Hydroxycarbamide for chronic myeloid leukaemia and other myeloproliferative disorders (adults)

It is vital for safe and appropriate patient care that there is a clear understanding of where clinical and prescribing responsibility rests between Consultants and General Practitioners (GPs). It is essential that a transfer or sharing of prescribing responsibilities should not take place without the sharing of information between the Haematology Prescriber and the individual GP, and their mutual agreement to this to ensure their full confidence when prescribing. These are not rigid guidelines. In all cases, Consultants and GPs should clearly communicate regarding the appropriate management of individual patients. As always, the doctor who prescribes the medication has the clinical responsibility for the drug and the consequences of its use.

1.0 Licensed indication:
Chronic myeloid leukaemia.
Polycythaemia vera
Essential thrombocythemia

2.0 Dosage and administration:
20-30mg/kg daily orally.
Continuous treatment if significant clinical effect after 6 weeks.

3.0 Cautions and contraindications:

3.1 Precautions
If WBC falls below 2.5x10$^9$/L or platelet count to <100x10$^9$/L, therapy should be interrupted. Counts should be rechecked after 3 days and treatment resumed when they rise significantly towards normal.
Severe anaemia must be corrected with whole blood replacement before initiating therapy with hydroxycarbamide. If, during treatment, anaemia occurs, correct without interrupting Hydroxycarbamide therapy (but a reduction in dose may be necessary).
Erythrocytic abnormalities; (raised MCV) megaloblastic erythropoiesis, which is self-limiting, is often seen early in the course of hydroxycarbamide therapy. The morphologic change resembles pernicious anemia, but is not related to vitamin B$_{12}$ or folic acid deficiency.
All Full Blood Count monitoring and appropriate dose adjustments will be made in secondary care, usually at least every 3 months.
Hydroxycarbamide should be used with caution in patients with marked renal dysfunction.
Hydroxycarbamide is not licensed for use in combination with antiretroviral agents for HIV disease and it may cause treatment failure and toxicities (in some cases fatal) in HIV patients.

3.2 Contra-indications
- Marked leucopenia (WCC <2.5x10$^9$/L),
- Thrombocytopenia (Platelets < 100x10$^9$/L),
- Severe anaemia
- Those who have previously shown hypersensitivity to Hydroxycarbamide.

4.0 Adverse effects:
- Cutaneous vasculitic toxicities including vasculitic ulcerations and gangrene in patients with myeloproliferative disorders (risk is increased if the patient is also receiving interferons). Due to potentially severe clinical outcomes for the cutaneous vasculitic ulcers reported in patients with myeloproliferative disease, hydroxycarbamide should be discontinued if cutaneous vasculitic ulcerations develop and alternative cytoreductive agents should be initiated as indicated.
- Increased uric acid which may lead to gout or uric acid nephropathy.
- Bone marrow suppression (leucopenia, thrombocytopenia, anaemia)
- Anorexia, nausea, vomiting, diarrhoea, constipation, headache, drowsiness, dizziness, stomatitis, alopecia, skin rash, melaena, abdominal pain, pulmonary oedema, hallucinations, convulsions, skin ulceration, dysuria, increased creatinine level, chills, malaise, increased hepatic enzymes.
- Rarely – diffuse pulmonary infiltrates or fibrosis and dyspnoea.
- In MDS treatment – vasculitic toxicities including ulcerations and gangrene.
- After long term treatment – hyperpigmentation, erythema, atrophy of the skin and nails, scaling, skin cancer, violet papules, alopecia, secondary leukaemia has been reported. It is unknown whether this leukaemogenic effect is secondary to hydroxycarbamide or associated with the patient's underlying disease.
5.0 Monitoring requirements:
The complete status of the blood, including bone marrow examination, if indicated, as well as kidney function and liver function should be determined prior to, and repeated during, treatment. Patients will be reviewed usually least every three months. All Full Blood Count monitoring and appropriate dose adjustments will be made in secondary care.

See section 3

6.0 Action to be taken if abnormal results/adverse effects:
All Full Blood Count monitoring and appropriate dose adjustments will be made in secondary care. If there are any concerns regarding interim blood counts contact referring Haematology Consultant for advice.

7.0 Drug interactions:
- Antiretrovirals for HIV - Cases of pancreatitis and hepatotoxicity (some with fatal outcomes) and severe peripheral neuropathy have been observed.
- May delay plasma iron clearance and decrease rate of iron utilization by erythrocytes but it does not appear to alter the red blood cell survival time.
- Effect of hydroxycarbamide potentiated by radiotherapy and cytotoxics.

8.0 Specialist responsibilities:
- To initiate hydroxycarbamide therapy and ensure monitoring requirements are met.
- To continue to prescribe hydroxycarbamide until the patient is stable (usually 3 to 6 months)
- To ensure regular hospital clinic follow up and appropriate clinical review.
- To communicate regularly with primary care colleagues on hospital visits and ongoing treatment plan.

9.0 GP responsibilities:
- Ensure receipt of regular communication from secondary care on hospital attendances and treatment plan prior to prescribing further supplies of hydroxycarbamide capsules. Clinic attendances usually occur at least every three months.
- To prescribe a supply of hydroxycarbamide capsules based on written communication from secondary care Haematology Prescribers.
- Liaison with the Haematology Consultant regarding any possible adverse effects of treatment.
- Reporting adverse drug reactions to the hospital.

10.0 Patient responsibilities:
- Report any adverse effects to their GP and/or specialist whilst treated with hydroxycarbamide
- Ensure they have a clear understanding of the indication for treatment and the prescribed dose.

11.0 Secondary care review:
- Enquire on any symptoms potentially attributable to treatment.
- Perform any necessary clinical examination.
- Perform routine Full Blood Count at each clinic visit.
- Perform further biochemical investigations if deemed clinically appropriate.
- Refer for appropriate further investigations based on abnormalities elicited above.

12.0 Availability/Other special considerations
If the patient prefers, or is unable to swallow 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

Counsel both female and male patients on the use of adequate contraception.

<table>
<thead>
<tr>
<th>Back up advice and support</th>
<th>Specialist</th>
<th>Telephone/Fax</th>
<th>Email address</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dr Ranjit Dasgupta</td>
<td>Consultant haematologist</td>
<td>0151 604 7679</td>
<td><a href="mailto:rdasgupta@nhs.net">rdasgupta@nhs.net</a></td>
</tr>
<tr>
<td>Dr David Galvani</td>
<td>Consultant haematologist</td>
<td>0151 604 7122</td>
<td><a href="mailto:david.galvani@nhs.net">david.galvani@nhs.net</a></td>
</tr>
</tbody>
</table>

Written By:
Simon Purcell: Lead Pharmacist, Haematology
Helen Dingle, Prescribing Adviser
Wirral University Teaching Hospitals NHS Foundation Trust
NHS Wirral