Specialised Medicines Service Guideline ~ Hydroxycarbamide in the treatment of essential thrombocythaemia, primary proliferative polycythaemia (polycythaemia vera), myelofibrosis and unclassified myeloproliferative disorders

This guideline highlights significant prescribing issues. Not all prescribing information and potential adverse effects are listed. Please refer to SPC/data sheet for full prescribing data.

Specialist: Please complete letter at the end of this document and send together with the guideline to the GP.

GP: Please indicate whether you wish to share patient's care by completing letter at the end of this document and return to specialist.

GPs are invited to participate. If a GP is not confident to undertake these roles, then they are under no obligation to do so. In such an event, the total clinical responsibility for the patient for the diagnosed condition remains with the specialist.

The doctor who prescribes the medication has the clinical and legal responsibility for the drug and the consequences of its use.

Introduction and aims of treatment

This guideline refers to the use of hydroxycarbamide 500mg capsules for the treatment of myeloproliferative disorders. The use of hydroxycarbamide for other indications is out of the scope of this guideline.

The licensed indications of the different brands of currently available hydroxycarbamide 500mg capsules differ, but include essential thrombocythemia or polycythemia vera with a high risk for thromboembolic complications. Treatment of other myeloproliferative disorders is unlicensed.

The precise mechanism of action of hydroxycarbamide is unknown however its most important effect appears to be in blocking the ribonucleotide reductase system resulting in the inhibition of DNA synthesis.

The aim of this guideline is to assist GPs who are sharing the care of a patient to maintain blood parameters within a pre-determined range by managing the dose of hydroxycarbamide.

Specialist responsibilities

- For female patients of child-bearing age, exclude pregnancy prior to initiating treatment
- Where appropriate, for both men and women discuss with the patient (and/or carer) the risks associated with pregnancy and the need for a reliable method of contraception
- Undertake baseline checks, and blood monitoring during initiation period as described in "Monitoring" section, below
- Discuss with the patient (and/or carer) the benefits, side effects, frequency of dosing and monitoring requirements of hydroxycarbamide treatment

- Provide patient (and/or carer) with relevant written information on use, side effects and need for monitoring of medication
- Provide chemotherapy record booklet for recording of monitoring and information. Ensure that the patient understands that they should bring the booklet to each hospital or GP practice appointment.
- Record the patient's confirmation of understanding of risks and benefits and consent to unlicensed use
- Ascertain immune status by enquiring about history of chicken pox. Measurement of antibodies to varicella-zoster is **not** recommended
- Initiate hydroxycarbamide treatment
- Send a letter to the GP, requesting the sharing of care for a particular patient after establishing a safe and stable dose (minimum 6 weeks), confirm with the GP (in writing) the frequency of ongoing monitoring
- Disease monitoring – response to treatment and need to continue therapy
- Continue to review the patient at agreed specified intervals (including response to treatment and need to continue therapy), sending a written summary to the GP whenever the patient is reviewed, including the current dose to be prescribed
  Inform the GP if the patient does not attend for a clinic appointment and confirm whether the GP should continue to prescribe hydroxycarbamide
- Provide any other advice or information for the GP if required.

General practitioner responsibilities

- Ensure a timely reply is sent to specialist in response to request for sharing of care.

If GP has agreed to share care:

- Continue to prescribe hydroxycarbamide in accordance with these guidelines
- Confirm if they are able to undertake the blood monitoring for the patient
- Set the relevant recalls on the practice system
- Where a patient has not attended for blood tests at the surgery within the last 3 months; request patient attends and prescribe a maximum of 1 weeks supply while awaiting blood result
- Prompt referral to a specialist if there is a change in the person's physical or mental health status
- Report to and seek advice from a specialist on any aspect of patient care which is of concern to the GP and may affect treatment
- Reporting adverse events to specialist, and to MHRA via yellow card scheme
- Stop treatment/amend dose in the case of a severe adverse event or as per prescribing guideline.

Monitoring

Baseline assessment & monitoring to be completed by the specialist service provider

All results should be recorded in patient's chemotherapy handheld record booklet.

At baseline:

- Full blood count (FBC)
- Liver function test (LFT)
- Urea and electrolytes (U&Es)
- Creatinine.

During initiation period:

- FBC – weekly until a safe and stable dose is established (minimum 6 weeks), reduce to a minimum of once every 3 months for the duration of therapy.

Ongoing monitoring to be completed by GP (once a safe and stable dose has been established).

