Hydroxycarbamide

Shared Care Guideline.

Specialist details	Patient identifier
Name: _____	
Location: _____	
Tel: _____	**Date:** _____

Introduction

This shared care guideline refers to the use of hydroxycarbamide in the treatment of dermatological and haematological amber list indications only.

Licensed indications include: myeloproliferative disorders: essential thrombocythaemia and polycythaemia vera where there is high risk of thrombo-embolic complications, sickle cell disease.

Unlicensed indications include: myelofibrosis, psoriasis, bullous pemphigoid.

Adult dosage and administration

Dermatology:
The usual adult dose is 500mg to 2g either daily, taken orally as a single dose, or divided into two doses (morning and evening).

Haematology:
Myeloproliferative disorders: dose is based on the patient's actual or ideal body weight, whichever is the less. Starting dose 15 - 20mg/kg/day. This should be adjusted according to response.
The usual adult dose in Haematology patients is 500mg to 2g daily. Occasionally over the course of each week there is variance in the daily dose, eg. 1.5g Monday / Wednesday / Friday, 1g Tuesday / Thursday / Saturday and Sunday or 500mg daily on five days only of the week. The treatment is taken orally either as a single dose, or divided into two doses (morning and evening).
Sickle cell disease: initially 15mg/kg daily, increased by steps of 2.5-5mg/kg daily, dose to be increased every 12 weeks according to response; usual dose 15-30mg/kg daily; maximum 35mg/kg per day.

Available as: hydroxycarbamide 500mg capsules and 100mg and 1000mg tablets. Hydroxycarbamide 100mg/ml oral solution (Xromi®) – for patients who are unable to swallow capsules only.
If the liquid formulation is used, provide training on safe handling, storage, spillage and waste disposal (provide a cytotoxic spill kit and cytotoxic sharps box if necessary).

Hospital specialist responsibilities

- Assess if the patient is suitable for treatment with hydroxycarbamide.
- Agree shared care with the patient's GP.
- Varicella Zoster immune status: if non-immune, consider immunisation prior to starting treatment.
- Advise GP on dose of hydroxycarbamide to be prescribed.
- Provide patient/carer with relevant (preferably written) information on use, side-effects and need for monitoring of medication.
- Undertake Baseline tests as indicated in monitoring table.
- Review results of safety monitoring and request additional tests as required.
- Monitor disease response to treatment and need to continue therapy.
- Continue to review the patient at agreed specified intervals, sending a written summary to the GP whenever the patient is reviewed.
- Provide any other advice or information for the GP if required.

Monitoring table		Hospital specialist	GP		Hospital specialist
Test	**Indication**	Pre-treatment baseline	During treatment		At review
			First 6 weeks	Thereafter	
FBC (including DWCC) LFTs U&Es, eGFR Uric Acid (Haematology only)	Baseline assessment, dose adjustment disease activity scoring	✓	Every week	Every 3 months	As part of review or as clinically indicated
Ask about oral ulceration, sore throat, unexplained rash or unusual bruising/bleeding		✓	At every consultation		✓
There may be clinical circumstances where the frequency of monitoring may vary and this should be specified by the initiating specialist.					

