# Hydroxycarbamide

Shared Care Guidelines: 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.

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**AREAS OF RESPONSIBILITY FOR THE SHARING OF CARE**

This shared care agreement outlines suggested ways in which the 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 with myeloproliferative neoplasms are under regular specialist follow-up, which provides an opportunity to discuss drug therapy.

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-day supply. |
| 2 | Discuss the benefits and side effects of treatment with the patient. |
| 3 | Ask the GP whether he or she is willing to participate in shared care and agree with the GP as to who will discuss the shared care arrangement with the patient. |
| 4 | Supply GP with summary within 14 days of a hospital out-patient review or in-patient stay. |
| 5 | Monitoring details |
| 6 | Review the patient's condition and monitor response to treatment regularly where indicated. |
| 7 | Give advice to the GP on when to stop treatment. |
| 8 | Report adverse events to the MHRA. |
| 9 | 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. |
| 3 | 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. |
| 4 | Liaise with specialist for the following issues: leg ulcers, unexpected leucopenia, anaemia or thrombocytopenia |
| 5 | 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. |
| 6 | Stop treatment on the advice of the specialist. |

| | Patient's role |
|---|---|
| 1 | Report to the specialist or GP if he or she does not have a clear understanding of the treatment. |
| 2 | Share any concerns in relation to treatment with medicine. |
| 3 | Report any adverse effects to the specialist or GP whilst taking the medicine. |

**BACK-UP ADVICE AND SUPPORT**

| Contact details | Telephone No. | Bleep: | Fax: | Email address: |
|---|---|---|---|---|
| Dr Jonathan Cullis<br>Dr Tamara Everington<br>Dr Effie Grand<br>Dr Louise Fraser | 01722 336262 extension 4043 or 2066 | Bleep via switch-board | 01722 333933 | jonathan.cullis@salisbury.nhs.uk<br>tamara.everington@salisbury.nhs.uk<br>effie.grand@salisbury.nhs.uk<br>louise.fraser@salisbury.nhs.uk |
| Hospital Pharmacy Dept: | 01722 336262 extension 4268 | N/A | 01722 333133 | N/A |
| Debra Robertson, Pharmacist | 01722 336262 extensions 4443 or 4275 | 1110 | 01722 333133 | debra.robertson@salisbury.nhs.uk |

**Shared Care Response Templates:**
Shared Care Agreements - Medicines

**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 10x 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.

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.

**Treatment Schedule (including dosage and administration)**
Hydroxycarbamide is prescribed in a variable dose. The required dose for an individual may vary between 2g 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.

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 and his/her clinical team through clinics/day ward attendances, and dose changes or interruptions to treatment will be communicated at each visit to the General Practitioner. The patients will continue to attend the Haematology clinics for blood tests and monitoring of their condition whilst on the drug, although for suitable patients, a shared care agreement opens up the possibility of telephone consultations.

**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

**Cautions:**

**Hydroxycarbamide should be used with caution in patients with marked renal dysfunction – 50% dose recommended if creatinine clearance <10ml/min**

- 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

**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 counselled 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 and leg ulcers

**Monitoring**

- Monitoring of the patient's blood count and other relevant parameters will remain the responsibility of the Consultant Haematologist in charge of the patient. 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, liver function tests may be checked annually
- Hydroxycarbamide will result in a red cell macrocytosis - the MCV may increase to values as high as 120 fl, with stable blood counts otherwise this is generally not of clinical concern and there is therefore no need to investigate this further

**Drug Interactions**

- Possibly reduced absorption of phenytoin
- Avoid concomitant use with clozapine
- Increased risk of toxicity with didanosine and stavudine
- Reduced absorption of digoxin

**Cost**

20 x 500mg capsules cost £2.22

**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**

http://www.bcshguidelines.com/documents/published_thrombocytosis_bjh_042010.pdf
http://www.bcshguidelines.com/documents/polycythaemia_amendment_07.pdf

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**Document details**

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