GIG CYMRU NHS WALES
Cyd-bwyllgor Comisiynu
Joint Commissioning Committee

Eculizumab for Paroxysmal Nocturnal Haemoglobinuria

Commissioning Policy: CP152

Policy Proposal

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Commissioning Team	Cancer and Blood
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Description	NHS Wales propose to routinely commission this specialised service in accordance with the criteria described in this policy
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GIG CYMRU NHS WALES | Cyd-bwyllgor Comisiynu Joint Commissioning Committee

Contents

Policy Statement

NHS Wales Joint Commissioning Committee (NWJCC) propose to commission Eculizumab for people with Paroxysmal Nocturnal Haemolglobinuria in accordance with the criteria outlined in this document.

In creating this document NWJCC has reviewed this clinical condition and the options for its treatment. It has considered the place of this treatment in current clinical practice, whether scientific research has shown the treatment to be of benefit to patients, (including how any benefit is balanced against possible risks) and whether its use represents the best use of NHS resources.

Welsh Language

NWJCC is committed to treating the English and Welsh languages on the basis of equality, and endeavour to ensure commissioned services meet the requirements of the legislative framework for Welsh Language, including the Welsh Language Act (1993), the Welsh Language (Wales) Measure 2011 and the Welsh Language Standards (No.7) Regulations 2018.

Where a service is provided in a private facility or in a hospital outside of Wales, the provisions of the Welsh language standards do not directly apply but in recognition of its importance to the patient experience, the referring health board should ensure that wherever possible patients have access to their preferred language.

In order to facilitate this, NWJCC is committed to working closely with providers to ensure that in the absence of a Welsh speaker, written information will be offered and people have access to either a translator or 'Language-line' if requested. Where possible, links to local teams should be maintained during the period of care.

Decarbonisation

NWJCC is committed to taking assertive action to reducing the carbon footprint through mindful commissioning activities. Where possible and taking into account each individual patient's needs, services are provided closer to home, including via digital and virtual access, with a delivery chain for service provision and associated capital that reflects the NWJCC commitment

Disclaimer

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

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, or Local Authority.

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

1. Introduction

This policy has been developed as a Policy Proposal for the planning and delivery of Eculizumab for Paroxysmal Nocturnal Haemoglobinuria (PNH) for people resident in Wales. This proposed service will only be commissioned by the NHS Wales Joint Commissioning Committee (NWJCC) and applies to residents of all seven Health Boards in Wales.

1.1 Plain Language Summary

Paroxysmal Nocturnal Haemoglobinuria (PNH) is a very rare blood disease (also sometimes referred to as an ultra-orphan disease) where blood cells are vulnerable to attack by a particular part of the body's immune system called "the complement system". The process whereby the red blood cells are destroyed is called haemolysis and is responsible for many of the symptoms of the disease.

Eculizumab, otherwise known as "Soliris", is administered by way of infusion once every two weeks on an ongoing basis. Eculizumab is an antibody which blocks the activation of the complement system. It therefore protects the blood cells affected by PNH from destruction or stimulation by the complement system.

Eculizumab has been proven to reduce the symptoms of PNH patients and improve their quality of life and their life expectancy. It also reduces the risks of many of the complications of PNH such as thrombosis, renal failure or pulmonary hypertension.

1.2 Aims and Objectives

This policy aims to define the commissioning position of NWJCC on the use of Eculizumab for people with Paroxysmal Nocturnal Haemoglobinuria.

The objectives of this policy are to:

- ensure commissioning for the use of Eculizumab is evidence based
- ensure equitable access to Eculizumab
- define criteria for people with Paroxysmal Nocturnal Haemoglobinuria to access treatment
- improve outcomes for people with Paroxysmal Nocturnal Haemoglobinuria

1.3 Epidemiology

PNH is an extremely rare condition and is thought to affect around 16 people per million in the United Kingdom. It is not an inherited condition, meaning it cannot be passed on

from parents to children. Equally, you cannot catch PNH from someone who has it. It can occur at any age. Men and women are affected equally[1].

1.4 Current Treatment

There are a number of different therapeutic interventions that patients with PNH may require. Some people, especially those with a lower proportion of PNH cells may require little or no intervention. Interventions include blood transfusions, folic acid, anticoagulation, iron supplements and iron removal, bone marrow transplantation and Eculizumab. Treatment options other than Eculizumab are described below. Eculizumab is described in 1.5.

