Anaemia Management Using Hypoxia Inducible Factor Prolylhydroxylase (HIF-PH) Inhibitor Therapy in Adults with Chronic Kidney Disease Clinical Guideline.

V1.0

Document reference code: CG/126/24

This is a joint policy between Cornwall Partnership NHS Foundation Trust and Royal Cornwall Hospitals NHS Trust.

This document replaces: N/A

Purpose: To ensure correct dosing and safe administration of this medication for staff responsible for prescribing/administering HIF-PH tablets.

Target audience: Renal physicians and patients.

Document author and role: Sharon Benton, Renal Clinical Nurse Specialist.
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Document definition: Guidelines.

Supporting committee: Medicine optimisation safety committee.
Supporting chairperson: Janine Glazier, Associate Medical Director
Executive director responsible for the policy: Chief Medical Officer.

Freedom of information: Can be released under the Freedom of Information Act 2000.
Document section: Clinical, clinical guidelines.

Audience:

☒ Cornwall Partnership NHS Foundation Trust

☒ Royal Cornwall Hospitals NHS Trust

Key words: hypoxia inducible factors, anaemia, chronic kidney disease.

Approval process

Approved at: CFT Medicines optimisation safety committee.
Date approved: 20 May 2024.
Executive approval: Dual Chief Nursing Officer / Deputy CEO RCHT. CFT Chief Medical Officer.
Date approved by: 3 June 2024
RCHT General manager confirming approval processes: Rachael Pearce.
RCHT Governance lead confirming approval process: Maria Lane.

Review date: January 2027 (6 months prior to the expiry date).

Expiry date: June 2027 (normally 3 years after ratification unless there are changes in legislation, NICE guidance or national standards or the document should only be valid for a specified period).

Publication location:

☒ Internet and intranet ☒ Intranet only

RCHT Document Library folder or sub-folder: Clinical / Renal

Version control

Version	Date	Author and/or reviewer	Section	Changes (key points)
V1.0	20/05/2024	Sharon Benton	None	New document

Contents

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For more information about your obligations under the Data Protection Act 2018 and UK General Data Protection Regulations 2016/679, contact the Information Governance team.

- Cornwall Partnership NHS Foundation Trust: Email cpn-tr.infogov@nhs.net
- Royal Cornwall Hospitals NHS Trust: Email rch-tr.infogov@nhs.net

1. Introduction

1.1. Normal functioning kidneys produce a hormone called erythropoietin (EPO). This endogenous hormone, in response to hypoxia, stimulates red blood cell production. EPO levels diminish when kidney function starts to deteriorate. Kidney function is ascertained by measuring the glomerular function rate (GFR). Recombinant human erythropoietin (rHuEPO), a biopharmaceutical, came into clinical practice for treating renal anaemia in chronic kidney disease (CKD) in 1990. This drug is a manufactured EPO which stimulates red blood cell production and improves haemoglobin (Hb) concentrations. Following its introduction there have been multiple EPO stimulating agents (ESAs) licensed. Unlike ESA's the newly available agent hypoxia-inducible factor (HIF) stabilizer stimulates endogenous EPO by mimicking hypoxia domain enzyme inhibition. This agent is abbreviated to HIF-PH therapy. It is unusual for ESAs or HIF-PH therapy to be required in patients with an eGFR >30ml/min (>45ml/min in patients with diabetes mellitus).

1.2. The investigation and management of anaemia should be considered in people with anaemia of CKD if their haemoglobin (Hb) level falls to 110 g/l or less or they develop symptoms attributable to anaemia. When determining individual aspirational Hb ranges for people with anaemia of CKD, take into account:

- Patient preferences.
- Symptoms and comorbidities.
- The required treatment.

1.3. Correction to physiologically normal Hb levels is not usually recommended in people with anaemia of CKD. Age alone should not be a determinant for treatment of anaemia of CKD. HIF-PH therapy should not be initiated in the presence of absolute iron deficiency without also managing the iron deficiency. In people with functional iron deficiency, iron supplements should be given concurrently when initiating HIF-PH's.

1.4. This version supersedes any previous versions of this document.

2. Aim/Purpose of this Guideline

2.1. All healthcare professionals have a duty of care which cannot be delegated at any time. The practitioners administering HIF-PH medication are responsible and accountable for their own clinical practice; including clinical competency. The Anaemia Management Nurse employed within renal services is responsible for policy review and update.

2.2. This policy is aimed at Staff responsible for prescribing/administering HIF-PH tablets. The policy objectives are to ensure correct dosing and safe administration of this medication. The policy Intended Outcomes are to ensure safe prescribing.

