Hydroxycarbamide

(AMBER with shared care)

Further copies can be obtained from:

Pharmacy Department, Great Western Hospital
NHS Swindon
NHS Wiltshire

Addressograph label

Patient's Name _____

Specialist Name _____

Specialist Signature _____

Date _____

I agree to prescribe Hydroxycarbamide in accordance with the attached shared care guideline:

GP Name _____

GP Signature _____

Date _____

Hydroxycarbamide (AMBER with shared care)

For the treatment of myeloproliferative neoplasms (polycythaemia rubra vera, essential (primary) thrombocythaemia, myelofibrosis and related disorders) Hydroxycarbamide is only licensed for Chronic Myeloid Leukaemia, but there is a considerable body of evidence to support the use of the drug for the treatment of other conditions covered by this shared care guideline.

AREAS OF RESPONSIBILITY FOR THE SHARING OF CARE

This shared care agreement outlines how responsibilities for managing the prescribing of hydroxycarbamide for the treatment of myeloproliferative neoplasms (polycythaemia rubra vera, essential (primary) thrombocythaemia, myelofibrosis and related disorders) may be shared between the specialist and general practitioner (GP). GPs are **invited** to participate. If the GP is not confident to undertake these roles, then he or she is 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. If a specialist asks the GP to prescribe this drug, the GP should reply to this request as soon as practicable.

Sharing of care assumes communication between the specialist, GP and patient. The intention to share care is usually explained to the patient by the doctor initiating treatment. It is important that patients are consulted about treatment and are in agreement with it. Patients will be given written information regarding their diagnosis & hydroxycarbamide therapy and give written consent before starting treatment. Patients with myeloproliferative neoplasms are under regular specialist follow-up, which provides an opportunity to discuss drug therapy.

Treatment is initiated by the Consultant Haematologist. Under his/her supervision the condition is stabilised; patients will then require a maintenance dose of hydroxycarbamide in the majority of cases. Stabilisation is undertaken by the Consultant Haematologist or Clinical Nurse Specialist through telephone reviews or clinics/day ward attendances, and dose changes or interruptions to treatment will be communicated at each visit to the GP.

GPs participating in the shared care agreement will be asked by the specialist to prescribe maintenance doses. The advantage of the shared care agreement will be shorter waits for patients attending hospital for outpatient appointments, reduced likelihood of patient running out of tablets e.g. when clinic appointments are rearranged, and possibly better awareness of any possible non-compliance.

The doctor who prescribes the medication legally assumes clinical responsibility for hydroxycarbamide and the consequences of its use.

RESPONSIBILITIES and ROLES

Specialist Responsibilities

1. Initiate treatment and provide at least 28 days' supply, including prescription via ARIA electronic prescribing system.
2. Discuss the benefits and side effects of treatment with the patient.
3. Patients will be given written information regarding their diagnosis & hydroxycarbamide therapy and must give written consent before starting treatment
4. Ask the GP whether he or she is willing to participate in shared care, and continue to prescribe until confirmation of the GP's agreement to participate has been received.
5. Supply GP with summary within 10 working days of a hospital out-patient review or in-patient stay.
6. Undertake monitoring as detailed on page 5 of this document, and liaise closely with the GP if there are concerns about the outcome of monitoring, especially if dose adjustment is necessary.
7. Review the patient's condition and monitor response to treatment regularly where indicated.
8. Give advice to the GP on when to stop treatment.
9. Report adverse events to the MHRA yellow card scheme: https://www.gov.uk/report-problem-medicine-medical-device .
10. Ensure that clear backup arrangements exist for GPs to obtain advice and support.

General Practitioner Responsibilities

1. Reply to the request for shared care as soon as practicable using the forms linked here (in writing or via secure email).
2. Prescribe medicine at the dose recommended by the specialist.
3. Encourage patient to attend all appointments, including appointment for blood tests and other monitoring.
4. Refer promptly to specialist when any loss of clinical efficacy is suspected (e.g. worsening of disease-related symptoms, new symptoms suggestive of disease recurrence or progression) or intolerance to therapy occurs.
5. Liaise with specialist for the following issues: leg ulcers, unexpected leucopenia, anaemia or thrombocytopenia
6. Report to and seek advice from the specialist on any aspect of patient care that is of concern to the GP and may affect treatment.
7. Stop treatment on the advice of the specialist.
8. Report adverse events to the specialist and MHRA yellow card scheme: https://www.gov.uk/report-problem-

Patient Responsibilities

1. Attend all appointments with GP and specialist, including appointments for blood tests & other monitoring.
2. Report to the specialist or GP if he or she does not have a clear understanding of the treatment.
3. Share any concerns in relation to treatment with medicine.
4. Report any adverse effects to the specialist or GP whilst taking the medicines.

