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Document Title:

**Hydroxycarbamide (Hydroxyurea) for
Haematological Conditions – Shared Care Guideline**

Version Number:
4

Status:
Ratified

Scope:

UHMB Haematology team and prescribers in primary care

Classification:
Departmental

Author / Title:

Andrea Scott, Medicines Management Pharmacist

Responsibility:
Pharmacy

Replaces:

Version 3.1, Hydroxycarbamide (Hydroxyurea) for Haematological Conditions – Shared Care Guideline, SCG/011

Head of Department:
Kam Mom, Trust Chief Pharmacist, CDAO

Does this document refer to and account for the prescribing, supply, storage or administration of medication (especially via electronic media)? **Yes**

If yes, Pharmacy Dept. must be consulted and provide approval date below.

Pharmacy Department approval code: CE11062024B

To be completed by Pharmacy Department staff

Date: 11/06/2024

Validated By:

Pharmacy Senior Management Team
Medicines Management, Drug & Therapeutics Group

Date:

13/02/2024
10/06/2024

Ratified By:

Core Clinical Services Quality and Governance Group

Date:

13/06/2024

Review dates may alter if any significant changes are made

Review Date:
01/06/2027

- Does this document meet the requirements under the Equality Act 2010 in relation to age, disability, gender reassignment, marriage and civil partnership, pregnancy and maternity, race, religion or belief, sex, and sexual orientation? **Yes**
- Does this document meet our additional commitment as a Trust to extend our public sector duty to carers, veterans, people from a low socioeconomic background, and people with diverse gender identities? **Yes**

Document for Public Display: No

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1. SUMMARY

Hydroxycarbamide (previously known as hydroxyurea) is used in the management of various haematological myeloproliferative disorders, under the management of the specialist Haematology team. Once the patient and dose have been stabilised, day-to-day prescribing and monitoring can be managed by the patient's GP and the primary care team.

2. PURPOSE

- To define the conditions which are suitable for shared care between the haematologist and primary care clinician
- Set out the responsibilities of the secondary care team and the primary care team regarding prescribing and monitoring for the patient.
- Outline the required monitoring and provide guidance on what to do if results fall outside the defined parameters.

3. SCOPE

Applies to Haematology team and prescribers in primary care

3.1 Roles and Responsibilities

Role	Responsibilities
Haematologist	Diagnose and stabilise patient and dose of hydroxycarbamide. Perform baseline monitoring
Primary Care Prescriber	Prescribe hydroxycarbamide as recommended by specialist. Provide ongoing monitoring

4. GUIDELINE

4.1 Introduction

Hydroxycarbamide is an oral cytoreductive agent used in the management of myeloproliferative neoplasms to control the blood count and reduce the incidence of vascular complications. Hydroxycarbamide is not licensed for all the conditions it is used to treat. However, its use for the indications below is established and supported by various sources and bodies including the British National Formulary (BNF) and the British Society for Haematology (BSH).

Indication: Used for the management of haematological myeloproliferative disorders including:

- Essential thrombocythaemia
- Chronic myeloid leukaemia
- Primary proliferative polycythaemia (polycythaemia vera)

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- Myelofibrosis*
- Unclassified myeloproliferative disorders*

* Off-label indications. The specialist must specify the indication for each patient when initiating shared care and clearly state when use is off-label.

4.2 Dosage & Administration

Hydroxycarbamide is available as 0.5g capsules.

Starting doses are typically 0.5g or 1.0g daily and subsequent dosing is determined by the full blood count (FBC), typically ranging from 0.5g – 2.0g daily. It is common for the dose to vary according to the day of the week.

Most patients require several dose adjustments in the first months of treatment and then fewer adjustments subsequently. The hospital will initiate treatment and will provide at least 6 weeks' supply, or longer if necessary to confirm that the medication is effective, tolerated, and likely to be continued. The hospital team will inform the GP (General Practitioner) when they wish them to take over prescribing.