2.3. Definitions / Glossary

- HIF-PH - a stabilizer that stimulates endogenous EPO by mimicking hypoxia domain enzyme inhibition.
- Erythropoietin - a endogenous hormone, in response to hypoxia, that stimulates red blood cell production.
- eGFR – estimated glomerular filtration ratio. Kidney function is ascertained by measuring the glomerular function rate (GFR).

2.4. Ownership and Responsibilities

2.4.1. Strategic and operational role responsible for the development, management and implementation of the policy/procedure will remain with the policy author.

2.4.2. Staff responsible for the implementation of this policy are:

- Lead healthcare professional employed in the role of renal anaemia management.
- Renal Governance Group.
- Medicines Practice Committee.
- Clinical staff who prescribe/administer Roxadustat.

2.4.3. Role of the Managers

Line managers are responsible for:

- Ensuring staff responsible for prescribing Roxadustat remain up to date with prescribing practice.

2.4.4. Role of the Renal Governance Group/Committee

The renal governance group is responsible for:

- Reviewing reports raised by the lead healthcare professional employed in the role of renal anaemia management highlighting deficiencies.
- Highlight recommendations to resolve deficiencies

2.4.5. Role of Individual Staff

All staff members are responsible for and accountable for their own clinical practice including clinical competency.

3. The Guidance

3.1. HIF PH therapy is indicated for the treatment of symptomatic anaemia in patients with CKD. The choice between Roxadustat and injectable ESA's for non-dialysis patients with CKD should be made with the patient. Published evidence suggests equivalent efficacy and safety outcomes between Roxadustat and Aranesp in this cohort (Barratt J et al, 2021) Roxadustat (the only HIF-PH inhibitor currently licensed for use in UK at the time of writing this guidance) is approved for use by NICE for adult patients if:

- They have stage 3 to 5 CKD (eGFR <60ml/min/1.73m2).
- They are iron replete.
- They are not receiving dialysis at the start of treatment.

3.2. Indications.

HIF-PH inhibitors are not licensed for use outside of CKD-associated anaemia. HIF-PH therapy should be considered in patients with symptomatic anaemia (Hb<105g/l) when other causes of anaemia are not suspected. Caution is required in initiating HIF-PH inhibitors in patients with uncontrolled hypertension, history of seizures, active malignancy, or history of thrombotic events.

3.3. Contraindications

Roxadustat should not be initiated in:

- Women planning on becoming pregnant or during pregnancy (ESA may be used instead).
- Patients with severe hepatic impairment.
- Roxadustat should not be offered to patients with a peanut allergy.
- Roxadustat is not recommended for patients receiving haemodialysis who are stable on ESA and is not approved by NICE for treatment initiation in patients receiving haemodialysis or peritoneal dialysis. Roxadustat may be continued in patients receiving dialysis if treatment was commenced prior to starting dialysis.

3.4. Route of administration

HIF-PH inhibitors are administered orally. Roxadustat is licensed to be given three times weekly, avoiding consecutive day dosing.

3.5. Dosing HIF-PH inhibitor

Choice of treatment	Initial correction dose	Maintenance dose
Roxadustat (non-dialysis)	70mg 3x/week oral if weight <100kg. 100mg 3x/week if weight >100kg.	Adjust by 1 to 2 steps (see Table 1) to achieve target haemoglobin.

3.6. Table 1:

Change in Hb over previous 4 weeks	Current Hb level (g/l)			
	Lower than 105	105 - 119	120 - 129	130 or higher
More than +10 g/l	No change	Reduce dose by one step	Reduce dose by one step	Withhold dosing, monitor Hb level and resume dosing when Hb is less than 120 g/l, at a dose that is reduced by two steps
Between -10 and +10 g/l	Increase by one step	No change	Reduce dose by one step	
Less than -10 g/l	Increase dose by one step	Increase dose by one step	No change	
The dose of Roxadustat should not be adjusted more frequently than once every 4 weeks, except if Hb increases by more than 20 g/l at any time within a 4-week period, in which case the dose should be reduced by one step immediately.				
Roxadustat dosing steps (3x/week oral, not on consecutive days)				
20 mg	40 mg	50 mg	70 mg	100 mg
150 mg	200 mg	250 mg	300 mg	400 mg*
*400mg dose only licensed for haemodialysis recipients.				

3.7. Monitoring of patients prescribed HIF-PH inhibitor therapy

During correction phase, haemoglobin should be monitored every 2 to 4 weeks until in target.

1. During maintenance phase, haemoglobin should be monitored every 4 weeks. Longer periods (up to 12 weeks) can be considered in patients established on a stable dose of treatment.
2. Dose adjustments should maintain haemoglobin in the aspirational target range of 100-120g/l (see Table 1).
3. Treatment should be paused in patients with haemoglobin >130g/l then recommenced at a lower dose when indicated.