1.4.1 Blood Transfusions

Anemia is one of the commonest symptoms of PNH. Blood transfusions may alleviate some of the symptoms experienced.

1.4.2 Folic Acid

Folic acid is a vitamin needed by the bone marrow to help make blood cells. In PNH, the bone marrow often produces more red blood cells than normal to try to compensate for the blood cells being destroyed in the bloodstream. Taking folic acid tablets helps to ensure that the bone marrow has enough folic acid to make blood cells.

1.4.3 Anticoagulation

Some patients are on blood thinning medication, such as warfarin, to reduce the risk of developing blood clots. These medications make people more likely to bruise and bleed.

1.4.4 Iron supplements and iron removal

Iron levels may be either too low or too high in PNH, usually depending on whether the patient is on a specific treatment for the PNH or not. Some patients therefore may require iron supplements and others may need medication to reduce the iron levels in the body.

1.5 Eculizumab

Eculizumab (or Soliris) is an intravenous infusion that is administered every two weeks in the long-term. Eculizumab blocks the activation of complement and therefore protects the PNH cells from destruction or stimulation. As soon as Eculizumab therapy is stopped, complement will become active and the PNH cells that were previously protected will be vulnerable to complement attack again. It is therefore usual that Eculizumab is a

[1] Information taken from the UK National PNH service website

treatment that needs to be given lifelong. Eculizumab has been proven to reduce the symptoms experienced in PNH and has been shown to improve people's quality of life. It also reduces the risks of many of the complications of PNH, such as thrombosis, renal failure or pulmonary hypertension and as a result can prevent death due to such complications.

1.6 What NHS Wales has decided

NWJCC has carefully reviewed the evidence of Eculizumab for Welsh residents with PNH. We have concluded that there is enough evidence to fund the use of Eculizumab, within the criteria set out in section 2.1.

1.7 Relationship with other documents

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

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

2. Criteria for Commissioning

The NHS Wales Joint Commissioning Committee propose to approve funding of Eculizumab for Welsh residents with Paroxysmal Nocturnal in line with the criteria identified in this policy.

2.1 Inclusion Criteria

Eculizumab (Soliris) is indicated for the treatment of patients with Paroxysmal Nocturnal Haemoglobinuria (PNH).

Patients fulfilling any of the following categories will be considered for treatment:

- Transfusion dependent due to PNH
- Thrombosis related to PNH
- Complications associated with haemolysis:
- Renal failure
- Pulmonary hypertension
- Pregnancy (and for at least 3 months post-partum)
- Haemolytic (LDH >1.5xULN) symptomatic PNH with **either** of the following:
  - Anaemia (Hb <9g/L) **or**
  - With agreement with Joint Service colleagues at MDT

If these criteria are not met, but the specialist PNH service believes that there are exceptional circumstances why Eculizumab should be prescribed for the patient, an application may be made to the Individual Patient Funding Request panel.

2.2 Exclusion Criteria

Referrals to the PNH service must be from a consultant haematologist (referrals from other specialties will not be funded). Any patient who does not meet the required criteria for Eculizumab therapy in 2.1 will not be considered appropriate for funding.

2.3 Stopping Criteria

A patient will discontinue Eculizumab if:

- they experience an anaphylactic reaction thought to be due to the treatment **or**
- they have a C5 polymorphism making them refractory to this treatment
- they have a spontaneous remission of PNH (rare)
- they have a bone marrow transplantation and PNH is no longer detectable or is at a very low level.

2.4 Continuation of Treatment

Healthcare professionals are expected to review a patient's health at regular intervals to ensure they are demonstrating an improvement to their health due to the treatment being given.

If no improvement to a patient's health has been recorded then clinical judgement on the continuation of treatment must be made by the treating healthcare professional.

2.5 Acceptance Criteria

The service outlined in this policy 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.

2.6 Patient Pathway (Annex i)

The referral pathway is described below and set out as a flow diagram in annex i.