4.3 Secondary Care Responsibilities

- Assess the patient and provide diagnosis; ensure that this diagnosis is within the scope of this shared care guideline and communicated to primary care.
- Conduct required baseline investigations and initial monitoring (see later).
- Initiate treatment and prescribe until dose is stable.
- Provide patient/carer with relevant written information on use, side effects, and the need for regular monitoring of medication.
- Ensure that all patients, male and female, are advised on the need to use contraception and that this is reinforced at each review visit
- Once treatment is optimised, complete the shared care documentation, and send it to the patient's GP practice detailing the diagnosis, current and ongoing dose, any relevant test results and when the next monitoring is required. Include contact information.
- Prescribe sufficient medication to enable transfer to primary care.
- Conduct the required monitoring/patient reviews at specified intervals and communicate the results to primary care. After each review, advise primary care whether treatment should be continued, confirm the ongoing dose, and whether the ongoing monitoring remains appropriate.
- Provide advice to primary care on the management of adverse effects if required

4.4 Primary Care Responsibilities

- Prescribe hydroxycarbamide as per the written dosage supplied by the hospital specialist.

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- Arrange and record ongoing monitoring as agreed with specialist (some specialists may choose to arrange their own monitoring instead).
- Identify and report adverse events to the specialist and the MHRA (Medicines and Healthcare products Regulatory Agency).
- Ensure no drug interactions with other medicines.
- Reinforce the advice to all patients regarding the need for contraception.
- Stop hydroxycarbamide and make an urgent referral to the specialist if bone marrow suppression is suspected.
- Refer management of the patient back to the specialist if the patient becomes or plans to become pregnant.
- Administer influenza vaccine annually and COVID-19 vaccination as recommended.
- Check the patient has had one dose of pneumococcal vaccine (re-vaccination is not recommended) – see BNF.
- Passive immunization using Varicella-Zoster immunoglobulin (VZIG) should be considered in non-immune patients if exposed to chickenpox or shingles. Contact virology for advice if exposure is suspected.
- Ask about oral ulceration/sore throats or unusual bruising at every consultation. If present, arrange urgent FBC.
- Stop treatment as advised by the specialist.

4.5 Monitoring

4.5.1 Baseline investigations

- Full blood count (FBC)
- Urea and electrolytes (U&Es)
- Liver function tests (LFTs)
- Serum ferritin

4.5.2 Initial monitoring

To be repeated every 2 weeks in secondary care until the dose has been optimised and all test results are stable (minimum of 8 weeks):

- FBC
- U&Es
- LFTs

4.5.3 Ongoing monitoring requirements to be undertaken by primary care

Blood count monitoring is usually performed on an 8-12 weekly basis for stable patients. However, the exact monitoring plan will be agreed and communicated individually between the Hospital Specialist and the GP.

Renal function tests and liver function tests should be monitored every 3-4 months as advised.

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If monitoring results are forwarded to the specialist team, please include clear clinical information on the reason for sending, to inform action to be taken by secondary care.

4.6 Adverse Effects

Adverse effect	Action for Primary Care
White cell count less than $4 \times 10^9/L$	Consider withholding and discuss urgently with specialist team
Neutrophil count less than $1.5 \times 10^9/L$	
Platelet count less than $100 \times 10^9/L$	
Haemoglobin level dropped by over 30g/L	
Signs or symptoms of bone marrow suppression, e.g., unexplained bleeding or bruising with or without sore throat or mouth ulcers.	Consider withholding. Check FBC immediately and discuss with the specialist team. See haematological monitoring above
Serum creatinine greater than 2x upper limit of normal or serial rise over 3 visits	Consider withholding and discuss urgently with specialist team
ALT or AST greater than 3x upper limit of normal or serial rise over 3 visits	Consider withholding and discuss urgently with specialist team
Leg ulcers or cutaneous vasculitic ulcerations	Consider withholding and discuss urgently with specialist team
GI disturbances including nausea, vomiting or diarrhoea	Review for reversible causes. Discuss with specialist team if persistent or severe

- **Macrocytosis** occurs in almost all patients and may persist for up to one year after stopping therapy. It is advised that vitamin B12 and folate levels should be checked.
- **Rarely:** anorexia, nausea, vomiting, diarrhoea, stomatitis, headache, drowsiness, dizziness, cutaneous hyperpigmentation, skin ulcers. If severe or persistent, refer to hospital.
- **Renal dysfunction:** hydroxycarbamide should be used with caution in patients with marked renal dysfunction.
- **Development of gout symptoms:** monitor uric acid levels regularly but be aware that hydroxycarbamide may affect results. Advise patient to maintain a high fluid intake during treatment. Treat symptoms appropriately. Discuss with specialist for advice if required.

4.7 Common Drug Interactions

The following list is not exhaustive. Please see BNF or SPC for comprehensive information and recommended management.

