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# **Rituximab and eculizumab for the prevention and management of delayed haemolytic transfusion reactions and hyperhaemolysis in people with hereditary anaemias**

## **Policy Position Statement: PPS237**

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## Abbreviations

<b>DHTR</b>	Delayed haemolytic transfusion reactions
<b>Hb</b>	Haemoglobin
<b>HCC</b>	Haemoglobinopathy Coordinating Centre
<b>HH</b>	Hyperhaemolysis
<b>IPFR</b>	Individual Patient Funding Request
<b>IVIg</b>	Intravenous Immunoglobulin
<b>LDH</b>	Lactate dehydrogenase
<b>MDT</b>	Multi-Disciplinary Team
<b>NHP</b>	National Haemoglobinopathy Panel
<b>IPFR</b>	Individual Patient Funding Request
<b>NWJCC</b>	NHS Wales Joint Commissioning Committee
<b>SCD</b>	Sickle Cell Disease/Disorder
<b>SHOT</b>	Serious Hazard of Transfusion
<b>SHT</b>	Specialist Haemoglobinopathy Team

## Policy Statement

NHS Wales Joint Commissioning Committee (NWJCC) will commission rituximab and eculizumab for the prevention and management of delayed haemolytic transfusion reactions and hyperhaemolysis in people with hereditary anaemias in accordance with the criteria outlined in this document.

In creating this document NWJCC has reviewed the relevant guidance issued by NHS England<sup>1</sup> and has concluded that rituximab and eculizumab should be made available.

### 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, 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. 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 judgement, knowledge and expertise when deciding whether it is appropriate to apply this document.

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<sup>1</sup> [NHS England » Rituximab and eculizumab for the prevention and management of delayed haemolytic transfusion reactions and hyperhaemolysis in patients with haemoglobinopathies](#)

This document 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 Position Statement has been developed for the planning and delivery of rituximab and eculizumab for people resident in Wales. This 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

Delayed haemolytic transfusion reactions (DHTR) and hyperhaemolysis (HH) are rare life threatening complications of a reaction to a blood transfusion. DHTR is defined as a significant drop in haemoglobin (blood count) with no alternative cause identified, within 21 days of the transfusion. Some patients will also go on to develop HH; the most severe form of DHTR, where the transfusion reaction triggers destruction of the patient's own red cells in addition to the new transfused red cells. The patient's haemoglobin (blood count) drops further to below the pre-transfusion baseline haemoglobin (Hb). Once a patient has experienced HH, they are at risk of recurrence in subsequent transfusions, even if several years later.

The new treatments available for use are rituximab and eculizumab. Rituximab is a drug that acts on the body's immune system and decreases DHTR by reducing the production of proteins that attack the red blood cells (alloantibodies). Eculizumab is a drug that reduces the activation of complement, a key part of activating the immune response involved in the red blood cell destruction. Rituximab has been used both to prevent the occurrence of DHTR in high risk patients and to manage severe ongoing DHTR/HH and eculizumab has been used to manage severe ongoing DHTR/ HH in patients at high risk of death and organ damage. Neither medicine is licensed for this intervention and will be used 'off label'.

## 1.2 Aims and Objectives

This Policy Position Statement aims to define the commissioning position of NWJCC on the use of rituximab and eculizumab for the prevention and management of delayed haemolytic transfusion reactions and hyperhaemolysis in people with hereditary anaemias.

The objectives of this policy are to:

- ensure commissioning for the use of rituximab and eculizumab is evidence based
- ensure equitable access to rituximab and eculizumab
- define criteria for people with hereditary anaemias to access treatment
- improve outcomes for people with hereditary anaemias

### 1.3 Epidemiology

In the UK, there is a national mandated reporting system where all transfusion reactions are reported to the Serious Hazard of Transfusion (SHOT) database, run by the National Blood Transfusion Service. In 2018, there were 28 cases of DHTR reported to SHOT<sup>2</sup>. Five of these cases were associated with HH, three of whom had Sickle Cell Disease (SCD), the other two had T-cell lymphoma and Rosai-Dorfman Syndrome and both non-SCD patients died. These were the first non-hereditary anaemia patients reported to SHOT with HH. There were no paediatric cases of DHTR reported in 2018. However, there was one reported in 2017 from a total of 23 cases of DHTR reported to SHOT in 2017, of which six were HH in patients with SCD<sup>3</sup>.