4. Doses should be reduced in patients with haemoglobin increases >20g/l/month irrespective of absolute haemoglobin level.

4. Related legislation and national and local guidance

None.

5. Training requirements

None.

6. Implementation

The document is available on the document library and shared during training sessions.

7. Monitoring arrangements

Information category	**Detail of process and methodology for monitoring compliance**
Element to be monitored	Appropriate use of HIF-PH therapy
Lead	Sharon Benton
Tool	Patient to be assessed to determine if ESA or HIF-PH therapy appropriate. Patient suitable to receive HIF-PH therapy if: • Has a severe needle phobia. • Would be reliant on community team to administer ESA. • Patient declines ESA with preference for HIF-PH therapy.
Frequency	Every outpatient prescription will be internally screened by a pharmacist before the drug is dispensed. Any discrepancies identified will be reported on within one month and shared with the renal governance team.
Reporting	If patient declines treatment or is unsuitable to receive either ESA

Information category	Detail of process and methodology for monitoring compliance
arrangements	or HIF-PH therapy Anaemia Management Nurse to inform referring health care professional. Patients prescribed Roxadustat will be reviewed to assess response to treatment. Haemoglobin (Hb) levels will be measured 1-3 monthly and haematinics measured every 3 months. HCP's involved in renal anaemia management will statistically analyse patient results. If Hb increases by more than 20 g/l at any time within a 4-week period the dose will be reduced by one step immediately. Roxadustat will be withheld if the Hb exceeds 130 g/L, blood tests will resume monthly, and the drug resumed at a reduced dose as per Table 1 when Hb <120g/L. Actions taken will be documented on Vitaldata. The renal anaemia nurse will identify and report deficiencies to the renal governance group. Completed reports will be sent to the Renal Governance group.
Acting on recommendations and lead(s)	The Anaemia Management Nurse will act on recommendations within 3 months of reporting deficiencies.
Change in practice and lessons to be shared	Report review to determine: • Number of patients suitable to receive HIF-PH therapy. • Number of patients opting for HIF-PH therapy. • Data analysis. Findings to be shared with the wider team.

8. Updating and review

This policy will be reviewed in 3 years. Earlier review may be required in response to exceptional circumstances, organisational change, or relevant changes in legislation and/or guidance, as instructed by the senior manager responsible for this policy.

9. Equality and diversity

9.1. This document complies with the Cornwall Partnership NHS Foundation Trust and Royal Cornwall Hospitals NHS Trust equality and diversity statements. The statements can be found in the RCHT Equality Diversity And Inclusion Policy and CFT Equality, Diversity and Inclusion Statement.

9.2. The initial equality impact assessment screening form is at appendix 1.

Appendix 1: Equality Impact assessment Form

Title of policy or document for assessment: Anaemia Management Using Hypoxia Inducible Factor Prolylhydroxylase (HIF-PH) Inhibitor Therapy in Adults with Chronic Kidney Disease Clinical Guideline V1.0

Document library section: Renal Medicine, Specialist Medicine Care Group.

Is this a new or existing document? New.

Date of assessment: 20 July 2023.

Person responsible for the assessment: Sharon Benton, Renal Clinical Nurse Specialist.

What is the main purpose of the document?
To ensure correct dosing and safe administration of medication for staff responsible for prescribing/administering HIF-PH tablets.

Who is affected by the document?

☒ Staff ☒ Patients ☐ Visitors ☐ Carers ☐ Other ☐ All

The document aims to improve access, experience and outcomes for all groups protected by the Equality Act 2010.

Concerns

Are there concerns that the procedural document could have a differential impact on the following areas?

If a negative impact has been identified, please complete a full EIA by contacting the Equality, Diversity, and Inclusion Team. For RCHT please contact rcht.inclusion@nhs.net and for CFT please contact cft.inclusion@nhs.net

Concern area	Response	If yes, what existing evidence (either presumed or otherwise) do you have for this?
Age	☐ Yes ☒ No	
Disability	☐ Yes ☒ No	
Sex	☐ Yes ☒ No	
Gender reassignment	☐ Yes ☒ No	
Pregnancy and maternity	☐ Yes ☒ No	
Race	☐ Yes ☒ No	
Religion and belief	☐ Yes ☒ No	
Sexual orientation	☐ Yes ☒ No	
Marriage and civil partnership	☐ Yes ☒ No	
Groups at risk of stigma or social exclusion such as offenders or homeless people	☐ Yes ☒ No	
Human rights	☐ Yes ☐ No	

Are there any associated objectives of the document? If yes, what existing evidence (either presumed or otherwise) do you have for this?

No

Signature of person completing the equality impact assessment:

Name: Sharon Benton, Renal Clinical Nurse Specialist

Date: 20 July 2023