- **Myelosuppressive agents or radiation therapy:** previous or concurrent use with hydroxycarbamide may increase the risk of bone marrow depression.
- **Antiretrovirals (such as didanosine and/or stavudine):** hydroxycarbamide may potentiate side effects of nucleoside reverse transcriptase inhibitors such as

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hepatotoxicity, pancreatitis, and peripheral neuropathy. Concomitant use should be avoided.

- **Live vaccines:** there is an increased risk of severe or fatal infections with the concomitant use of live vaccines. Live vaccines are not recommended in immunosuppressed patients and should be avoided for at least 6 months after treatment with hydroxycarbamide has finished.

4.8 Cautions & Contra-indications

4.8.1 Pregnancy/contraception

Hydroxycarbamide is contraindicated in pregnancy. It is recommended that patients of childbearing potential use effective contraception before starting and during treatment with hydroxycarbamide and for 6 months after treatment has stopped.

4.8.2 Breastfeeding

Hydroxycarbamide is excreted in human milk. Owing to the potential for serious adverse effects in infants, breastfeeding should be discontinued during hydroxycarbamide treatment.

4.8.3 Paternal exposure

Men are advised to use effective contraception during and for at least 3 months after therapy. Fertility in males might be affected by treatment. Reversible oligo- and azoospermia are very commonly observed.

4.8.4 Live vaccines

Should be avoided by patients receiving hydroxycarbamide.

Hydroxycarbamide should be used with caution in patients with:

- Myelosuppression (reduced dose may be required)
- Renal impairment (reduced dose may be required)
- Hepatic impairment
- Skin ulceration

Skin cancer has been reported in patients receiving long-term hydroxycarbamide. Patients should be advised to protect their skin from sun exposure. In addition, patients should conduct self-inspection of the skin during treatment and after discontinuation of hydroxycarbamide and be screened for secondary malignancies during routine follow-up visits.

4.9 References

This guidance does not replace the SPCs, which should be read in conjunction with this guidance.

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References:

British National Formulary (BNF) '[Hydroxycarbamide \(Hydroxyurea\)](#)' (accessed 18.06.24)
Electronic Medicines Compendium (emc) (2023) '[Hydroxycarbamide medac 500 mg capsule, hard](#)' (accessed 18.06.24)

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5. ATTACHMENTS		
Number	Title	Separate attachment
1	Monitoring	N
2	Values and Behaviours Framework	N
3	Equality & Diversity Impact Assessment Tool	N

6. OTHER RELEVANT / ASSOCIATED DOCUMENTS	
The latest version of the documents listed below can all be found via the Trust Procedural Document Library intranet homepage.	
Unique Identifier	Title and web links from the document library

7. SUPPORTING REFERENCES / EVIDENCE BASED DOCUMENTS	
Every effort been made to review/consider the latest evidence to support this document?	Yes
If 'Yes', full references are shown below:	
Number	References
1	Medicines Complete BNF > Drug: Hydroxycarbamide (accessed 25/07/2024)
2	Electronic Medicines Compendium (emc) Hydroxycarbamide medac 500 mg capsule, hard - Summary of Product Characteristics (SmPC) (accessed 25/07/2024)

8. DEFINITIONS / GLOSSARY OF TERMS	
Abbreviation or Term	Definition
SMT	Senior Management team

9. CONSULTATION WITH STAFF AND PATIENTS		
Enter the names and job titles of staff and stakeholders that have contributed to the document		
Name/Meeting	Job Title	Date Consulted
David Howarth	Clinical Lead for Haematology	06/09/2023
Pharmacy SMT	Vickie Rose, Kam Mom, Jenny Bowler, Carrie Eddy	11/06/2024

10. DISTRIBUTION & COMMUNICATION PLAN	
Dissemination lead:	Andrea Scott
Previous document already being used?	Yes
If yes, in what format and where?	Trust Procedural Document Library
Proposed action to retrieve out-of-date copies of the document:	Archive previous document and replace in library

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To be disseminated to:	
Document Library	
Proposed actions to communicate the document contents to staff:	Include in the UHMB Weekly News. New documents uploaded to the Document Library.