There have been five known cases of eculizumab being used in the UK to treat HH in the last two years. It is expected that there will be fewer than five patients per year who will require eculizumab and fewer than two patients that will need rituximab per year.<sup>4</sup>

### 1.4 Current Treatment

#### Management of established DHTR/HH

Current first line treatment for established DHTR/HH consists of supportive care (fluids, pain relief) with erythropoietin and haematinic replacement to improve new red cell production. Treatments such as steroids and intravenous immunoglobulin (IVIg) are also used to reduce the immune system breaking down red cells. These drugs are not always effective and haemolysis may continue despite treatment.

#### Prevention of DHTR/HH

Some patients are at high risk of DHTR/HH because of previous history of this complication and a need for further transfusion therapy. In this situation, steroids and IVIg are used to prevent future DHTR/HH.

### 1.5 Proposed Treatment

Rituximab is a drug that acts on the body's immune system by depleting B cells. It decreases DHTR by reducing the production of alloantibodies and by preventing the antibody mediated red blood cell destruction. Therefore, it is also useful in preventing further delayed haemolytic transfusion reactions. Rituximab is licensed for the

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<sup>2</sup> [https://www.shotuk.org/wp-content/uploads/myimages/SHOT-Report-2018\\_Web\\_Version.pdf](https://www.shotuk.org/wp-content/uploads/myimages/SHOT-Report-2018_Web_Version.pdf)

<sup>3</sup> <https://www.shotuk.org/wp-content/uploads/myimages/SHOT-Report-2017-WEB-Final-v4-25-9-18.pdf>

<sup>4</sup> Clinical opinion from the CVUHB haematology directorate.

treatment of diseases such as non-Hodgkin's Lymphoma, chronic lymphocytic leukaemia and rheumatoid arthritis; it is unlicensed for the treatment of DHTR/HH.

Eculizumab is a drug that has been shown to significantly reduce the activation of complement, which is a key mechanism involved in the immune response causing red blood cell destruction and there is evidence of its efficacy in other conditions with marked complement activation. Eculizumab led to rapid resolution of HH in a case report<sup>5</sup>. Eculizumab is licensed for the treatment of other diseases such as Paroxysmal nocturnal haemoglobinuria<sup>6</sup> and atypical haemolytic uremic syndrome<sup>7</sup>; it is unlicensed for the treatment of DHTR/HH.

A recent paper recommended rituximab as first line treatment for prevention of DHTR and eculizumab as second line treatment for management of DHTR/HH<sup>8</sup>.

### **Treatment of DHTR/HH**

Intravenous immunoglobulin (IVIg) and steroids with supporting treatment are the usual first line treatment. This policy recommends eculizumab for all ages as a second line treatment for the management of DHTR/HH in patients where first line treatment has failed to prevent rapid haemolysis. Rituximab is recommended as third line treatment for adult and post pubescent patients.

### **Prevention of DHTR/HH in patients requiring elective blood transfusion**

IVIg and steroids are first line preventative treatment. Where this has previously failed, this policy commissions the use of rituximab for adult and post-pubescent patients only, as a second line treatment instead of using IVIg and steroid therapy for the prevention of DHTR/HH in patients requiring elective blood transfusion.

## **1.6 Off-label use**

Eculizumab and rituximab are not licensed to treat DHTR/HH and are therefore "off – label". A clinician considering prescribing these medications outside of the terms of a product licence (off-label) should do so in accordance with the [Medicines and Healthcare Products Agency \(MHRA\)](#) and the [General Medical Council](#) (GMC) guidance which applies throughout the UK.