- The local haematologist makes a diagnosis of symptomatic PNH or identifies a PNH clone: decision to refer to the specialist PNH service.
- The specialist PNH service will provide advice on investigation and management at the PNH clinic (or Outreach Clinic). It will also provide specialist monitoring and follow-up at clinics through shared care arrangements with local haematology services.
- The designated centre for Wales is the PNH service at Leeds Teaching Hospitals NHS Trust. The Leeds PNH service also provides outreach clinics in Bristol and Liverpool.
- If the specialist PNH service confirms that Eculizumab is indicated for the patient (criteria in 2.1), the first infusion is usually delivered by the specialist PNH service. On-going prescribing of Eculizumab will be undertaken by the local haematologist.
- Patients receiving Eculizumab will continue to be monitored in accordance with the shared care protocol, as appropriate (annex v).
- If Eculizumab is not indicated, the patient will continue to be monitored in accordance with the shared care protocol, as appropriate (annex v).

The referral pathway is supported by the administrative and funding arrangements outlined in annex ii.

If the local haematologist or patient wishes to be referred to a provider outside the agreed pathway, an Individual Patient Funding Request should be submitted.

2.7 Designated Centre

PNH National Service
Level 3, Bexley Wing
St James's Institute of Oncology
Leeds Teaching Hospitals NHS Trust
Beckett Street
Leeds
LS9 7TF

2.8 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, an IPFR should be submitted.

Further information on making IPFR requests can be found at: Individual Patient Funding Requests

2.9 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.

2.10 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.

Clinicians considering treatment should:

- discuss all alternative treatments with the patient;
- 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 NWJCC for the treatment.

In all other circumstances an IPFR must be submitted.

3. Evidence

NWJCC is committed to regularly reviewing and updating all of its commissioning policies based upon the best available evidence of both clinical and cost effectiveness.

3.1 References

- Kelly RJ, Hill A, Arnold LM, Brooksbank GL, Richards SJ, Cullen M, Mitchell LD, Cohen DR, Gregory WM, Hillmen P. Long-term treatment with Eculizumab in paroxysmal nocturnal haemoglobinuria: sustained efficacy and improved survival. Blood. 2011;117:6786–6792[2]

3.2 Date of Review

This document is scheduled for review before 2023, where we will check if any new evidence is available. If no new evidence or intervention is available the review date will be progressed.

If an update is carried out the policy will remain extant until the revised policy is published.

[2] Long-term treatment with eculizumab in paroxysmal nocturnal hemoglobinuria: sustained efficacy and improved survival. - PubMed - NCBI

4. 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 NHS Wales Joint Commissioning 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.

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 NWJCC.