BACK-UP ADVICE AND SUPPORT

Shared Care Response Templates: Shared Care Agreements - Medicines

Contact details	Telephone No.	Email address:
Triage Line Mon–Fri 09.00-17.30 Traige Line out of hours	01793-604348 01793-604400	n/a
Haematology Clinical Team	01793-604020, ask for registrar via switchboard	gwh.haematologyadviceandguidance@nhs.net
Haematology Clinical Nurse Specialist	01793-604341 01793-604020, ask for CNS via switchboard	HaemCNS@gwh.nhs.uk
GWH Cancer Pharmacy Team	01793-605026	gwh.pharmacistscancer@nhs.net
GWH Medicines Information Service	01793-605029	medinfo@gwh.nhs.uk

SUPPORTING INFORMATION

Summary of condition and licensed indications.
Hydroxycarbamide is used to treat patients with active myeloproliferative neoplasms (polycythaemia rubra vera, essential thrombocythaemia or myelofibrosis) or chronic myeloid/granulocytic leukaemia and selected cases of myeloid leukaemia. It is only licensed to treat chronic myeloid leukaemia, but is very rarely used in this condition since the advent of imatininb.

Another preparation of Hydroxycarbamide (Siklos®) is also licensed for treatment of sickle cell disease: this product is 10 x more expensive than other preparations of hydroxycarbamide and only comes as 1000mg and 100mg size tablets. THIS PREPARATION SHOULD NOT BE PRESCRIBED TO PATIENTS WITH MYELOPROLIFERATIVE NEOPLASMS DUE TO EXPENSE AND POSSIBLE CONFUSION OVER TABLET SIZE.

In order to reduce the likelihood of prescribing an incorrect product please consider setting an alert on the patient record to indicate that this patient should only receive hydroxycarbamide 500 mg capsules

Treatment Aims (Therapeutic plan)
Hydroxycarbamide is cytotoxic and works by reducing cellular proliferation in the bone marrow. The aims of hydroxycarbamide therapy are the control of blood count and associated clinical abnormalities in patients with myeloproliferative neoplasms e.g. in polycythaemia reduction of elevated haematocrit, in thrombocythaemia control of platelet count and in myelofibrosis reduction in spleen size. Normalising the blood count will limit/abolish symptoms associated with the condition and will reduce the risk of complications associated with the disorder.

Treatment Schedule (including dosage and administration)
Hydroxycarbamide is prescribed in a variable dose. The required dose for an individual may vary between 500mg to 21g per week, with most requiring around 5-10g per week. Hydroxycarbamide is best taken as a single dose by mouth but can be divided if convenient and possible. Dosage may be daily or on selected days each week. The drug is available as 500mg capsules.

Contra-indications
- Marked leucopenia (<2.5 x 10^9/L), thrombocytopenia (<100 x 10^9/L), or severe anaemia and those who have previously shown hypersensitivity to hydroxycarbamide
- Pregnancy and breast feeding