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<sup>5</sup> Chonat S, Quarmyne MO, Bennett CM, Dean CL, Joiner CH, Fasano RM, Stowell SR. Contribution of alternative complement pathway to delayed hemolytic transfusion reaction in sickle cell disease. *Haematologica*. 2018 Oct;103(10):e483-e485

<sup>6</sup> See [NWJCC Commissioning Policy CP152](#)

<sup>7</sup> See [NWJCC Commissioning Policy CP98](#)

<sup>8</sup> Pirenne, F. & Yazdanbakhsh, K. 2018. How I safely transfuse patients with sickle-cell disease and manage delayed hemolytic transfusion reactions. *Blood* 131(25) 2773-2781

The risk and benefits of off-label use of eculizumab and rituximab should be clearly stated and discussed with the patient to enable informed consent.

Should clinicians consider the treatments appropriate for their patients and they have followed local medicines governance arrangements for off-label use, NWJCC will meet the cost under the criteria set out in 2.1.

### **1.7 What NHS Wales has decided**

NWJCC has carefully reviewed the relevant guidance issued by NHS England. We have concluded that rituximab and eculizumab should be made available within the criteria set out in section 2.1.

## 2. Criteria for Commissioning

The NHS Wales Joint Commissioning Committee approve funding of rituximab and eculizumab for people with hereditary anaemias in line with the criteria identified in this policy.

### 2.1 Inclusion Criteria

DHTR and HH are rare, life threatening complications of blood transfusion associated with red cell alloantibody formation and activation of complement. DHTR is defined as a significant drop in haemoglobin (Hb) in the absence of an alternative cause within 21 days of transfusion associated with one or more additional clinical criteria and with the exclusion of an alternative cause. The five defining criteria for treatment are:

- new red cell alloantibody (or antibodies)
- haemoglobinuria
- Hb level that decreases more rapidly than expected post transfusion
- relative reticulocytopenia or reticulocytosis from baseline
- significant rise in lactate dehydrogenase (LDH) from baseline.

### Prevention of DHTR/HH

Rituximab should be considered as second line treatment, given instead of IVIg and steroid for the prevention of DHTR/HH in adults and post-pubescent patients requiring elective blood transfusion who have:

- had DHTR/HH previously despite pre-transfusion treatment with IVIg and steroids

**or**

- multiple red cell alloantibodies where compatible blood is not available.

### Management of DHTR/HH

- Second line treatment with eculizumab should be considered for patients of all ages when the rate of rapid haemolysis WITH symptomatic anaemia OR compromise of another organ system (e.g. respiratory failure, renal failure, neurological symptoms) continues despite first line treatment with IVIg and steroids.
- Third line treatment with rituximab should be considered for adult and post-pubescent patients when all criteria for giving eculizumab has been met AND there is a need for ongoing blood transfusion therapy.

### Dose

- Rituximab in adult and post-pubescent patients:

- PREVENTION: 2 doses of 375mg/m<sup>2</sup> given 7-14 days apart.
- MANAGEMENT: 2 doses of 375mg/m<sup>2</sup> to a maximum of 4 doses given 7 days apart, depending on response and the need for further blood transfusions.
- Eculizumab in adult patients: 900mg IV ONCE and a second dose 7 days later if there is evidence of efficacy of treatment but ongoing haemolysis. No further doses/ courses are permitted.
- Eculizumab in paediatric patients based on weight: patients <10kg = 300mg, 10-40kg = 600mg; >40kg adult dose of 900mg dose. A maximum of two doses are commissioned and no further doses/ courses permitted.

## 2.2 Exclusion Criteria

- Patients who do not have a hereditary anaemia.
- Patients previously treated without a response.
- For rituximab, pre-pubescent paediatric patients.

There is no well-controlled data for either drug when used in pregnancy. In both instances, this would be a risk benefit judgement balancing the clear and present danger to the mother with the unknown but theoretical risk of complement inhibition or B-cell depletion in the baby.

## 2.3 Stopping Criteria

### **Eculizumab**

One dose to be given initially and no further dose given if there is:

- a complete response in line with the five defining criteria (2.1 above)
- no evidence of response
- an adverse event.

