Barking, Havering and Redbridge University Hospitals NHS Trust

# DRUG NAME: HYDROXYCARBAMIDE
## Indication/s: Myeloproliferative disorders and Sickle Cell Disease

***DOCUMENT TO BE SCANNED INTO ELECTRONIC RECORDS AS AND FILED IN NOTES***

**Patient Name :** **Date of Birth:** **NHS No:**

**Name of Referring Consultant:** **Contact number:**

## INTRODUCTION

Hydroxycarbamide has a number of licensed indications, not all of which are suitable for shared care. It is available as 500mg capsules. This guideline includes treatment for the following:

**1. Sickle cell anaemia**: Hydroxycarbamide is given primarily to reduce the incidence of painful episodes of sickle-cell crisis. It is usually commenced when patients have:

- 3 or more hospital admissions with painful crises within 1 year, or
- Frequent days of pain at home, leading to a lot of time off work, or
- Recurrent acute chest syndrome

It works by either increasing the Haemoglobin F% or by altering red blood cell hydration. It may also:

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

**2. Myeloproliferative disorders,** including: Primary Proliferative Polycythaemia (PRV), Essential Thrombocythaemia, Myelofibrosis, Chronic Myeloid Leukaemia (CML), Acute Myeloid Leukaemia, Chronic Eosinophilic Leukaemia, Hypereosinophilic Syndrome.

## PATIENT PATHWAY

| Indications | Prescribing Initiated by | Prescribing Continued by : | Monitored by : | Duration of treatment |
|---|---|---|---|---|
| Sickle cell anaemia; Myeloproliferative disorders (see above) | Haematology Consultant or Haematology Specialist Registrar | General Practitioner | Haematology Consultant or Specialist Registrar, Clinical Nurse Specialist and GP. | Dependent on diagnosis and risk factors |

## DOSE AND ADMINISTRATION

Sickle cell anaemia: The initial dose is 15mg/kg once a day (to the nearest 500mg). If there is no response or a poor response the dose is increased by increments of 5mg/kg/day every 4 to 6 weeks provided blood values are in the acceptable range until a haematologically safe stable dose is established. Usual dose is 15 to 30 mg/kg/day. Maximum dose should not exceed **35mg/kg/day**.

The aim is to reach the maximum tolerated dose (MTD), but if haematological and clinical responses are achieved at a lower dose, consider using this dose.

Myeloproliferative disorders: Doses in the order of 20 to 30mg/kg per day have been used (to the nearest 500mg). The initial dose is dependent on the disease, the level of abnormality (platelet count/haemoglobin level/haematocrit/white cell count) and patient age.

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This will be decided by the Haematology Consultant or Haematology Specialist Registrar initiating the drug. Only when the patient is on a stable dose will the GP be requested to continue the prescription. Usually a higher dose is given initially and then this dose is reduced to maintain a target count.

If the patient prefers, or is unable to swallow the 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

- Should be administered with caution to patients who receive concomitant or have received previous therapy with other antineoplastic drugs or irradiation
- Haematological impairment [see table below]
- Renal or hepatic impairment

## CONTRA-INDICATIONS

- Blood dyscrasias; [marked leucopaenia (Neutrophils <1.5 $x10^9$/L), thrombocytopaenia (< $100x10^9$/L), severe anaemia].
- Previous hypersensitivity to hydroxycarbamide
- Pregnancy and lactation
- Genotoxic – therefore men and women undergoing therapy are advised to use safe contraceptive measures during and for at least **3 months** after therapy
- Rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption.

## KEY ADVERSE EFFECTS AND ACTIONS

- There is no evidence that hydroxycarbamide is leukaemogenic despite earlier reports of an association.
- The possibility of an increase in serum uric acid, resulting in the development of gout or at worst, uric acid nephropathy, should be borne in mind in patients with myeloproliferative neoplasms treated with hydroxycarbamide, especially when used with other cytotoxic agents.

| **Adverse effect** | **Management** |
|---|---|
| Skin changes | **Stop** and discuss with specialist |
| Fever and hepatitis | |
| Hyper-pigmentation of skin and nails | This is common and is not an indication for stopping treatment |
| Development of gout or uric acid nephropathy (especially when used with other cytoxic agents). | Monitor uric acid levels regularly (at least every 3 months) and advise patient to maintain a high fluid intake during treatment. |

**This only lists the key important ADRs - For comprehensive information on cautions, contra-indications and interactions, please refer to the <u>current</u> British National Formulary (BNF) and Summary of Product Characteristics (SPC).**

## GENERAL MONITORING (applicable when prescribing for either indication)

The following standards have been agreed for the monitoring of hydroxycarbamide. This drug has haematological, renal and hepatic toxicity which will be monitored in secondary care.

