

Management of Patients with Essential Thrombocythaemia with hydroxycarbamide

Shared Care Protocol

ONLY the **100mg** and **500mg** hydroxycarbamide formulations should be **PRESCRIBED** for safety reasons (See Prescribing Information and Administration section below)

This protocol provides prescribing and monitoring guidance for hydroxycarbamide therapy for patients with Essential Thrombocythaemia (ET). It should be read in conjunction with the Summary of Product Characteristics (SPC) available on www.medicines.org.uk/emc and the [BNF](#).

See also [Hydroxycarbamide for Polycythaemia Vera \(PV\) SCP](#) and [Hydroxycarbamide Therapy in Sickle Cell Disease SCP](#)

Shared Care Responsibilities

Shared care assumes communication and agreement between the specialist, GP and patient. The intention to share care should be explained to the patient and accepted by them. Patients are under regular follow-up and this provides an opportunity to discuss drug therapy. Specialists must contact GPs as soon as decision is made to commence treatment with the antibiotic regimen to ensure adequate time for full communication, support and agreement to be made. Specialists must retain prescribing until the patient's clinical condition is stable or predictable.

Specialist

- Complete pre-treatment assessment
- Initiate treatment and prescribe until the dose is stable and/or the GP formally agrees to shared care (*The expectation would be for the specialist to prescribe the first 28 days of treatment*)
- Ensure the patients understand the nature and complications of drug therapy and their role in reporting adverse effects promptly
- Provide copy of patient information leaflet and drug monitoring card where appropriate
- Send a letter to the GP requesting shared care. Outline shared care protocol criteria
- Liaise with GP regarding changes in disease management, drug dose, missed clinic appointments
- Be available to give advice to GP and patient throughout treatment

GP

- **Prescribe medication once the dose is stable or shared care is agreed**
- Ensure all monitoring is completed in accordance to the specific shared care protocol (listed under on-going monitoring).

- Check and record results then advise the specialist of any deteriorations or abnormal results
- Notify the specialist to any changes in patients condition, any adverse drug reactions or failure to attend tests

Patient

- Agree to treatment and monitoring after making an informed decision
- Agree to being under the shared care of the GP and specialist
- Attend for blood tests and monitoring when required
- Ensure monitoring card is kept up to date and is brought to all appointments
- Report any side effects to the GP or a member of the specialist team

Background for Use

Essential Thrombocythaemia (ET) is a myeloproliferative disorders characterised by a persistently elevated platelet count. Vascular events including venous and arterial thromboembolism and also bleeding are among the main clinical complications, although there is a small risk of evolution to myelofibrosis (5-10%) and to acute myeloid leukaemia (<5%). In many patients, the diagnosis is made incidentally from a routine full blood count, and management is undertaken in the outpatient setting.

Hydroxycarbamide is a cytoreductive agent used for the treatment of myeloproliferative disorders to control the platelet count, and occasionally other blood counts

Supporting Information

Further information on the shared care of patients with Essential Thrombocythaemia who require Hydroxyurea (Hydroxycarbamide) therapy is provided below and in the flow chart at the end of this document

Contraindications and Precautions

Contraindication	Action
Renal Impairment	Dose should be reduced if GFR <50mL/min, but any dose reduction as a result of renal impairment should be carried out by haematology dept only
Pregnancy and Lactation	These patients should be under specialist management only

Dosage

Indication	Dose
Myeloproliferative Neoplasm e.g. ET	20-30mg/kg/day PO, adjusted to platelet and neutrophil counts. Lower starting doses are often used in elderly patients. For the majority of patients this is in the order of 0.5-2g/day

Prescribing Information and Administration

Hydroxycarbamide formulations are available in three strengths:

- 100mg tablets - Siklos
- 500mg capsules – (non-proprietary)
- 1000mg tablets – Siklos

ONLY the 100mg and 500mg hydroxycarbamide formulations should be prescribed for safety reasons

- For a sample prescription – see below
- Hydroxycarbamide should be taken once daily, preferably in the morning before breakfast and, where necessary, with a glass of water or a very small amount of food.
- For patients who are not able to swallow the Siklos tablets, these can be disintegrated immediately before use in a small quantity of water in a teaspoon. Adding a drop of syrup or mixing with food can mask a possible bitter taste.

Sample prescription

For a dose of 1200mg daily prescribe as

Hydroxycarbamide 500mg capsules
Two to be taken in the morning before breakfast

Hydroxycarbamide 100mg tablets
Two to be taken in the morning before breakfast

Time to Response

Variable, most patients respond within 1-2 weeks but require longer to achieve stable dose

Pre-Treatment Assessment is done by the specialist team

Ongoing Monitoring in Shared Care

The rationale for treatment is primarily to prevent arterial and venous thrombosis and haemorrhage, which are all increased in these patients. Some patients with ET have significant symptoms which is also an indicated for treatment in certain cases.

Treatment will be initiated by the Haematology service. If cytoreductive therapy is commenced, the patient will be monitored until his/her platelet count has stabilised. At this point, if considered appropriate by the patient's haematologist and general practitioner, shared care may be possible with Primary Care services. Patients are typically managed primarily through the hospital nurse-led telephone and/or face-to-face clinic, with input from consultant specialists and GP as required. Although dose

changes are usually made in the nurse-led clinic, a flow chart for the ongoing monitoring of Hydroxycarbamide (Hydroxyurea) treatment is included on page 7. Patients will be on a dose usually between 0.5g/day to 2.5g/day. Often, patients will need a dose that varies daily (e.g. 0.5g/1.0g alternate days, or 0.5g/0.5g/1.0g every 3 days).

****Blood test monitoring and dose adjustments are typically done in the nurse-led clinics for suitable patients under shared care, but it is helpful for the GP to continue to prescribe hydroxycarbamide for these patients.****

A major aspect of managing these patients, be it in specialist clinics or in the community, involves **reducing their thromboembolic risk factors, in particular smoking, diabetes, high cholesterol and hypertension**. Blood pressure monitoring, fasting lipid and glucose levels and smoking cessation advice where appropriate as just as important for these patients as cytoreductive therapy and aspirin.

The main **complication** with treating patients with cytoreductive therapy is the possible development of neutropenia, which can be life-threatening if severe (neutrophils $<0.5 \times 10^3/\text{mm}^3$). Managing these patients in the community therefore requires a high degree of awareness of this complication and an appropriate management plan should the neutrophil count begin to drop.

Patients being looked after in the community will remain under shared care with the Haematology Specialists and **a clear set of indications for specialist review** is important. These include:

- ***the patient requires ever increasing doses of cytoreductive therapy to control the counts***
- ***the counts cannot be controlled by cytoreductive therapy***
- ***the patient develops any adverse effects (e.g. GI disturbance, skin rash/leg ulcer)***
- ***the patient complains of abdominal discomfort/has an enlarging spleen***
- ***the patient develops any thrombotic event***
- ***the neutrophil count drops to $<1.0 \times 10^3/\text{mm}^3$ or Hb $< 10.0\text{g/dL}$***

There will always be open access to the Clinical Haematology Department in the Cancer and Haematology Centre at the Churchill Hospital, and the Laboratory Haematology Specialist Registrar will always be contactable through the switchboard during normal working hours to answer any query, large or small.

Monitoring and Actions to be taken

Regular full blood count monitoring is required (minimum of 3-monthly if stable, otherwise more often as per flow-chart)

Possible Side Effects

Side Effects	Action
<i>Neutropenia (see flow chart for levels)</i>	<i>Can be severe and life-threatening, requires regular monitoring and dose adjustment as per flow chart.</i>
<i>Anaemia</i>	<i>Requires dose adjustment as per flow chart.</i>
<i>Gastro-intestinal e.g. anorexia, nausea, diarrhoea</i>	<i>Usually most prominent when patient commences treatment and then settle within a couple of weeks</i>
<i>Skin rash or skin ulcers, sun sensitivity</i>	<i>Skin ulcers require cessation of treatment. Caution patients regarding sun exposure</i>

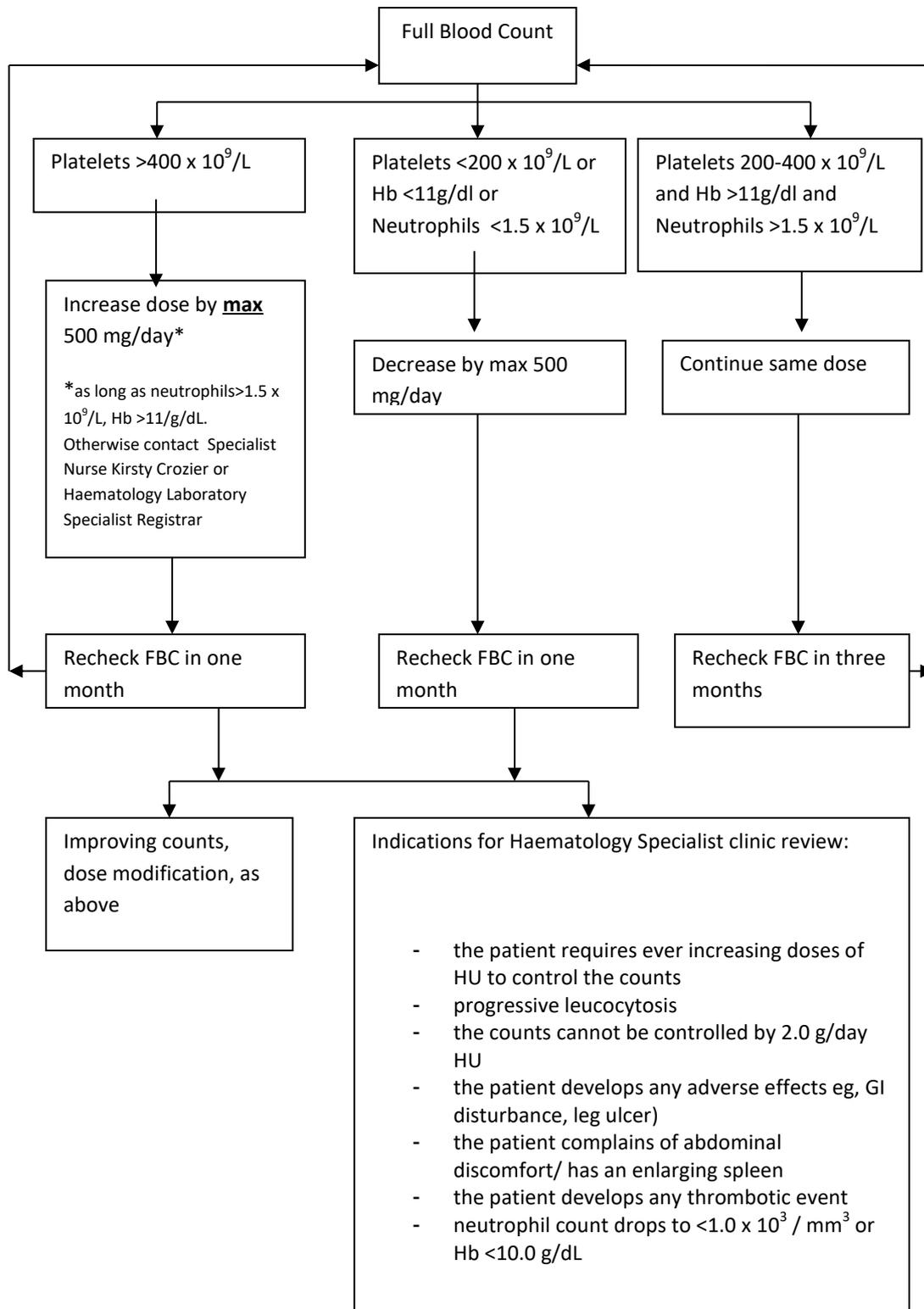
Notable Drug Interactions (Refer to [BNF](#) and [SPC](#))

Drug Interactions	Please also refer to BNF or SPC
Other cytotoxic drugs	Can cause more severe myelosuppression if taken with other cytotoxic drugs
Uricosuric drugs	May need dose adjustment

FLOW CHART FOR ADJUSTING HYDROXYCARBAMIDE DOSES ACCORDING TO BLOOD COUNTS.

Please contact the nurse specialist for advice if required.

- For the majority of patients, monitoring of counts and dose adjustments are done in the nurse-led hospital clinic although in some cases patient care is GP led.
- Careful history should be sought to identify stressors e.g. illnesses/new medications that have caused the changes in blood counts in previously stable patients.
- The flowchart below indicates the ***maximum*** recommended dose change. Dose adjustments should be decided on a case-by-case basis. For elderly patients / patients with renal impairment, dose adjustments may need to be modest (e.g. 500mg per week) with interim FBC checks to avoid dramatic fluctuations in blood counts.



Back-up Information and Advice

Oxford Radcliffe Hospital Haematology Department Contact details	
Haem Registrar on call	Bleep Haematology SpR on call: Bleep 1836 via switchboard 01865 741841
Advanced Nurse Practitioner for Myeloid Disorders	Kirsty Crozier: 01865 235287 and 07766 632856 (available Tues, Wed, Thurs) Email: kirsty.crozier@nhs.net
Haematology Clinical Nurse Specialist	Caroline Allman – 01865 235287; bleep 5095 via switchboard. Email: caroline.allman@ouh.nhs.uk
Consultant contact details: Adam Mead MRCP, FRCPath, PhD Consultant Haematologist	Level 2, Cancer and Haematology Centre Churchill Hospital Old Road, Headington Oxford OX3 7LJ Phone: +44 (0) 1865 222325 Fax: +44 (0) 01865 235260 Clinical Secretary: James Harker 01865 235880

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