### **Rituximab**

Following initial dose(s) no further doses given if there is:

- no further transfusion is needed
- an adverse event of a severity such that the balance of risks and benefit do not support further use.

## 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 Monitoring

Principal long-term adverse effects of rituximab include neutropenia and hypogammaglobulinaemia from prolonged B-cell depletion. The product license for rituximab recommends regular measurement of blood neutrophils which would be part of ongoing monitoring.

Following eculizumab administration, long term prophylactic antibiotics may be required based on clinical decision and local guidelines. Patients receiving eculizumab should be vaccinated with Meningitis ACWY and Meningitis B<sup>9</sup>.

## 2.6 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.

## 2.7 Transition arrangements

Transition arrangements should be in line with [Transition from children's to adults' services for young people using health or social care services, NICE guidance NG43](#) and the [Welsh Government Transition and Handover Guidance](#)

Transition involves a process of preparation for young people and their families for their transition to adulthood and their transition to adult services. This preparation should start from early adolescence 12-13 year olds. The exact timing of this will ideally be dependent on the wishes of the young person but will need to comply with local resources and arrangements.

The transition process should be a flexible and collaborative process involving the young person and their family as appropriate and the service.

The manner in which this process is managed will vary on an individual case basis with multidisciplinary input often required and patient and family choice taken into account together with individual health board and environmental circumstances factored in.

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<sup>9</sup> [NHS England » Rituximab and eculizumab for the prevention and management of delayed haemolytic transfusion reactions and hyperhaemolysis in patients with haemoglobinopathies](#)

For the specialised paediatric services it commissions, the JCC will routinely commission treatment up until a patient is 16 years old. The JCC does not commission specialised paediatric services for patients aged 18 and older. For patients aged 16 or 17 years of age, the JCC will continue to commission ongoing specialised treatment initiated before the patient's 16<sup>th</sup> birthday and under the ongoing care of a specialised paediatric team.

## 2.8 Patient Pathway (Annex i)

See Annex (i) for pathways for:

- Management of DHTR/HH in patients with hereditary anaemias
- Prevention of DHTR/HH in patients with hereditary anaemias

## 2.9 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](#)

## 2.10 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.

A prospective data collection process with an agreed dataset will be required to inform prescribing in the future. All cases of DHTR/HH in Wales will be reported to the National Haemoglobinopathy Panel (NHP). The dataset will be completed by the NHP and the reporting provider. That dataset will include information on usage, indications and outcomes. Outcome measures will include mortality, NHS utilisation (e.g. ICU admission and length of stay), clinical complications (including side effects of eculizumab and rituximab) and prevention of post transfusion haemolysis 24 hours to 21 days following

transfusion. The NHP will produce an annual report that will be used to inform future policy developments.

In the UK there is a national mandated reporting system whereby all transfusion reactions are reported to the SHOT database run by the National Blood Transfusion Service. Cases must continue to be reported to allow outcomes to be compared with those in patients with DHTR/HH who are not treated with these therapies or who do not have a hereditary anaemia.

## 2.11 Responsibilities

Due to the urgent nature with which the condition can occur, NWJCC will commission treatment from any acute hospital. However, it is expected that all cases and treatment planning should be discussed with the Specialist Haemoglobinopathy Team (SHT) and/or the appropriate Haemoglobinopathy Co-ordinating Centre (HCC).

All cases will be required to seek approval (ideally before administering treatment) from the appropriate HCC.

Provider organisations should register all patients using prior approval software (Blueteq®) and ensure monitoring arrangements are in place to demonstrate compliance against the criteria as outlined. All cases must be referred to the NHP for retrospective discussion of indications and outcomes.

In the non-emergency situation, patients with previous DHTR/HH despite pre-transfusion treatment with IVIg's and steroids who need elective transfusion therapy should be referred to the HCC MDT for discussion/approval and also (if time allows) to the NHP prior to treatment being given. As with the above, all cases must then be referred to the NHP for retrospective discussion of indications and outcomes. Provider organisations must register all patients using prior approval software (Blueteq®) and ensure monitoring arrangements are in place to demonstrate compliance against the criteria as outlined.