11. TRAINING

Is training required to be given due to the introduction of this procedural document? **No**

If 'Yes', training is shown below:

Action by	Action required	To be completed (date)

12. AMENDMENT HISTORY

Version No.	Date of Issue	Section/Page Changed	Description of Change	Review Date
4	13/06/2024	Throughout	New format	01/06/2027

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Appendix 1: Monitoring

Section to be monitored	Methodology (incl. data source)	Frequency	Reviewed by	Group / Committee to be escalated to (if applicable)
Compliance with defined responsibilities in secondary care	Feedback from primary care	Quarterly	Andrea Scott	Medicines Management, Drug & Therapeutics Group

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Appendix 2: Values and Behaviours Framework

To help create a great place to work and a great place to be cared for, it is essential that our Trust policies, procedures and processes support our values and behaviours. This document, when used effectively, can help promote a positive workplace culture. By following our own policies and with our **ambitious** drive we can cultivate an **open, honest and transparent culture** that is truly **respectful and inclusive** and where we are **compassionate** towards each other.

<p>We are... Compassionate</p>  <p>We will:</p> <ul style="list-style-type: none"> • Be kind and caring to each other; our patients and families and our partners • Consider the feelings of others • Work together to deliver safe care and a safe working environment • Be proud of the role we do and how this contributes to patient care <p>www.uhmb.nhs.uk</p>	<p>We are... Respectful and inclusive</p>  <p>We will:</p> <ul style="list-style-type: none"> • Show respect to and for everyone • Act professionally at all times • Communicate effectively – listen to others and seek clarity when needed • Value each other and the contribution of everyone 	<p>We are... Ambitious</p>  <p>We will:</p> <ul style="list-style-type: none"> • Go beyond traditional boundaries; being positively receptive to change and improvement • Work with colleagues and system partners to improve services for our patients, families and carers • Support each other to listen, learn and develop • Collaborate with and empower each other 	<p>We are... Open, honest and transparent</p>  <p>We will:</p> <ul style="list-style-type: none"> • Seek out feedback and act on it • Take personal responsibility and accountability for our own actions • Not be afraid to be challenged • Ensure consistency and fairness in our approach <p>@UHMBT  </p>
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Appendix 3: Equality & Diversity Impact Assessment Tool



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Equality Impact Assessment Form

Department/Function	Pharmacy	
Lead Assessor	Andrea Scott	
What is being assessed?	Hydroxycarbamide Shared Care Guideline	
Date of assessment	05/06/2024	
What groups have you consulted with? Include details of involvement in the Equality Impact Assessment process.	Patient Experience and Involvement Group?	NO
	Staff Side Colleague?	NO
	Service Users?	NO
	Staff Inclusion Network(s)?	NO
	Personal Fair Diverse Champions?	NO
	Other (including external organisations):	

1) What is the impact on the following equality groups?

	Positive:	Negative:	Neutral:
	<ul style="list-style-type: none"> ➢ Advance Equality of opportunity ➢ Foster good relations between different groups ➢ Address explicit needs of Equality target groups 	<ul style="list-style-type: none"> ➢ Unlawful discrimination / harassment / victimisation ➢ Failure to address explicit needs of Equality target groups 	<ul style="list-style-type: none"> ➢ It is quite acceptable for the assessment to come out as Neutral Impact. ➢ Be sure you can justify this decision with clear reasons and evidence if you are challenged
Equality Groups	Impact (Positive / Negative / Neutral)	Comments	
Race (All ethnic groups)	Neutral	<ul style="list-style-type: none"> ➢ Provide brief description of the positive / negative impact identified benefits to the equality group. ➢ Is any impact identified intended or legal? 	
Disability (Including physical and mental impairments)	Neutral		
Sex	Neutral		
Gender reassignment	Neutral		
Religion or Belief	Neutral		
Sexual orientation	Neutral		
Age	Neutral		
Marriage and Civil Partnership	Neutral		
Pregnancy and maternity	Neutral	Not suitable for use during pregnancy	
Other (e.g. carers, veterans, people from a low	Neutral		

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socioeconomic background, people with diverse gender identities, human rights)		
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2) In what ways does any impact identified contribute to or hinder promoting equality and diversity across the organisation?	No effect
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3) If your assessment identifies a negative impact on Equality Groups you must develop an action plan to avoid discrimination and ensure opportunities for promoting equality diversity and inclusion are maximised.
➤ This should include where it has been identified that further work will be undertaken to further explore the impact on equality groups
➤ This should be reviewed annually.

Action Plan Summary		
Action	Lead	Timescale

This form will be automatically submitted for review once approved/noted by Trust Procedural Document Group. For all other assessments, please return an electronic copy to EIA.forms@mbht.nhs.uk once completed.

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