWMSG (please enter the published recommendation)
Cost of treatment:

I confirm that as the patient's Consultant, I have discussed this application and consent has been provided to obtain further clinical information pertinent to this funding request if required.

Clinicians signature:

Date:

Please return this form with a copy of the referral letter to:

Please return completed form to:

Patient Care Team
Welsh Health Specialised Services
Unit G1, The Willowford
Treforest Industrial Estate
Pontypridd
CF37 5YL

Email: whssc.ipc@wales.nhs.uk or whssc.ipc@nhs.net

If you have any questions, please telephone 01443 443443 ext.78123