Health Boards and NWJCC are to circulate this Policy Position Statement to all Hospitals/MDTs to inform them of the conditions under which the treatment will be commissioned.

Referrers should:

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

Clinician considering treatment should:

- discuss all the alternative treatment with the patient and/or their parent or guardian
- advise the patient and/or their parent or guardian of any side effects and risks of the potential treatment
- inform the patient and/or their parent or guardian 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. Documents which have informed this policy

The following documents have been used to inform this policy:

- **NHS Wales Joint Commissioning Committee policies and service specifications**
  - [Sickle Cell Disorders, Thalassaemia Disorders and other Rare Hereditary Anaemias: all ages](#) CP179 Service Specification December 2020
- **NHS England policies**
  - [Rituximab and eculizumab for the prevention and management of delayed haemolytic transfusion reactions and hyperhaemolysis in patients with haemoglobinopathies](#) [URN 1821] [200602P], September 2020
- **Scottish Paediatric & Adult Haemoglobinopathy Network**
  - [Paediatric and Adult Guideline Management of Hyperhaemolysis in patients with Sickle Cell Disease](#) , June 2020

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 is scheduled for review every three years, unless information is received which indicates that the policy requires revision.

If an update is carried out, this version of the policy will remain extant until the revised policy is published.

## 5. Listening to People:

### 5.1 Complaints, Incidents and Redress Process

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 [Listening to People, The NHS Wales Complaints, Incidents and Redress Process – People’s Guidance 2026](#). 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.

## **6. Equality Impact and Assessment**

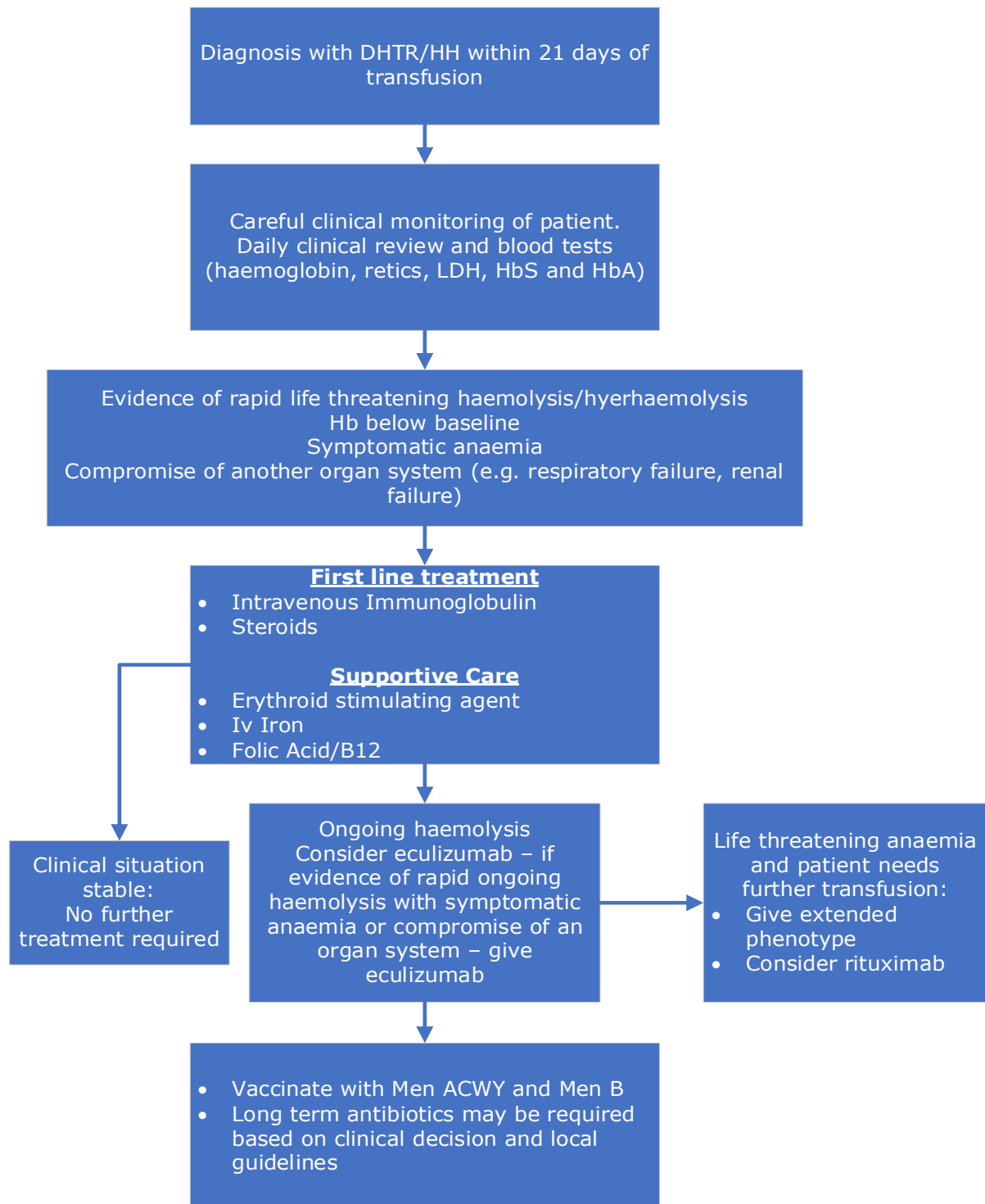
The Equality Impact Assessment (EIA) process has been developed to help promote fair and equal treatment in the delivery of health services. It aims to enable NHS Wales Joint Commissioning Committee to identify and eliminate detrimental treatment caused by the adverse impact of health service policies 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.