Cautions
- Hydroxycarbamide should be used with caution in patients with marked renal dysfunction – 50% dose recommended if creatinine clearance <10ml/min.
- Severe anaemia should be corrected with whole blood replacement prior to the patient starting hydroxycarbamide.
- Self-limiting megaloblastic erythropoeisis may be seen early in the course of hydroxycarbamide therapy. It is not related to vitamin B_{12} or folic acid deficiency, but may mask incidental folic acid deficiency, so regular monitoring of serum folic acid is recommended.
- In patients receiving long-term therapy with hydroxycarbamide for myeloproliferative neoplasms, such as polycythemia, secondary leukaemia has been reported. It is unknown whether this leukaemogenic effect is secondary to hydroxycarbamide or associated with the patient's underlying disease.
- Skin cancer has also been reported in patients receiving long-term hydroxycarbamide. Patients should be advised to protect skin from sun exposure, conduct self-inspection of the skin and be screened for secondary malignancies during routine follow-up visits.
- Cutaneous vasculitic ulcerations and gangrene have been reported in patients receiving hydroxycarbamide. Due to the potentially severe clinical outcomes of cutaneous vasculitic ulcers, hydroxycarbamide should be discontinued if cutaneous vasculitic ulcers develop and alternative agents initiated as indicated.
- An increase in serum uric acid may be seen in patients treated with hydroxycarbamide, especially when used with other cytotoxic agents. As this could result in gout or, at worst, uric acid nephropathy, it is important to monitor uric acid levels regularly and maintain a high fluid intake during treatment.

Please see SPC for full list of cautions and more detailed information.

Common adverse effects

- Hydroxycarbamide is generally well tolerated with few side effects – the main side effect is myelosuppression; in the above haematological indications it is being administered to achieve controlled myelosuppression. It is short acting so that effects of overdosage are quickly reversed on drug withdrawal; where necessary patients will be managed supportively and expectantly pending recovery. If WBC falls below $2.5x10^9$/L or platelet count to $<100x10^9$/L, therapy should be interrupted and advice sought from a Haematologist
- Patients are counseled to maintain a high fluid intake. Allopurinol may be recommended for shorter or longer periods to minimise secondary hyperuricaemia in active myeloproliferative states.
- Other side effects are rare, but include mouth ulcers, gastrointestinal disturbance, abdominal pain, anorexia, pyrexia, chills, malaise, asthenia, digital or leg ulcers, raised LFTs, cholestasis, pancreatitis, hepatitis, hepatotoxicity and skin cancer.

Please see SPC for full list of adverse effects and more detailed information.

Monitoring

- **Monitoring and advice on the action to be taken following monitoring of the patient's blood count and other relevant parameters will remain the responsibility of the Consultant Haematologist in charge of the patient's care.** Initially weekly blood counts may be required. The frequency will reduce as the condition is stabilised.
- Long term monitoring for stable patients generally involves blood counts every 3 months.
- Renal function is normally checked 3 monthly, and liver function tests are checked at least annually.
- Hydroxycarbamide will result in a red cell macrocytosis - the MCV may increase to values as high as 120fl, with stable blood counts otherwise this is generally not of clinical concern and there is therefore no need to investigate this further.
- GPs are kindly asked to report to the Consultant Haematologist any suspected loss of efficacy and any adverse effects which may be attributable to hydroxycarbamide.

Drug Interactions

- Possibly reduced absorption of phenytoin
- Avoid concomitant use with clozapine, as increased risk of agranulocytosis
- Increased risk of toxicity with didanosine, stavudine and other anti-retrovirals
- Increased risk of vasculitis with interferon alfa
- Reduced absorption of digoxin
- Avoid live vaccine during hydroxycarbamide therapy and at least for 6 months after stopping therapy

Cost

100 x 500mg capsules cost £12.12 (Drug Tariff -Aug 17)

Do not prescribe as the 1000mg tablets (Siklos®) which are only licensed for the treatment of sickle cell syndrome and cost £500 for 30 x 1000mg tablets.

References

1. http://www.bcshguidelines.com/documents/published_thrombocytosis_bjh_042010.pdf
2. http://www.bcshguidelines.com/documents/polycythaemia_amendment_07.pdf
3. http://www.b-s-h.org.uk/guidelines/guidelines/diagnosis-and-management-of-myelofibrosis/
4. http://www.macmillan.org.uk/cancerinformation/cancertreatment/treatmenttypes/chemotherapy/individualdrugs/hydroxycarbamide.aspx
5. http://www.mpnvoice.org.uk/
6. Summary of Product Characteristics. Hydrea monograph. Accessed on 6th July 2016 via http://www.medicines.org.uk/emc/medicine/19081.
7. British National Formulary June 2016. Hydroxycarbamide monograph. Accessed on 6th July 2016 via https://www.medicinescomplete.com/mc/bnf/current/PHP5470-hydroxycarbamide.htm?q=hydroxycarbamide&t=search&ss=text&tot=10&p=1#_hit

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Document details

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