HYDROXYCARBAMIDE

INDICATION

1. Non-leukaemic myeloproliferative neoplasms (MPN):
    - Essential Thrombocythaemia (ET)
    - Primary Polycythaemia Vera (PV)
    - Rarely: Myelodysplastic Syndromes/Myeloproliferative Neoplasm (MDS/MPN overlap), Myelofibrosis
2. Chronic myeloid leukaemia (CML)
3. Chronic myelomonocytic leukaemia (CMML)
4. Palliative chemotherapy for Acute Myeloid Leukaemia (AML)

Hydroxycarbamide can also be prescribed by GPs as part of a shared care protocol by primary care for ET and PV. [Link]

Available as 500mg capsules

Note on prescribing: When used to treat haematological neoplasms (ET, PV, myelofibrosis, MDS/MPN, CML, CMML, AML) hydroxycarbamide must be prescribed on ARIA.

TREATMENT INTENT

Disease Modification

PRE-ASSESSMENT

1. Investigations to include FBC, blood film, urea and electrolytes, liver function tests, bone profile, HIV, Hepatitis B (including HB surface Ag and HB core antibodies) and Hepatitis C antibody.
2. Ensure diagnosis confirmed prior to administration of oral systemic anti-cancer treatment (SACT), and document in notes.
3. Bone marrow aspirate and trephine may be indicated.
4. Molecular diagnostic tests as appropriate.
5. Urine pregnancy test – before cycle 1 of each new therapy course for women of child-bearing age unless they are post-menopausal, have been sterilised or undergone a hysterectomy.
6. Record performance status (WHO/ECOG).
7. Record weight and height.
8. Fertility - it is very important the patient understands the potential risk of infertility. All patients should be offered fertility advice.
9. Consent (CRUK consent form) – ensure patient has received adequate verbal and written information regarding their disease, treatment and potential side effects. Document in notes all information that has been given. Obtain written consent prior to treatment.
10. Hydration - in patients with bulky disease pre-hydrate with sodium chloride 0.9% 1 litre over 4-6 hours. Patients at high risk of tumour lysis refer to Tumour Lysis Syndrome protocol.
11. Treatment should be agreed in the relevant MDT.
12. Patients prescribed oral SACT, ensure appropriate pre-SACT counselling and handling advice has been provided.

DRUG REGIMEN

Variable dosing depending on blood count, response and indication:

MPN: Recommended starting dose is typically 500mg OD which can be titrated upwards as required. Higher starting doses may be used in patients requiring more urgent count reduction.

CML: Hydroxycarbamide is usually given at an initial dose of 40 mg/kg daily dependent on the white cell count. The dose is reduced by 50% (20 mg/kg daily) when the white cell count has dropped below 20 x 10^9/L. The dose is then adjusted individually to keep the white cell count at 5-10 x 10^9/L. Hydroxycarbamide dose should be reduced if white cell counts fall below 5 x 10^9/L and increased if white cell counts >10 x 10^9/L are observed.

CMML/AML: Hydroxycarbamide may either be used in the palliative setting to control a rising white cell count (e.g. 500mg to 1000mg daily) or used at diagnosis to control a very high white cell count (for example out of hours) whilst other treatment options are discussed (usually requiring 40 mg/kg/day or 2000mg to 3000mg daily in the short term).

CYCLE FREQUENCY

Continuous treatment until significant disease progression or intolerable side effects.

RESTAGING/ASSESSING RESPONSE

Therapy should be monitored regularly by repeat blood counts and LFT's, and the dose adjusted accordingly. Initially monitor response 1-2 weekly, if response is achieved treatment should continue indefinitely with the monitoring frequency is reduced to a maximum of 4 monthly when the blood count is fully stable.

CML	To maintain WCC between 5 -10 x10^9/L
ET	To maintain PLT < 400 x10^9/L and WCC > 4 x10^9/L. See BSH guidelines for more information.
PV	To maintain Haematocrit at < 0.45 and PLT < 400 x 10^9/L and normal WBC count. See BSH guidelines for more information.

DOSE MODIFICATIONS

Haematologic

Therapy should be interrupted if the WBC drops below 2.5 x 10^9/L, or the platelet count below 100 x 10^9/L.
Adjust dose with anaemia.
Where these are the result of bone marrow suppression secondary to haematological disease, at the discretion of a consultant haematologist treatment may commence cautiously.

Non- Haematologic

Renal impairment – Although, in practice, the dose will be titrated according to response, note that impaired renal function may affect drug clearance and the following information is available:

Renal Impairment	Hepatic Impairment
GFR ≥ 60mL/min: 100% dose GFR < 60mL/min: 50% dose Haemodialysis (HD): 50% of the original dose following HD	No dose adjustment necessary. Monitor for haematological toxicity

INVESTIGATIONS & ON-TREATMENT MONITORING

FBC, U&Es and LFTs

CONCURRENT MEDICATION

Consider Allopurinol 300mg OD for 7-28 days (starting 24-48 hours before chemotherapy) if high white cell count. Refer to Tumour Lysis Syndrome Protocol.
ET/PV: Aspirin 75mg daily (Consider prescribing concomitant PPI if appropriate). Assess bleeding risk individually.

EMETIC RISK

Minimal

DRUG INTERACTIONS

(Consult with pharmacist and refer to SmPC for full details)

Hydroxycarbamide should be given with caution to patients with previous or concomitant radiotherapy or cytotoxic therapy. In these cases the patients have an increased risk to develop bone marrow depression, gastric irritation and mucositis (more severe, higher frequency). Furthermore, an exacerbation of erythema caused by previous or simultaneous irradiation may occur.

ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS

- Leukopenia: this can be severe and life-threatening and patients' total white cell counts should be regularly monitored
- Anaemia: requires dose-adjustment
- Gastro-intestinal symptoms: e.g. anorexia, nausea, diarrhoea. These are usually most prominent when the patient commences the treatment and settle within a couple of weeks
- Potentially mutagenic and genotoxic: Female patients should be advised to avoid pregnancy, and male patients should avoid causing pregnancy whilst taking hydroxycarbamide and for three months after stopping the drug. Hydroxycarbamide is present in breast milk and should be avoided when breast feeding.
- Leukaemogenesis: Myeloproliferative Neoplasms have an inherent risk of transformation to acute myeloid leukaemia. A number of lines of evidence support that single agent hydroxycarbamide does not increase the risk of secondary leukaemia. However, it is difficult to exclude a minor increased risk associated with hydroxycarbamide and patients should be informed of this.
- Mouth and leg ulcers with chronic use, ovarian failure, infertility
- Skin rash or skin ulcer (requires cessation of treatment)
- Increased risk of skin cancer with prolonged use, consider surveillance
- Interstitial lung disease: pulmonary fibrosis, lung infiltration, pneumonitis, and alveolitis/allergic alveolitis

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TREATMENT RELATED MORTALITY

Very low

REFERENCES

1. Medac Pharma LLP . Hydroxycarbamide 500mg capsules Summary of Product Characteristics. Updated 04/11/2024. Accessed on 25/06/2025 via http://www.medicines.org.uk/
2. Giraud, E.L. et al. (2023) 'Dose recommendations for anticancer drugs in patients with renal or hepatic impairment: An update', The Lancet Oncology, 24(6). doi:10.1016/s1470-2045(23)00216-4
3. Harrison CN, Bareford D, Butt N, Campbell P, Conneally E, Drummond M, Erber W, Everington T, Green AR, Hall GW, Hunt BJ. Guideline for investigation and management of adults and children presenting with a thrombocytosis. British journal of haematology. 2010 May 1;149(3).
4. McMullin M, Harrison C, Ali S, Cargo C, Chen F, Ewing J, Garg M, Godfrey A, Knapper S, McLornan D, Nangalia J. A guideline for the diagnosis and management of polycythaemia vera. A British Society for Haematology Guideline. British journal of haematology. 2018 Nov 27;184(2).

REVIEW

Name	Revision	Date	Version	Review date
Prof Vyas	New document	Feb 2016	1.0	

Cheuk-kie Jackie Cheung, Haematology Pharmacist.	Typo correction, reformatting	Jul 2018	1.1	
Cheuk-kie Jackie Cheung, Haematology Pharmacist. NSSG Myeloid Group	Annual protocol meeting	Oct 2019	1.2	Oct 2021
Yen Lim, Haematology Pharmacist. NSSG Myeloid Group	Updated renal dosing. Annual protocol meeting	Nov 2021	1.3	Nov 2023
Godwin Chun Wing Leung, Haematology Pharmacist. Dr Beth Psaila, Consultant Haematologist. NSSG Myeloid Group	Updated pre-assessment to align with current practice. Annual protocol meeting 2025	Jul 2025	2.0	Jul 2028