SACT PROTOCOL

The Clatterbridge Cancer Centre NHS Foundation Trust

Systemic Anti Cancer Therapy Protocol

Hydroxycarbamide Myeloproliferative Neoplasms (MPN)

PROTOCOL REF: **MPHAHYDHA**
(Version No. 2.0)

Approved for use in:

Patients with essential thrombocythaemia (ET), polycythaemia vera (PV), myelofibrosis (PMF) at high risk of thrombosis. Intermediate risk ET patients on the basis of PT1 amended trial.

Blueteq request is NOT required

Dosage:

Drug	Dose	Route	Frequency
Hydroxycarbamide	**500mg to 2500mg***	PO	Daily **continuous**

*Higher doses may rarely be needed for resistant patients/ urgent cytoreduction, but these patients should be monitored very closely.

Administration/counselling points:

- Hydroxycarbamide is available as 500mg capsules
- An unlicensed specials liquid formulation is also available (note short expiry)
- If liquid unavailable or unsuitable, as a last resort capsules may be opened and contents dispersed in water, but patients should be advised wear gloves whilst preparing, to wash their hands and the glass thoroughly after use, avoid direct contact with the skin and inhalation (note off-label use)
- Can be taken on an empty stomach or with food

- Can be used in combination with anagrelide/ other cytoreductive therapies. See separate individual protocols for dosing.
- Skin cancer reported in patients receiving long-term treatment. Patients should be advised to protect their skin from the sun and regularly self-inspect their skin for any abnormalities and report to their prescriber if any concerns.
- Patients should be advised to regularly self-inspect their legs for signs of leg ulcers and report to their prescriber if any concerns.
- Secondary leukaemias have been reported in patients receiving long-term treatment for myeloproliferative disorders, causality not established.
- Prescribers should ensure intended dose, intended length of supply and next clinic appointment are recorded in patient's notes to facilitate the clinical check of each prescription.

Emetogenic risk:

Low risk

Supportive treatments:

- Allopurinol 300mg daily until counts are controlled (reduce dose if renal dysfunction)
- Antiplatelet therapy is usually indicated if PV/ET (ask GP to prescribe, consider addition of gastro-protection where appropriate)
- Some patients may require PRN antiemetic therapy (e.g. metoclopramide)

Dosing in renal and hepatic impairment:

Renal Impairment
Since renal excretion is a pathway of elimination, consideration should be given to decreasing the starting dose of hydroxycarbamide in this population. Patients who develop renal dysfunction during therapy may be more at risk of cytopenias, dose reduction should be considered depending on blood counts.
Hepatic Impairment
No dose adjustment necessary

Interactions:

Administration of live vaccinations whilst on hydroxycarbamide can result in severe and potentially life threatening infections – avoid the use of live vaccines

Caution should be used when treating patients on concomitant HIV medication. Refer to SPC for more detailed information.

Please refer to the relevant SPC for more drug-drug interaction information

Main toxicities:

- Drowsiness – dose reduction or consider dosing at night only. Affected patients should be counselled on taking more care when driving
- Leg ulcers – would require cessation of hydroxycarbamide to allow ulcers to heal
- Skin cancers – patients should be advised to protect skin from sun exposure. In addition, patients should conduct self-inspection of the skin during the treatment and after discontinuation of the therapy with hydroxycarbamide
- Hydroxycarbamide is contraindicated in patients with marked bone marrow depression, or severe anaemia; or in patients who have demonstrated a previous hypersensitivity to hydroxycarbamide or any other component or its formulation.
- Hydroxycarbamide is genotoxic, fetotoxic, teratogenic in animals and has the potential to be mutagenic. It should not be used in pregnancy; its effects on fertility have not been established.
- Breast feeding is not recommended due to the secretion into breast milk.
- When appropriate both male and female patients should be counselled concerning the use of contraceptive measures before and during treatment with hydroxyurea and for at least 6 months (women) to 12 months (men) after treatment has stopped.
- Elderly patients and patients with extensive prior radiation or chemotherapy may be more sensitive to the effects of hydroxycarbamide

Please refer to the relevant SPC for more information on toxicities.

Investigations and treatment plan:

	Pre	Cycle 1	Cycle 2 onwards	Ongoing
Informed Consent	X			
Clinical Assessment	X	X	X	Prior to every cycle
SACT Assessment (including toxicity assessment and PS)	X	X	X	Prior to every cycle
FBC	X	X	X	Prior to every cycle. A cycle may extend to three months in length once patients are stable on treatment. FBC should be taken within 7 days of prescribing but may be taken up to 14 days prior to prescription at clinician's discretion. **Prescribers must check FBC prior to prescribing and document that this check has taken place in the medical notes. SACT assessment will not include checking of this parameter in this instance.**
U&E & LFTs	X			Must have had within 6 months of prescription. **Prescribers must check the most recent U+E & LFT prior to prescribing. SACT assessment will not include checking of these parameters in this instance.**
Height	X			
Weight	X	X	X	Prior to every cycle
Pregnancy test	X			If clinically indicated

Dose Modifications and Toxicity Management:

Haematological toxicity:

- Hydroxycarbamide causes macrocytic red cell indices and may mask iron, B12 or folic acid deficiency.
- Consider reducing the dose/ interrupting therapy if the patient develops leukopenia <2.5 x10^9/L, neutropenia <1.5 x 10^9/L or thrombocytopenia <100 x 10^9/L.
- For non-medical prescribers (NMPs) reviewing MPN patients there is a separate SOP to guide when consultant input should be sought and guidance on target parameters – available via the intranet
- Patients with PV/ ET may have differing Hct/ Plt/ WCC treatment targets. It may be helpful to document these targets in the patient's medical notes to ensure continuity of care.

These haematological guidelines assume that patients are well with good performance status, that other acute toxicities have resolved and the patient has not had a previous episode of neutropenic sepsis.

References:

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2. Cortelazzo, S., Finazzi, G., Ruggeri, M., Vestri, O., Galli, M., Rodeghiero, F. & Barbui, T. (1995). Hydroxyurea for patients with essential thrombocythemia and a high risk of thrombosis [see comments]. New England Journal of Medicine, 332, 1132-1136.
3. MRC Working Party on Leukaemia in Adults. Primary Thrombocythaemia Trial. http://www.ctsu.ox.ac.uk/projects/pt1/
4. Barosi,G., Besses,C., Birgegard,G., Briere,J., Cervantes,F., Finazzi,G., Gisslinger,H., Griesshammer,M., Gugliotta,L., Harrison,C., Hasselbalch,H.,

Lengfelder,E., Reilly,J.T., Michiels,J.J., & Barbui,T. (2007) A unified definition of clinical resistance/intolerance to hydroxyurea in essential thrombocythemia: results of a consensus process by an international working group. Leukemia, 21, 277-280.

5. Summary of Product Characteristics Hydrea© updated 01/03/2023 Hydrea 500 mg Hard Capsules - Summary of Product Characteristics (SmPC) - (emc) (medicines.org.uk)
6. Krens S D, Lassche, Jansman G F G A, et al. Dose recommendations for anticancer drugs in patients with renal or hepatic impairment. *Lancet Oncol* 2019; **20:** e201–08.

Circulation/Dissemination

Date added into Q-Pulse	For completion by DCM
Date document posted on the Intranet	For completion by DCM

Version History

		Author name and designation	Summary of main changes
1.0	Oct 2019	**David Breen**	**Protocol created**
2.0	Aug 2023	**Jade Marsh**	**Protocol reviewed, new protocol template used**