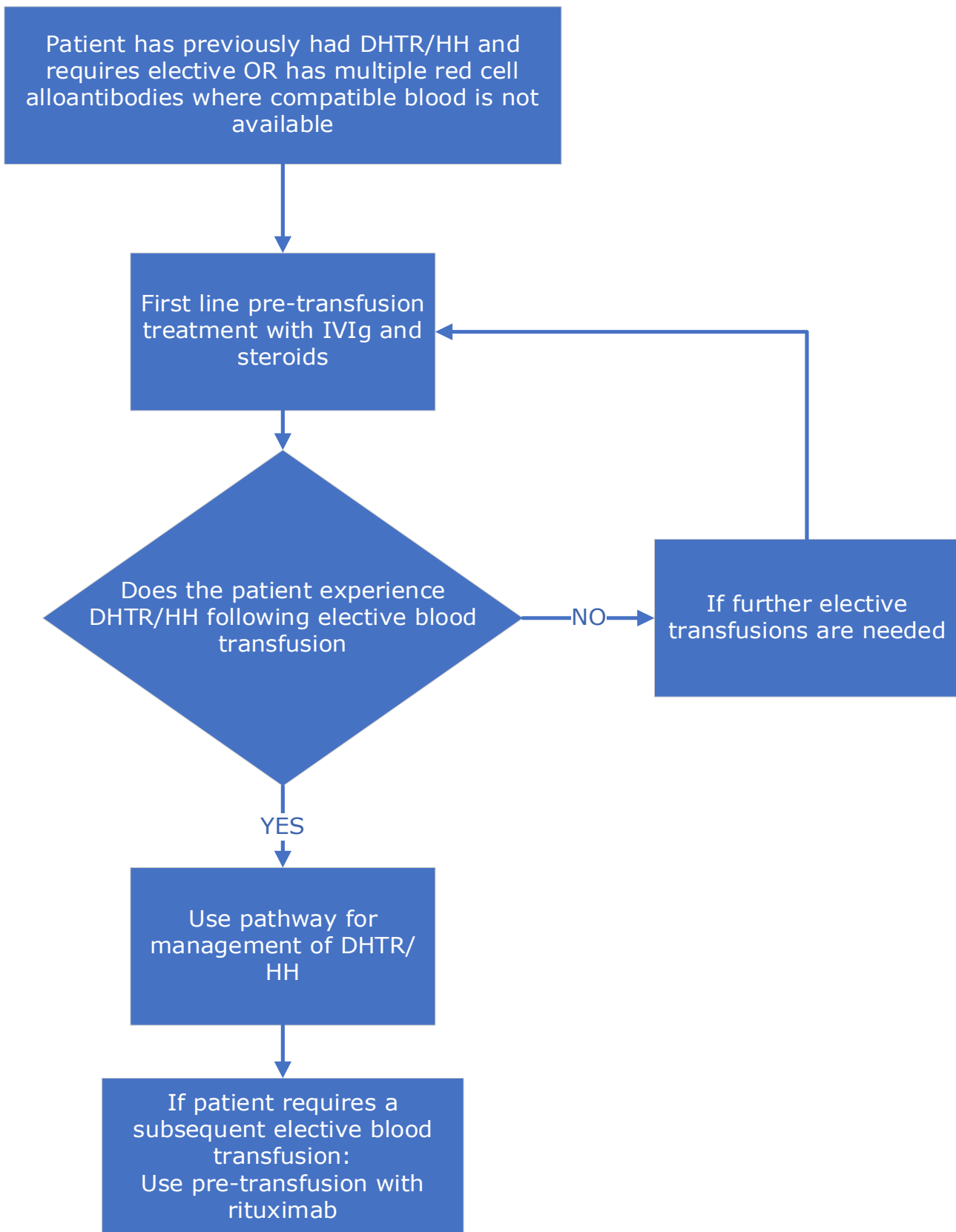
The Assessment demonstrates the policy is robust and there is no potential for discrimination or adverse impact. All opportunities to promote equality have been taken.

