City and Hackney Integrated Care Partnership, North East London Clinical Commissioning Group
Homerton University Hospital NHS Foundation Trust

SHARED CARE GUIDELINE

Hydroxycarbamide
Sickle cell disorders and myeloproliferative disorders

DOCUMENT TO BE SCANNED INTO ELECTRONIC RECORDS AND FILED IN NOTES

INTRODUCTION – Indication and Licensing

Hydroxycarbamide has a number of licensed indications. This guideline includes treatment for the following:

Sickle cell anaemia - Hydroxycarbamide is given primarily to reduce the incidence of painful episodes by either increasing the Haemoglobin F% or by alterations in RBC hydration. It may also:

- Increase the haemoglobin concentration
- Prevent or possibly reverse chronic organ damage
- Reduce the incidence of the acute chest syndrome
- Decrease the need for blood transfusion
- Reduce mortality (40% decrease over 6-8 years follow up)

Myeloproliferative disorders – e.g. Primary Proliferative Polycythaemia (PRV), Essential Thrombocythaemia and Chronic Myeloid Leukaemia (CML).

PATIENT PATHWAY

Patients on hydroxycarbamide require regular monitoring and access to medicines this is easier for the patients if an established pathway exist between primary and secondary care. This will improve patient experience and outcomes.

Clinical Speciality / Indication	**Prescribing Initiated by**	**Prescribing Continued by**	**Monitored by** ***(detail when suitable for transfer to occur IF APPROPRIATE)***	**Duration of treatment**
Sickle cell disorders	Haematology Consultant/Lead Nurse	Lead Nurse/ GP when patient established on stable dose	Lead Nurse/GP	indefinitely
Myeloproliferative disorders	Haematology Consultant	Haematology/ GP when patient established on stable dose	Haematology/GP	Lifelong or until intolerant or progression of condition

A review of the outcome of treatment will be made at all hospital outpatient appointments. At these appointments adherence and response to therapy will be determined whether treatment will stop or continue.

For patients out of area this may differ and some GPs may prefer to monitor and in some cases perform their own phlebotomy. However, this must be agreed with the relevant teams and any concerns discussed immediately. The patient must attend follow up at the hospital at least every 6 months.

Hydroxycarbamide
Sickle Cell Disorders & Myeloproliferative Disorders

ORAL DOSE AND ADMINISTRATION

Sickle cell disorders – initially 15mg/kg daily, increased in steps of 5mg/kg daily, dose to be increased every 8 weeks according to response; maximum 35mg/kg per day.

Myeloproliferative disorders

Polycythaemia vera - Initially 15–20 mg/kg daily, adjusted according to response. Usual dose 500–1000 mg daily.

Essential thrombocythaemia - Initially 15 mg/kg daily, adjusted according to response.

Hydroxycarbamide is available as 500mg capsules, it is also available in liquid form but this is usually reserved for paediatric patients due to the volume of suspension required to be consumed.

If the patient prefers, or is unable to swallow capsules, the contents of the capsules may be emptied into a glass of water and taken immediately. The contents of capsules should not be inhaled or allowed to come into contact with the skin or mucous membranes. Spillages must be wiped immediately.

CAUTIONS

- Patients who have had radiotherapy or chemotherapy, or are currently taking any other **medicines for cancer treatment**, especially interferon therapy.
- Haematological impairment.
- Renal or hepatic impairment.
- In general patients should try to avoid 'live' vaccines during treatment and at least 6 months after treatment. *Examples of live vaccines include:* oral polio, MMR, BCG and yellow fever [passive immunization should be carried out using Varicella zoster immunoglobulin (VIZIG) in non-immune patients exposed to active chickenpox or shingles].
- Leg ulcers (review treatment if cutaneous vasculitic ulcerations develop)
- Protect the skin from the sun and regularly inspect the skin during treatment (skin cancer reported in patients receiving long-term hydroxycarbamide).
- Hydroxycarbamide contains lactose so lactose intolerant patients may suffer side effects.
- Patients on hydroxycarbamide should be offered the annual flu vaccine and the pneumoccocal vaccine every 5 years. **This will be lifelong for sickle cell patients.**

CONTRAINDICATIONS

- Avoid if planning to become pregnant or are breastfeeding.
- Both male and female patients are advised to use safe contraceptive measures before and during treatment with hydroxycarbamide and **at least 3 months** after discontinuation.
- If a woman is pregnant, planning to be or breastfeeding they should not handle the capsules.
- Blood dyscrasias [marked leucopenia (WBC $<2.5x10^9$/L), thrombocytopenia (platelets $< 100x10^9$/L), severe anaemia)
- Rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucosegalactose malabsorption.
- Previous hypersensitivity to hydroxycarbamide.

