Oxford University Hospitals NHS
NHS Trust

NHS
Oxfordshire
Clinical Commissioning Group

Hydroxycarbamide for Polycythaemia Vera (PV)
Shared Care Protocol

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

This protocol provides prescribing and monitoring guidance for management of patients with polycythaemia vera (PV) treated with hydroxycarbamide. 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 Management of Patients with Essential Thrombocythaemia with hydroxycarbamide 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.

Patients with PV being treated with venesection and/or hydroxycarbamide may be suitable for shared care between the haematology specialist team and their GP, with specialist input only when required.

Typically, stable patients who are suitable for shared care are managed primarily in the nurse-led telephone and face-to-face clinics to monitor blood results and arrange for venesections/hydroxycarbamide dose adjustments as required.

For patients managed in the nurse-led clinic, it is very helpful if the GP can continue to prescribe hydroxycarbamide.

Flow charts for the management of venesection and hydroxycarbamide in shared care are shown below, although dose adjustments will typically be done by the hospital haematology team.

For advice, please contact the haematology team - Nurse Practitioner Kirsty Crozier (available Tues, Wed, Thurs); Haematology Clinical Nurse Specialist Caroline Allman or the Haematology Secretary James Harker (see contact details at the end of this document).

Please notify the specialist to any changes in patients condition, any adverse drug reactions or failure to attend tests

Shared Care responsibilities

Specialist

- Complete pre-treatment assessment (detailed below)
- 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

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

Polycythaemia Vera (PV) is a myeloproliferative disorder characterized by an increased red blood cell production and increased haematocrit (Hct) due to mutations in a gene called JAK2 (e.g. JAK2V617F mutation). Vascular events including venous and arterial thromboembolism are the main clinical complications. In a minority of patients, PV can transform to myelofibrosis (~10% patients) and acute myeloid leukaemia (~5%)

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

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. Often a lower dose is 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
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ONLY the **100mg** and **500mg** hydroxycarbamide formulations should be prescribed for safety reasons

- For a sample prescription – see below
- Only Hydrea capsules are licensed for chronic myeloid leukaemiadisease. They are licensed for children >2 years old.
- 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 2-4 weeks but may 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 PV 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 blood counts have 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 8. 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 x10^3/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 x10^3 /mm^3 or Hb < 10.0 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
Neutropenia (see flow chart for levels)	*Can be severe and life-threatening, requires regular monitoring and dose adjustment as per flow chart.*
Anaemia	*Requires dose adjustment as per flow chart.*
Gastro-intestinal e.g. anorexia, nausea, diarrhoea	*Usually most prominent when patient commences treatment and then settle within a couple of weeks*
Skin rash or skin ulcers, sun sensitivity	*Skin ulcers require cessation of treatment. Caution patients regarding sun exposure including risk of skin tumours with long term use.*

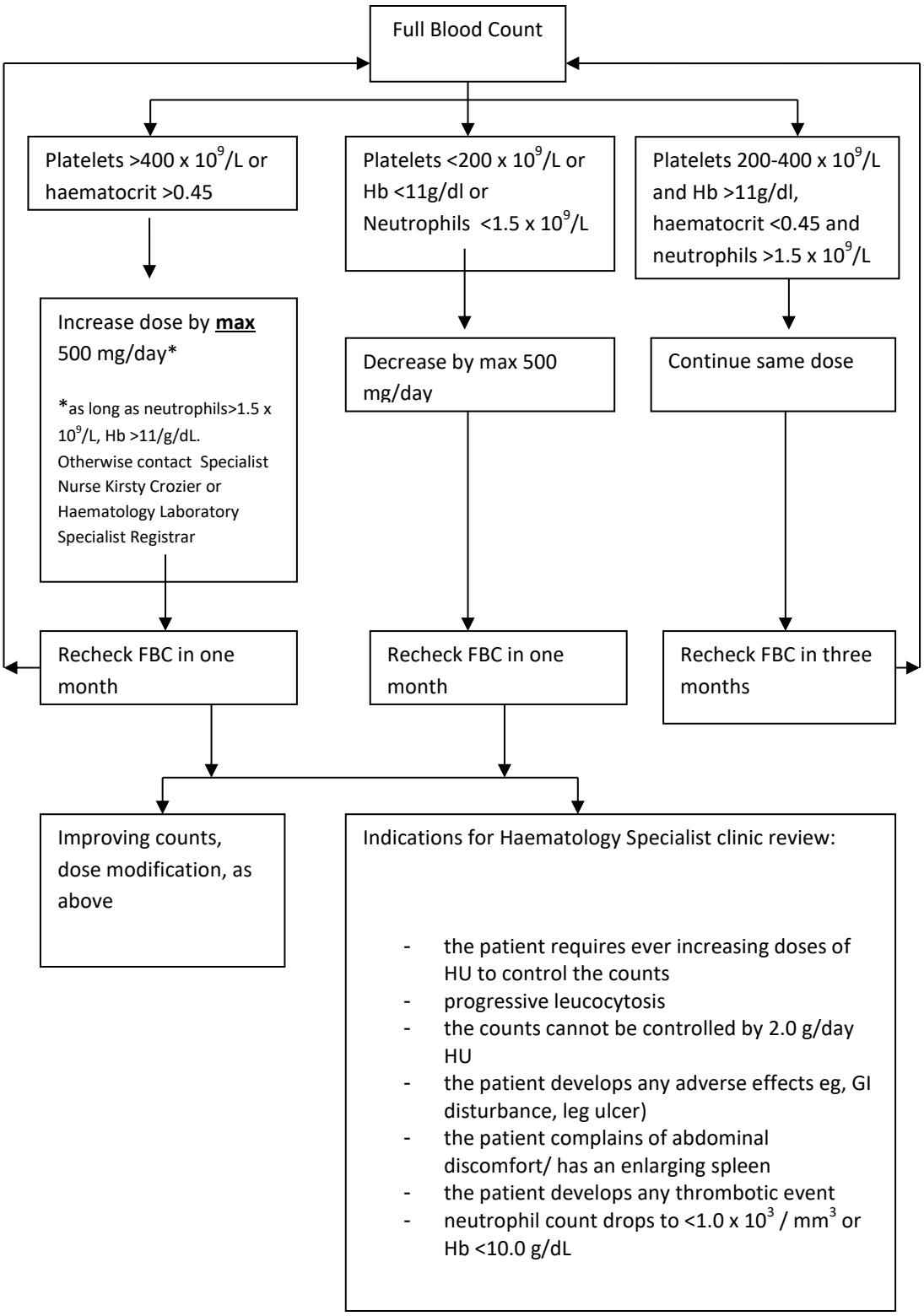
Notable Drug Interactions (Refer to BNF and SPC)

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. This will be made clear in the initial communication from the haematology clinic.
- 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.


Full Blood Count
Platelets >400 x 10^9/L or haematocrit >0.45
Platelets <200 x 10^9/L or Hb <11g/dl or Neutrophils <1.5 x 10^9/L
Platelets 200-400 x 10^9/L and Hb >11g/dl, haematocrit <0.45 and neutrophils >1.5 x 10^9/L
Increase dose by max 500 mg/day*
*as long as neutrophils>1.5 x 10^9/L, Hb >11/g/dL. Otherwise contact Specialist Nurse Kirsty Crozier or Haematology Laboratory Specialist Registrar
Decrease by max 500 mg/day
Continue same dose
Recheck FBC in one month
Recheck FBC in one month
Recheck FBC in three months
Improving counts, dose modification, as above
Indications for Haematology Specialist clinic review:
- the patient requires ever increasing doses of HU to control the counts
- progressive leucocytosis
- the counts cannot be controlled by 2.0 g/day HU
- the patient develops any adverse effects eg, GI disturbance, leg ulcer)
- the patient complains of abdominal discomfort/ has an enlarging spleen
- the patient develops any thrombotic event
- neutrophil count drops to <1.0 x 10^3 / mm^3 or Hb <10.0 g/dL

Back-up Information and Advice, Contact Details

Oxford Radcliffe Hospital Haematology Department Contact Details	
Registrar on call	Bleep Haematology SpR on call: Bleep 1836 via switchboard 01865 741841
Advanced Nurse Practitioner for Myeloid Disorders	Kirsty Crozier: 01865 235287; Mobile – 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

References

Change Control			
Input	Dr Adam Mead (OUHT), Kirsty Crozier (OUHT), Dr Beth Psaila (OUHT), Louisa Griffiths (OCCG)		
Approved by	Oxfordshire Area Prescribing Committee		
Notes	Version 2		
Date published	October 2018	**Review Date**	October 2020

Amendment to the diagnosis and investigation of polycythaemia/erythrocytosis *British Journal of Haematology* 2007; 138 (6): 821-2

Guidelines for the Diagnosis, Investigation and Management of Polycythaemia/ Erythrocytosis. *British Journal of Haematology 2005; 130(2): 174-95 [New updated guidelines to be published soon]*