GP responsibilities

- Prescribe hydroxycarbamide.
- Arrange and record ongoing monitoring as agreed with specialist. For haematology patients, ongoing monitoring and frequency of monitoring will be confirmed by initiating consultant, otherwise see monitoring table above.
- Ensure practice systems are in place to recall patients for monitoring blood tests.
- Follow-up any non-compliance with the monitoring schedule. The risks of cessation of therapy versus risks of toxicity should be considered. Contact the specialist if treatment is stopped or further advice required.
- Report any adverse drug reactions to the initiating specialist and the usual bodies (eg. MHRA/CHM).
- Ensure no drug interactions with other medicines.
- Administer **inactivated** influenza vaccine annually unless otherwise advised by the initiating specialist.
- Check patient has had ONE DOSE of pneumococcal vaccine (revaccination is not recommended except every five years in patients whose antibody levels are likely to have declined more rapidly eg. asplenia), see BNF or Green Book.
- Provide COVID 19 and **inactivated** shingles (Shingrix®) vaccination as appropriate as per local arrangements and Green Book
- Post exposure prophylaxis (antivirals or VZIG if antivirals are contraindicated) should be considered in non-immune at risk patients if exposed to chickenpox or shingles. Contact the consultant virologists, Regional Virus Laboratory, Royal Group of Hospitals on 07889 086 946 for advice if exposure is suspected. For other queries eg. those concerning exposure, infection or any recommendations relating to healthy susceptible household contacts, consult the Green Book and/or take additional advice from Regional Virus Laboratory, Royal Group of Hospitals
- Ask about oral ulceration, sore throat, skin ulceration or unusual bruising/bleeding at every consultation.

Withhold hydroxycarbamide and contact specialist if:

- Hb decrease by 30g/L or more
- WCC < 3.5 x 10^9/L
- Neutrophils < 1 x 10^9/L
- Platelets < 100 x 10^9/L
- If renal impairment develops (not always appropriate to stop but may need dose adjustment)
- Unexplained oral ulceration / sore throat / skin ulceration
- Unexplained bruising / unexplained rash.

Normal reference range may vary slightly between labs.
Please note an unusual fall or rise or a consistent downward or upward trend in any value should prompt review of the patient and extra vigilance. Some patients may have abnormal baseline values, specialist will advise.

Adverse effects, precautions and contraindications

Leucopenia, anaemia, and thrombocytopenia. GPs should be alert to any unexplained bruising, bleeding or signs of infection.
Cutaneous vasculitis including vasculitic ulcerations may occur when treating myeloproliferative disorders.
Macrocytosis occurs in almost all patients and may persist for up to one year after stopping therapy.
Common: diarrhoea, constipation.
Rarely: anorexia, nausea, vomiting, headache, drowsiness, dizziness, cutaneous hyperpigmentation. If severe or persistent, refer to the specialist. Interstitial lung disease including pulmonary fibrosis, lung infiltration, pneumonitis, and alveolitis/allergic alveolitis have been reported in patients treated for myeloproliferative neoplasm and may be associated with fatal outcome. Patient developing pyrexia, cough, dyspnoea or other respiratory symptoms should be closely monitored, investigated and treated. Prompt discontinuation of hydroxycarbamide and treatment with corticosteroids appears to be associated with resolution of the pulmonary events.
Renal dysfunction. Hydroxycarbamide should be used with caution in patients with marked renal dysfunction.
Pregnancy / Contraception. Patients discovered or planning to become pregnant should be referred to the initiating specialist at the earliest opportunity. Female patients must be advised not to conceive whilst receiving hydroxycarbamide. A reliable form of contraception should be used by men and women whilst on hydroxycarbamide. Men should be advised to continue contraception for 3 months following discontinuation of treatment.
Breastfeeding. Patients should not breastfeed whilst receiving hydroxycarbamide.
Cancer risk. Patients receiving hydroxycarbamide are at increased risk of lymphomas and malignancies of the skin; avoiding excessive exposure to the sun and use of high factor sunscreens are advised. Adherence to population screening programmes is particularly important in this population.
Live vaccines. Consult the Green Book and take additional advice from initiating specialist if required.

Common drug interactions

Toxicity may be potentiated by previous / concomitant radiotherapy or cytotoxic therapy.
Clozapine: increased risk of agranulocytosis - avoid concomitant use.
Didanosine and stavudine: increased risk of toxicity - avoid concomitant use.

Communication

For any queries relating to this patient's treatment with hydroxycarbamide, please contact the specialist named at the top of this document.

This information is not inclusive of all prescribing information and potential adverse effects.
Please refer to full prescribing data in the SPC at www.medicines.org.uk or the BNF

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