INTERACTIONS

- Previous or concomitant radiotherapy, cytotoxic therapy or other drugs that can cause myelosuppression – potentiation of myelosuppression.
- Antiretroviral agents
- If patient is HIV positive to contact Specialist team for HIV
- Studies have shown that there is an analytical interference of hydroxycarbamide with the enzymes (urease, uricase, and lactic dehydrogenase) used in the determination of urea, uric acid and lactic acid, rendering falsely elevated results of these in patients treated with hydroxycarbamide.
- Live vaccines - Increased risk of severe or fatal infections with the concomitant use of live vaccines. Live vaccines are not recommended in immunosuppressed patients.
- Both men and women will be counselled about contraception and what to do if pregnancy occurs. The counselling should be documented in the patient notes.
- Women who are breastfeeding or pregnant are not suitable for treatment with hydroxycarbamide.

Please refer to the current British National Formulary and Summary of Product Characteristics for comprehensive information on cautions, contraindications, interactions and adverse effects.

MONITORING STANDARDS FOR MEDICATION AT THE ACUTE NHS TRUST

The following standards have been agreed for the monitoring of hydroxycarbamide.

Haematology (sickle cell disorders, myeloproliferative disorders)

Pre-treatment - then 3 monthly	
FBC, U&E, LFT, Haemoglobin F%, Haemoglobin S%, LDH	
Ongoing monitoring	
FBC, reticulocyte count and Haemoglobin F%, Haemoglobin S%	Every 2 weeks until a haematologically safe and stable dose is achieved then every month Extend duration to every 3 months when established on an effective dose with good adherence

KEY ADVERSE EFFECTS & ACTIONS

Laboratory Events	**Values**	**Action**
Serum creatinine	>150 micromol/L	**Stop** + seek advice.
Haemoglobin	< 45* g/dl (limit applicable to sickle cell anaemia patients only)	**Stop** + seek advice.
Neutrophils	<1.5 x10^9/L	**Stop** + seek advice.
Reticulocytes	< 80** x 10^9/L	**Stop** + seek advice.

Platelets	<80x10^9/L	**Stop** + seek advice.
Elevation in liver enzymes (AST, ALT, GGT)	Serial rise over 3 visits	**Stop** + seek advice.

***** Values between 45 and 53 g/dl are not considered toxic provided the reticulocyte count is > 320 x 10^9/L
****** Not considered toxic if the haemoglobin concentration is >90 g/dl

Symptoms	**Management**
Symptoms of anaemia, unexpected bruising or bleeding, fever, sore throat or other symptoms of infection	Should be seen urgently and an FBC checked. Discuss with specialist immediately.
Leg ulcer or severe mouth ulcers	GP to discuss with specialist within 72 hours
Skin changes	Stop and discuss with specialist.
Fever & Hepatitis	
Hyper pigmentation of skin and nails	This is common and is not an indication for stopping treatment.
Hair thinning	This is common and is not an indication for stopping treatment.
Development of gout or uric acid nephropathy (generally only seen in treatment of myeloproliferative disorders, especially when used with other cytotoxic agents. Less common in sickle cell disease.)	Advise patient to maintain a high fluid intake during treatment. If any episode of clinical gout occurs, treat with urate lowering therapy. Routine monitoring of urate levels not recommended.

REMEMBER if unsure at any point: Contact the various Specialists and or Specialist Nurse/Nurse Practitioner via the Homerton Hospital switchboard on 020 8510 5555.