5.2 Individual Patient Funding Request (IPFR)

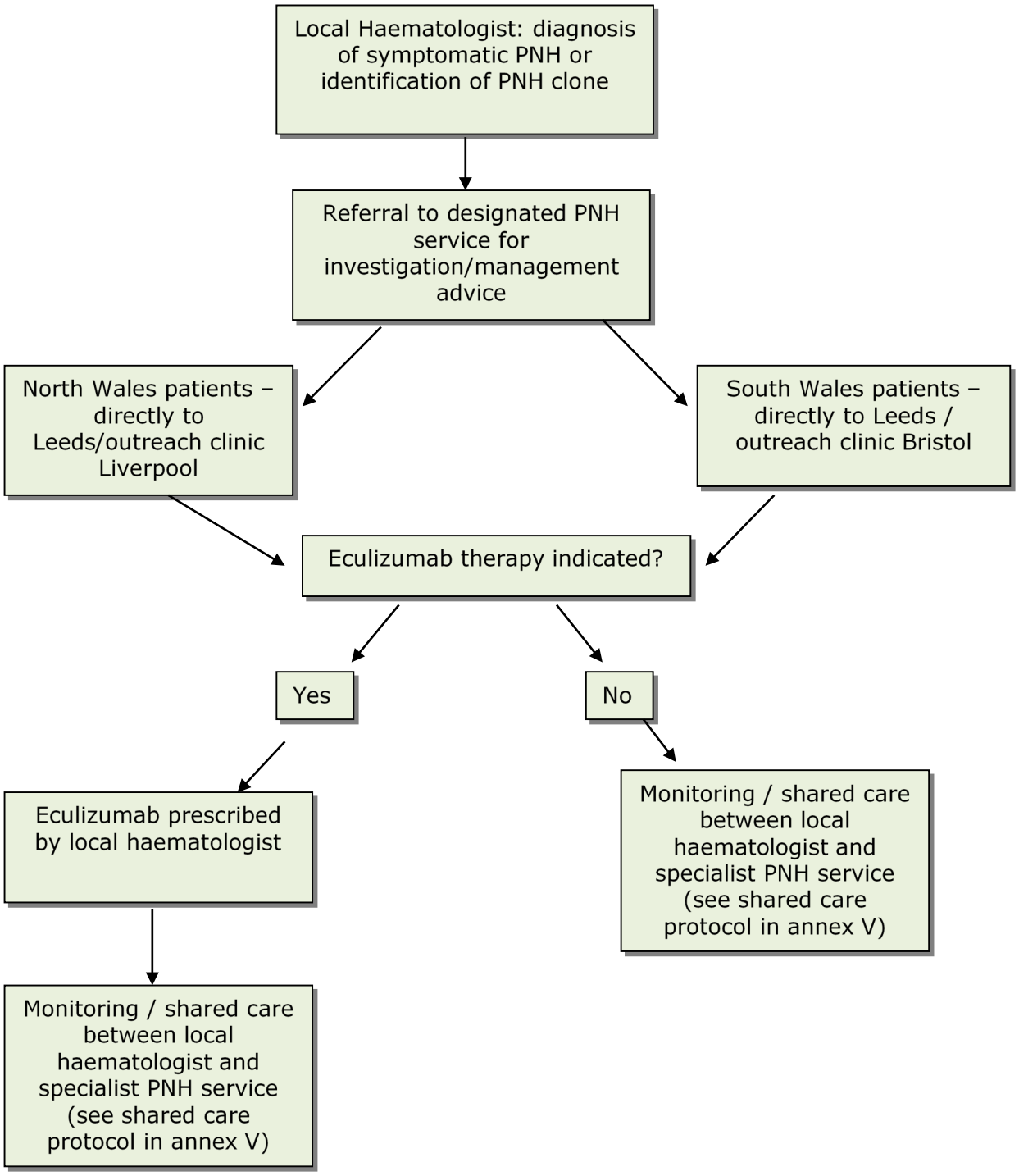
If the patient does not meet the criteria for treatment as outlined in this policy, an Individual Patient Funding Request (IPFR) can be submitted for consideration in line with the All Wales Policy: Making Decisions on Individual Patient Funding Requests. The request will then be considered by the All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

Further information on making IPFR requests can be found at: Individual Patient Funding Requests

Annex i Patient Pathway



Annex ii Referral protocol: roles and responsibilities

A: Process for referral to the specialist PNH service (South Wales/North Wales)

- Local haematology referral to PNH centre, Leeds Teaching Hospitals NHS Trust, for confirmation of diagnosis/initiation of treatment.
- PNH service determines whether the patient should be seen at a suitable outreach clinic (Bristol/Liverpool) or at the PNH centre in Leeds.
- Funding provided within WHSSC contract with Leeds Teaching Hospitals.

B: Process for commencing a patient on Eculizumab (all Wales)

- Local haematologist refers patient to specialist PNH service for clinical advice (Process A above).
- PNH service confirms to referring haematologist that Eculizumab treatment is indicated once the patient has been reviewed in clinic (unless a clinical emergency) and patient meets the criteria in section 2.1of this policy.
- Local haematologist informs WHSSC that the patient is commencing Eculizumab (copy of clinical letter and completed checklist in annex 1 sent to WHSSC – WHSSC.IPC@wales.nhs.uk)
- WHSSC confirm funding for treatment (within 24 hrs). An application for funding must be submitted as soon as possible (retrospective applications will be considered in an emergency setting).
- Local haematology/Health Board arranges home care delivery.
- If emergency Eculizumab therapy is required for breakthrough haemolysis, or for a new patient, such cases must be discussed and a treatment plan agreed with the PNH consultant on call. An application for funding must be submitted as soon as possible (retrospective applications will be considered in an emergency setting).
- Eculizumab can be accessed within 24 hours. In the event the drug is not available at a site, the on-call duty pharmacist/haematologist on call should contact the Alexion on-call team.

