NHS Herefordshire Clinical Commissioning Group

Wye Valley NHS Trust

Shared Care Guidelines

HYDROXYCARBAMIDE (Hydroxyurea)
In MYELOPROLIFERATIVE DISORDERS

INTRODUCTION

This shared care guideline sets out details for the sharing of care of patients with myeloproliferative disorders prescribed ***hydroxycarbamide.*** The exact 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.

Hydroxycarbamide is used in the treatment of Myeloproliferative disorders (MPD) include Essential Thrombocythaemia (ET), Polycythaemia Vera (PV) and Myelofibrosis (MF).

Hydroxycarbamide is currently licensed for the treatment of adults with chronic myeloid leukaemia (CML), treatment of essential thrombocythaemia or polythaemia vera with a high risk for thrombo-embolic complications in adults.

DOSE AND ADMINISTRATION

Variable dose depending on indication, clinical response and effects on full blood count (FBC).

20–30 mg/kg daily or 80 mg/kg every third day

Hydroxycarbamide 500mg capsules 1x100 capsules £11.08 (Nov2014) *[not to be confused with hydroxycarbamide 100mg or 1000mg tablets Siklos® licensed for use in sickle cell syndrome]*

Typical doses range from 500mg up to a maximum of 4000mg orally once daily. A small number of patients may require alternate day dosing. Doses are adjusted to clinical response and will be provided in writing by the reviewing Consultant Haematologist or Specialist Registrar (SpR).

Allopurinol may be co-prescribed for the first 1-2 months.

All patients with essential thrombocythaemia and those with polycythaemia vera receive aspirin 75mg once daily (OD) to prevent vascular events unless contraindicated or commenced on anticoagulant.

ADVERSE EFFECTS

Common: bone marrow suppression (usually mild), anaemia, leukopenia, thrombocytopenia, megaloblastosis (raised median cell volume (MCV)) - General Practitioners (GPs) should be alert to any unexplained bruising or bleeding

Less common: nausea, vomiting, anorexia, stomatitis, mouth ulcers, fever, chills, malaise, maculopapular rash, facial erythema, peripheral erythema, altered liver function tests (LFTs), reduction in renal tubular function, diarrhoea, constipation, leg ulceration, altered nail colour (brown) Patients who develop mouth or leg ulcers need to be monitored very closely. If lesions worsen or do not improve within 7 days then the treatment may need to be withhold temporarily. In all cases the management should be discussed with the Consultant Haematologist conshaem.advicewvt@nhs.net.

See BNF and SPC for comprehensive list

CAUTIONS

- Leukopenia (White blood cells (WBC) less than 2.5x109 cells/l)
- Thrombocytopenia (Platelets (PLT) less than 100x109 cells/l)
- Severe Anaemia
- Previous hypersensitivity to hydroxycarbamide
- Patients currently receiving anti-retroviral therapy with didanosine and/or stavudine
- Pregnancy and breast feeding: women must be advised not to conceive whilst receiving hydroxycarbamide. A reliable form of contraception should be used by men and women whilst on hydroxycarbamide and for 3 months after treatment. Nursing mothers should not breastfeed if taking hydroxycarbamide.

CONTRAINDICATIONS

- Hypersensitivity to the active substance or to any of the excipients listed in SPC
- Marked leucopenia (<2.5wbcx109/L), thrombocytopenia (< 100x109/L), or severe anaemia

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MONITORING STANDARDS FOR AT WYE VALLEY NHS TRUST		
Monitoring is performed in secondary care and consists of:		
Pre-treatment Monitoring	see Consultant request letter to GP for these results	
Subsequent Monitoring	FBC	minimum 3 monthly when stable
	U&E	minimum 6 monthly when stable
	LFT	minimum 6 monthly when stable

ACTION AND ADVICE FOR GP'S IN RESPONSE TO BLOOD MONITORING/SIDE-EFFECTS	
Blood Test Results	**Action**
Plt > 450 or Hct > 0.45	Contact consultant haematologist for advice
Symptoms	**Action**
Bruising, bleeding, purpura	Check FBC and contact Consultant Haematologist conshaem.advicewvt@nhs.net
Sore throat, fever, malaise	
Low FBC (neutropenia, thrombocytopenia, anaemia)	

Patients who recently started hydroxycarbamide or required dose modifications are monitored more frequently within secondary care depending on the clinical decision of the Consultant Haematologist; e.g. FBC to be reviewed after 2 weeks.

Patients must report immediately any evidence of infection, unexpected bruising/bleeding or other manifestations of bone marrow suppression.

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SHARED CARE RESPONSIBILITIES

Consultant / Specialist

1. Diagnosis of condition and ensuring other treatment options have been fully explored
2. Discuss with the patient if the indication is out of license and document agreement in the patient's medical record
3. Initiation of treatment and titration of dose to the optimum level
4. Monitoring for response and adverse drug reactions (ADRs) during titration period
5. Ask the GP if they are willing to participate in Shared Care when a stable dose has been achieved
6. Respond to issues raised by GP after care of patient has been transferred
7. Ensure clear arrangements for GP back-up, advice and support.
8. Send a letter to the GP after each clinic attendance ensuring current dose, most recent blood results and frequency of monitoring are stated
9. Evaluate any reported adverse effects by GP or patient
10. Advise GP on review, duration or discontinuation of treatment where necessary
11. Inform GP of patients who do not attend clinic appointments

General Practitioner

1. Hydroxycarbamide should not be initiated in the primary care setting
2. Reply to the request for Shared Care within 14 days of request
3. Monitoring the patient's overall health and well being and observing patient for evidence of ADRs / abnormalities (such as myelosuppression, pulmonary oedema, skin rash and ulceration) and raising with secondary care clinician if necessary
4. Report any suspected adverse reactions to the hospital Consultant
5. Remind patient to protect skin from sun exposure
6. GP is **not** expected to undertake any specific clinical monitoring
7. Prescription of drug after achievement of a stable dose regime by secondary care, in accordance with written instructions ie clinic letter [not more than 3 months old]
8. **Before issuing a repeat prescription confirm that a full blood count has been taken within the last 3 months.** Do not issue a prescription if a full blood count has not been taken within the preceding 3 months and contact the secondary care clinician as soon as possible
9. Liaise with the hospital Consultant regarding any complications of treatment
10. Stop treatment on advice of the Consultant

CONTACT NUMBERS FOR ADVICE AND SUPPORT

Wye Valley NHS Trust	
Consultant Haematologist	01432 364435 conshaem.advicewvt@nhs.net
Medicines Information, Pharmacy dept	01432 364017 ruth.bader@wvt.nhs.uk

This document should be read in conjunction with the BNF: http://evidence.nhs.uk/formulary/bnf/current, the Summary of Product Characteristics: https://www.medicines.org.uk/emc/ and relevant NICE guidance http://www.nice.org.uk/

Prepared by Dr Lisa Robinson and Ruth Bader October 2014