Relevant contact details

Consultant or Registrar on-call *via* switchboard	020 8510 5555
Lead Nurse – Sickle Cell & Thalassaemia Services	0207 683 4570
Clinical Nurse Specialist- Sickle Cell & Thalassaemia	0207 683 4570 0208 510 5555 - Homerton bleep 362
Homerton University Hospital NHS Foundation Medicines Information	020 8510 7000
City and Hackney Medicines Management Team	0203 816 3224

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SHARED CARE

Shared care guideline*:* is a document which provides information allowing patients to be managed safely by primary care, secondary care and across the interface. It assumes a partnership and an agreement between a hospital specialist, GP and the patient and also sets out responsibilities for each party. The intention to shared care should be explained to the patient and accepted by them. Patients are under regular follow-up and this provides an opportunity to discuss drug therapy. Intrinsic in the shared care agreement is that the prescribing doctor should be appropriately supported by a system of communication and cooperation in the management of patients. The doctor who prescribes the medicine has the clinical responsibility for the drug and the consequence of its use**.**

Consultant

1. Ensure that the patient/carer is an informed recipient in therapy.
2. Ensure that the patient/carer understands their treatment regimen and any monitoring or follow up that is required (using advocacy if appropriate). Issue any local patient information leaflets where appropriate.
3. Ensure baseline investigations are suitable before commencing treatment.
4. Initiate treatment and prescribe until the patient is stabilised on their most effective dose.
5. Send a letter to the GP requesting shared care for this patient.
6. Clinical and laboratory supervision of the patient by blood monitoring (if applicable) and routine clinic follow-up on a regular basis.
7. Send a letter/results notification to the GP after each clinic attendance ensuring current dose, most recent blood results and frequency of monitoring are stated (unless otherwise available via ELPR or covered by letter e.g. from Clinical Nurse Specialist or Drug Monitoring Service).
8. Where the GP is out of area and is not performing the phlebotomy, the blood test form/EPR request MUST specify that blood results are also copied to the GP. Specialist team to check with pathology IT if unsure on how to do this.
9. Evaluation of any reported adverse effects by GP or patient.
10. Advise GP on review, duration or discontinuation of treatment where necessary. Where urgent action is required following tests the hospital team will telephone the patient and inform GP.
11. Inform GP of patients who do not attend clinic appointments.
12. Counsel the patient on contraception (if applicable) and what to do if pregnancy occurs. Document in the notes.
13. Ensure that backup advice is available at all times.
14. Advise that the patient receives appropriate vaccination in primary care either prior to commencing treatment and/or during a treatment that is likely to cause immunosuppression.

General Practitioner

1. Ensure that the patient understands the nature, effect and potential side effects of the drug before prescribing it as part of the shared care programme and contact the specialist for clarification where appropriate.
2. Monitor patient's overall health and well-being.
3. Report any adverse events to the consultant, where appropriate.
4. Report any adverse events to the MHRA / CHM, where appropriate.
5. Help in monitoring the progression of disease.
6. Prescribe the drug treatment as described.

7. Provide contraception advice and prescription as appropriate.
8. Provide appropriate vaccinations to patients receiving treatments likely to cause immunosuppression.

City and Hackney Medicines Management Team

1. To provide feedback to acute trusts via the Joint Prescribing Group.
2. To support GPs to make the decision whether or not to accept clinical responsibility for prescribing.
3. To support acute trusts in resolving issues that may arise as a result of shared care.

Patient/ Carer

1. Report any adverse effects to their GP and/or specialist
2. Ensure they have a clear understanding of their treatment.
3. Report any changes in disease symptoms to GP and/or specialist
4. Alert GP and/or specialist of any changes of circumstance which could affect management of disease e.g. plans for pregnancy.
5. Take/ administer the medication as prescribed.
6. Undertake any monitoring as requested by the GP and/or specialist.

Costs

Drug Product	Cost in primary care
Hydroxycarbamide 500mg Capsules	£12.14 (100 capsules) – Drug Tariff price
Hydroxycarbamide 100mg/ml Oral solution	£250.00 (150ml)

Please note that we do not prescribe SIKLOS.

Based on BNF edition 79 (30th March 2020)

RESOURCES AVAILABLE

www.bad.org.uk
https://www.sicklecellsociety.org/sicklecellstandards/
https://www.macmillan.org.uk/cancer-information-and-support/treatments-and-drugs/hydroxycarbamide

References

- SCG template adapted from NELMMN and Barts Health NHS Trust
- British National Formulary, available at https://bnf.nice.org.uk/ (accessed 20/04/2020)
- Summary of product characteristics - Hydroxycarbamide medac 500 mg capsule, hard. Available at www.medicines.org.uk (accessed 20/04/2020)

Date SCG approved by Joint Prescribing Group (JPG): 12/2020 **Review date:** 12/2022