Annex iii Checklist

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The following checklist should be completed for every patient to whom the policy applies:

- Where the patient meets the criteria **and** the procedure is included in the contract **and** the referral is received by an agreed centre, the form should be completed and retained by the receiving centre for audit purposes.
- The patient meets the criteria **and** is received at an agreed centre, but the procedure is not included in the contract. The checklist must be completed and submitted to WHSSC for prior approval to treatment.
- The patient meets the criteria but wishes to be referred to a non contracted provider. An Individual Patient Funding Request (IPFR) Form must be completed and submitted to WHSSC for consideration.
- 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.

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The following checklist should be completed for ***all*** *patients to whom the policy applies*, before treatment, by the responsible clinician.

Please complete the appropriate boxes:

Patient NHS No:		
Patient is Welsh Resident registered with an NHS Wales GP	Post Code:	
Patient is English Resident registered with NHS Wales GP	GP Code:	

Patient meets the following access criteria for treatment:	**Yes**	**No**
Transfusion dependent due to PNH **and/or**		
Thrombosis related to PNH **and/or+**		
Complications associated with haemolysis 1. Renal failure 2. Pulmonary Hypertension **and/or**		

Pregnancy (and for at least 3 months post partum) **and/or**		
Haemolytic (LDH >1.5xULN) symptomatic PNH with **either** of the following 1.Anaemia (Hb <9g/L) **or** 2. With agreement with Joint Service colleagues at MDT		
Patient wishes to be referred to non-contracted provider		
An Individual Patient Funding Request (IPFR) Form must be completed and submitted to WHSSC for consideration.		
Patient does not meet access criteria but has exceptional circumstances		
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.		

Name: _____ Designation: _____

Signature: _____ Date: _____

Annex ii Codes

Code Category	Code	Description
ICD-10	D59.5	Paroxysmal nocturnal haemoglobinuria

Annex v: shared Care Protocol

The first infusion of Eculizumab is usually delivered via the PNH centre. To allow convenient access to long-term treatment, Eculizumab is then administered in the patient's home via a home care provider.

The PNH team will be responsible for liaising with the local haematologist regarding arrangements for admission of the patient to the PNH centre and proposed discharge date. The PNH team will also advise on supportive care medication such as antimicrobial prophylaxis and arrangements for relevant vaccinations at review at clinic visits.

It is the responsibility of the local haematologist with support from local pharmacists to ensure all relevant paperwork and prescriptions are completed and forwarded to the home care provider.

The PNH team will be responsible for determining the frequency of visits to the outreach clinics for patients on treatment with Eculizumab and those under observation alone. It is usual for visits to occur between 3-6 months once established on therapy or if on monitoring alone.

PNH patients will be given contact numbers for local haematology services in the event of the patient being taken unwell or developing a potential complication of PNH. Patients will also be given contact details for the PNH service to address concerns or queries related to PNH between visits that cannot be answered by the local haematology team. The PNH service operates a 24/7 on call service whereby a PNH consultant or haematologist is always available for emergency advice for local haematology teams.

Screening for PNH related complications will be undertaken at local hospitals following advice from the PNH service. Routine haematology follow up between PNH clinics will occur locally as required. Routine follow up and monitoring for underlying bone marrow disorders such as aplastic anaemia/myelodysplastic syndrome will continue as per local practice.

For emergency cases, the PNH centre will provide the local haematology team with advice with regard to management, and once stable the patient will be referred and seen in a specialist PNH clinic. It is expected that junior medical staff would first contact the local on-call haematology consultant for advice before contacting the PNH centre.

Advice on dose of Eculizumab for maintenance if not adequately controlled is provided during monitoring clinic appointments. Advice is available from the PNH centre outside these visits.

Annex vi Abbreviations and Glossary

Abbreviations

AWMSG All Wales Medicines Strategy Group

IPFR Individual Patient Funding Request

NWJCC – NHS Wales Joint Commissioning Committee

SMC Scottish Medicines Consortium

PNH Paroxysmal Nocturnal Haemoglobinuria

Glossary

Individual Patient Funding Request (IPFR)

An IPFR is a request to NHS Wales Joint Commissioning Committee (NWJCC) to fund an intervention, device or treatment for patients that fall outside the range of services and treatments routinely provided across Wales.

NHS Wales Joint Commissioning Committee (NWJCC)

NWJCC is a joint committee of the seven local health boards in Wales. The purpose of NWJCC is to ensure that the population of Wales has fair and equitable access to the full range of Tertiary Services. NWJCC ensures that services within our portfolio 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.