<u>Pre-treatment:</u>
U&E's, LFT's, Hb concentration + reticulocyte count, Haemoglobin S%, Haemoglobin F%, neutrophil count and platelet count.

<u>During treatment</u>:
FBC and reticulocytes, U&E's, LFT's and Haemoglobin F% until a haematologically safe and stable dose is achieved.

| **EVENTS AND ACTION TABLE** | | |
|---|---|---|
| **Laboratory parameter** | **Values** | **Action** |
| Serum creatinine | >150 micromol/L | **Stop** + seek advice from Consultant Haematologist |
| Haemoglobin | < 4.5 g/dl (limit applicable to sickle cell anaemia patients only)* | |
| | Hb drops by more than 20% from baseline or > 2g/dl | |
| Neutrophils | < 1.5 $x10^9$/L | |
| Reticulocytes | < 80 x $10^9$/L* | |
| Platelets | < 80 x $10^9$/L | |
| Elevation in liver enzymes | Serial rise over 3 visits | |

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* These limits apply for sickle cell anaemia patients only: Hb values between 4.5 and 5.3 g/dl are acceptable provided the reticulocyte count in >320 x$10^9$/L; Reticulocytes < 80 x $10^9$/L acceptable if the Hb concentration is > 9.0 g/dl

This frequency of monitoring can be gradually increased up to 3 to 4 monthly blood counts when the patient has been established on a stable and safe dose.

If treatment is interrupted:
Check FBC weekly and consider restarting after the counts recover at a lower dose than the patient was on at the time of toxicity.

## DURATION OF THERAPY

Sickle cell anaemia patients who achieve a good response to hydroxycarbamide are likely to remain on it long term.

Myeloproliferative patients should remain on hydroxycarbamide as long as the desired haematological and clinical responses are met; otherwise alternative treatment options may be considered.

## 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 patients understand 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 investigation requirements are met before commencing treatment.
4. Initiate treatment and prescribe until the GP formally agrees to share care (as a minimum, supply the first month of treatment or until patient is stabilised).
5. Send a letter to the GP requesting shared care for this patient.
6. Clinical and laboratory supervision of the patient by blood monitoring 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 covered by letter e.g. from Haematology Clinical Nurse Specialist). All dose adjustments will be made either by a Haematology Consultant or Haematology Specialist Registrar.
8. Monitor for side effects and evaluate any adverse effects reported by GP or patient.
9. 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.
10. Inform GP of patients who do not attend clinic appointments.
11. Counsel the patient on contraception and what to do if pregnancy occurs. Document in the notes.
12. Ensure that backup advice is available at all times.
13. Ensure, where timing is appropriate, that the patient has received a flu vaccine prior to commencing treatment that is likely to cause immunosuppression. Document this in the patient notes and inform the GP it has been given

**General Practitioner**

1. Reinforce the patient's understanding of 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 CSM, where appropriate.
5. Help in monitoring the progression of disease
6. Prescribe the drug treatment as described.

**PCT**

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

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**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. Attend clinic appointments

**Costs**

| Drug Product | Cost in primary care |
|---|---|
| Hydroxycarbamide capsules 500mg | |

Based on BNF edition 64

*Give the cost of a 1 month course of treatment for each drug listed*

***RESOURCES AVAILABLE***

| **Barking, Havering & Redbridge University Hospitals Trust** | |
|---|---|
| Consultant via switchboard:<br>Dr Khalid Saja, Consultant Haematologist<br><br>Dr Claire Hemmaway, Consultant Haematologist<br><br>Registrar on-call during working hours | Telephone Queens Hospital switchboard:<br>01708 435000 and request by name.<br><br><br><br>DECT 6837 via switchboard |
| Clinical Nurse Specialist: | DECT 6328 or 6228 via switchboard |
| NHS ONEL Prescribing Team | To confirm new number |

**References:**

1. Shared Care Guidelines for Hydroxycarbamide - Homerton University Hospital; NHS City and Hackney
2. Hydroxycarbamide Summary of Product Characteristics (SPC).

**Refer to the NHS ONEL website to obtain the latest version of this guideline**

**This guideline is version 1**

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