Test	**Frequency**
FBC	At least every 3 months (in line with advice from specialist)
U&Es/creatinine/LFT	6 monthly (in line with advice from specialist)

Action to be taken by GP in response to blood monitoring/side effects:

Blood test results	**Action**
Hb decreases by 30g/dL from baseline	If concerned about sequential drops in FBC indices (possibly still within the normal range) consider an early re-test **If blood test results meet specified criteria, urgently contact the specialist for advice** (if out of hours, contact on-call specialist) If unable to contact the specialist advise the patient to withhold treatment.
WCC < 4 x 10^9/L	
Neutrophils < 1 x 10^9/L	
Platelets < 100 x 10^9/L	
MCV > 105fl	Check for other causes (B12, folate, and alcohol consumption); if results are normal, refer to specialist.
U&Es/creatinine/LFTs	If significant renal or hepatic dysfunction develop, discuss with specialist
Symptoms/Side effects	
Oral/skin ulceration (especially leg ulcers); unexplained sore throat, bruising, or bleeding; and/or any other concern thought to be associated with hydroxycarbamide (see also adverse effects, below)	Urgently contact the specialist for advice (if out of hours, contact on-call specialist) If unable to contact the specialist, advise the patient to withhold treatment.

Contact microbiology if a patient not known to be immune to chickenpox comes into contact with shingles or chickenpox, for advice on whether varicella-zoster immune globulin or other treatment is indicated.

Patient/carer responsibilities

- Ensure they have a clear understanding of the treatment, expected benefits and potential side effects
- Take (or support administration of) medication as directed by the prescriber
- Report any adverse effects to the GP and/or specialist regarding their treatment
- Ensure prescribed medication is stored safely and securely

- Ensure they understand the importance of monitoring treatment and attend appointments to ensure timely monitoring can be completed (in accordance with this guideline)
- Understand that treatment will be stopped if patient does not attend for monitoring and treatment reviews.

Supporting Information

Please refer to individual product SPCs for full prescribing data; these can be accessed at www.medicines.org.uk

Dosage and administration

Refer to the current BNF or individual product SPC. Patient specific guidance will be provided to the GP by the specialist.

Contraindications and precautions

Refer to individual product SPCs.

hydroxycarbamide should be used with caution in patients with marked renal or hepatic dysfunction.

Pregnancy and lactation

Refer to individual product SPCs.

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.

Women should not breastfeed whilst receiving hydroxycarbamide.

Adverse effects

Refer to individual product SPCs.

Leucopenia, anaemia and thrombocytopenia: GPs should be alert to any unexplained bruising or bleeding.

Macrocytosis occurs in almost all patients and may persist for up to one year after stopping therapy.

Rarely: anorexia, nausea, vomiting, diarrhoea, headache, drowsiness, dizziness, cutaneous hyperpigmentation. If severe or persistent, refer to hospital.

Drug interactions

This list is not exhaustive, for additional information, and further interactions, consult the BNF and individual product SPCs.

Toxicity may be potentiated by previous or concomitant radiotherapy or cytotoxic therapy.

The following drug interactions are classified in the online version of the BNF as **potentially serious;** concomitant administration of the drugs involved should be **avoided** (or only undertaken with caution and appropriate monitoring).

- **Didanosine:** increased risk of toxicity when hydroxycarbamide given with didanosine
- **Stavudine:** increased risk of toxicity when hydroxycarbamide given with stavudine
- **Vaccines:** risk of generalised infections when hydroxycarbamide given with live vaccines
- **Clozapine:** increased risk of agranulocytosis

Support

Contact details	
Yarty ward	01392 402850

Date ratified: June 2017

Shared Care Agreement Letter - overleaf

Shared Care Agreement Letter - Consultant Request

To:	**Dr:**
	Practice Address:
Patient Name:	
NHS Number:	
Date of birth:	
Address:	

Diagnosed condition: ……

I recommend treatment with the following drug: …….

At the following dosage: ……..……

I request your agreement to continue the care of this patient according to the Specialised Medicines Service Guidelines for this drug. The patient has been initiated on treatment and stabilised in accordance with the appropriate Specialised Medicines Service Guidelines.

The results of any relevant baseline tests and any additional supportive information (target range, date of last blood test etc.) are included below:

Principles:
GPs are invited to participate, but **if the GP is not confident to undertake these roles then they are under no obligation to do so.** If so, the total clinical responsibility for the patient for the diagnosed condition remains with the specialist. If asked to prescribe this drug the GP should reply to this request as soon as practical. Continuing the care assumes communication between the specialist, GP and patient; the intention should be explained to the patient and accepted by them.

Remember: the doctor who prescribes the medication has the clinical and legal responsibility for the drug and the consequences of its use.

Signed:			**Date:**
Consultant name:			
Telephone number:		**Fax number**	
Email address			

Please sign below and return promptly. Remember to keep a copy of this letter for the patient's records. If this letter is not returned sharing of the care for this patient will not commence.

GP Response

I agree / do not agree* to share the care of this patient in accordance with the Specialised Medicines Service Guideline.

Signed: …….. Date: …….

GP name: …… *Delete as appropriate.

Patient agreement

I understand and agree to my responsibilities as described above.

Signed: …….. Date: …….

Name: