

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

- Ensure histology confirmed prior to administration of chemotherapy and document in notes.
- Bone marrow aspirate and trephine may be indicated
- Molecular diagnostic tests as appropriate
- Blood tests: FBC, U&Es, LFTs.
- Record stage of disease
- Urine pregnancy test – for all women of childbearing age unless they are postmenopausal, have been sterilised or undergone a hysterectomy.
- Record performance status (WHO/ECOG).
- Record weight and height.
- Fertility - it is very important the patient understands the potential risk of infertility. All patients should be offered fertility advice (see fertility guidelines).
- Consent – 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.
- 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 protocol.
- Treatment should be agreed in the relevant MDT.
- For patients prescribed oral chemotherapy, ensure pre-chemotherapy counselling in line with NPSA recommendation and chemotherapy measures

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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 $20 \times 10^9/L$. The dose is then adjusted individually to keep the white cell count at $5-10 \times 10^9/L$. Hydroxycarbamide dose should be reduced if white cell counts fall below $5 \times 10^9/L$ and increased if white cell counts $>10 \times 10^9/L$ 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 $5-10 \times 10^9/L$
ET	To maintain $PLT < 400 \times 10^9/L$ and $WCC > 4 \times 10^9/L$. See BSH guidelines for more information.
PV	To maintain Haematocrit at < 0.45 and $PLT < 400 \times 10^9/L$ and normal WBC count. See BSH guidelines for more information.

DOSE MODIFICATIONS

Haematologic

Therapy should be interrupted if the WBC drops below $2.5 \times 10^9/L$ (neutrophil $<1.5 \times 10^9/L$), or the platelet count below $100 \times 10^9/L$.

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 $\geq 60\text{mL/min}$: 100% dose GFR $< 60\text{mL/min}$: 50% dose	No dose adjustment necessary. Monitor for haematological toxicity

INVESTIGATIONS

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

ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS

- Neutropenia: this can be severe and life-threatening and patients' neutrophil 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: Non-leukaemic 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

TREATMENT RELATED MORTALITY

Very low

REFERENCES

1. Bristol-Myers Squibb. Hydroxycarbamide 500mg capsules Summary of Product Characteristics. Updated 29/7/2021. Accessed on 5/11/2021 via <http://www.medicines.org.uk/>
2. Krens S D et al (2019). Dose recommendations for anticancer drugs in patients with renal or hepatic impairment. *Lancet Oncol*; **20**: e201–08

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

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