# Annex i Patient Pathway

## Pathway for management of DHTR/HH in patients with hereditary anaemias



**Pathway for prevention of DHTR/HH in patients with hereditary anaemias**



## Annex iii Codes

The list of ICD codes below is indicative and is not exhaustive. The ICD10 codes have been provided and verified by the Information Standards Team at Digital Health and Care Wales (DCHW). Additional codes may be used for contract monitoring purposes, furthermore some codes may cover indications not included within this policy.

Code Category	Code	Description
ICD-10	D56	Thalassaemia
	D57	Sickle Cell Disorders
	D58	Other hereditary haemolytic anaemias

## Annex iv Glossary

### **Alloantibodies**

An antibody that occurs against foreign tissues from a person of the same species.

### **Haemoglobin (Hb)**

A protein responsible for transporting oxygen in the blood.

### **Haemoglobinuria**

Presence of haemoglobin in the urine.

### **Haemolysis**

The destruction of red blood cells.

### **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.

### **Lactate Dehydrogenase (LDH)**

An enzyme involved in energy production found in almost all cells in the body and which increases during haemolysis.

### **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.

### **Sickle Cell Disease**

A group of inherited health conditions that affect the red blood cells and are associated with the production of abnormal haemoglobin.

### **Thalassaemia**

An inherited blood disorder in which the body makes an abnormal form of haemoglobin due to the production of abnormal amounts of globin chains.

### **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.

## Contact Us

If you have a question related to this document you can contact us using one of the methods outlined below.

If you would like this document in an alternative format and/or language, please contact us for assistance.

### **Email:**

NWJCC consultation mailbox – [NWJCC.Consultation@wales.nhs.uk](mailto:NWJCC.Consultation@wales.nhs.uk)

### **Telephone:**

General Enquiries – 01443 433112

### **Website:**

[Contact us - NHS Wales Joint Commissioning Committee](#)

### **Writing:**

If you wish to contact the NHS Wales Joint Commissioning Committee, you can write to us at one of our locations below, we welcome correspondence in Welsh or English:

#### **South Wales Offices**

Unit 1, Charnwood Court, Heol Billingsley, Nantgarw, CF15 7QZ

Unit G1 The Willowford, Main Avenue, Treforest Industrial Estate, Pontypridd, CF37 5YL

#### **North Wales Offices**

Unit 3, Media Point - Unit 3, Mold Business Park, Mold, CH7 1XY

Preswylfa, Hendy Road, Mold, CH7 1PZ