The Princess Alexandra Hospital NHS NHS Trust

NHS West Essex Clinical Commissioning Group

Shared Care Agreement

HYDROXYCARBAMIDE – MYELOPROLIFERATIVE NEOPLASMS

For up to date version of Shared Care Agreement contact specialist team or latest version on website https://westessexccg.nhs.uk/your-health/medicines-optimisation-and-pharmacy/shared-care-medicines

Referral Criteria

- Shared Care is only appropriate if it provides the optimum solution for the patient.
- Prescribing responsibility will only be transferred when it is agreed by the consultant and the patients' GP
- Safe prescribing must be accompanied by effective monitoring

When transfer is agreed, the patient will be given a supply of hydroxycarbamide sufficient for 4 weeks maintenance therapy

The doctor who prescribes the medication has the clinical responsibility for the drug and the consequences of its use.

These guidelines are for treating patients over 16 years of age with the following conditions:

polycythaemia vera – an increase above the normal in the number of red cell in the blood (normal range 4.50 - 5.50 x 10^{12}/L)

essential thrombocythaemia – Increase in the number of platelets in the circulating blood (normal range 150 – 450 x 10^{9}/L)

primary myelofibrosis – fibrosis of the bone marrow

Sharing of care depends on communication between the Specialist, GP and the patient or their parent/carer. 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.

SHARED CARE RESPONSIBILITIES

Consultant

Undertake the necessary testing to confirm a diagnosis for which hydroxycarbamide treatment is recommended.

Ensure the patient's concurrent drug therapy is stabilised and there are no contra-indications to treatment with hydroxycarbamide

Ensure that patient is aware of risks and benefits of medication and has read appropriate information leaflet.

Ensure women of childbearing potential have to use effective contraception before the start of and during treatment with hydroxycarbamide; and Men under therapy are advised to use effective contraception during and for at least 3 months after therapy. They should be informed about the possibility of sperm conservation before the start of therapy. BNF and SPC do not report interactions between hydroxycarbamide and hormonal contraceptives.

Ensure the patient understands the shared care agreement and has signed the Patient Agreement Letter

Perform baseline tests (see Monitoring section) and provide results to GP

Initiate treatment and prescribe until initiation phase is complete and patient is in maintenance phase.

Send a letter to the GP requesting shared care for this patient.

Review the patient in outpatients as clinically appropriate and advise the GP promptly after these reviews on when to adjust the dose, stop treatment or consult with the Specialist.

Inform GP, by letter, of each clinic attendance and action taken for the management of the patient ensuring current dose, most recent blood results and frequency of monitoring are stated.

Evaluate any reported adverse effects by GP or patient.

Inform GP of patients who do not attend clinic appointments, admin to contact patient to rearrange.

Ensure that backup advice is available at all times. (see Contacts section)

12. To report any adverse events to the CHM and GP (see link) Yellow Card MHRA

General Practitioner

Monitor patient's overall health and well-being.

Respond to the request for Shared Care as soon as practicable. If concerns regarding shared care, urgently contact the Consultant and complete attached letter with clinical reasons and return to Consultant and Pharmacy department.

Ensure compatibility with other concomitant medication.

Prescribe at the dose recommended.

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Monitor U&E, creatinine, FBC and LFTs at recommended frequencies (see monitoring section) and refer if abnormal.
Adjust the dose as advised by the Specialist.
Stop treatment on advice of Specialist or immediately if any urgent need to stop treatment arises (see monitoring section).
Report any adverse events to the Specialist and CHM. Yellow Card MHRA
Inform Specialist of any change in the medical condition of patient which may have effect on disease / medications.

Patient

Report to Specialist if there is not a clear understanding of their treatment and discuss any concerns in relation to treatment
Report any adverse effects to their Specialist whilst taking hydroxycarbamide especially unexplained bruising/bleeding.
Report any changes in disease symptoms to Specialist whilst taking hydroxycarbamide
Alert GP and/or Specialist of any changes of circumstance which could affect management of disease
Inform GP or Specialist of any other medicines being taken including over-the-counter products.
Attend for regular reviews and blood monitoring tests.

CONTACT NUMBERS FOR ADVICE AND SUPPORT

Princess Alexandra Hospital NHS Trust - Haematology	
Haematology Consultant	01279 827035/ 01279 444455 Ext 2891

Princess Alexandra Hospital NHS Trust - Pharmacy	
Medicines Information (for medicines related queries)	01279 827054

Licensed indication

From SPC Licensed for the treatment of chronic myeloid leukaemia and cancer of the cervix in conjunction with radiotherapy. https://www.medicines.org.uk/emc/medicine/19081

Therapeutic Summary

Hydroxycarbamide is an oral cytoreductive agent used for the treatment of myeloproliferative neoplasms (MPN) eg polycythaemia vera, essential thrombocythaemia and primary myelofibrosis. These are unlicensed indications.

The Philadelphia-negative MPNs - polycythaemia vera, essential thrombocythaemia and primary myelofibrosis – are haematological disorders characterised by increased blood counts, which may include haemoglobin / haematocrit, neutrophil count and/or platelet count. They are associated with an increased incidence of vascular complications, predominantly thrombosis but also haemorrhage. Thrombotic risk can be reduced by the use of low-dose aspirin, together with additional therapy to control the blood counts in the majority of patients. Blood count control frequently requires the use of cytoreductive medication, of which the most frequently prescribed is hydroxycarbamide, an orally administered inhibitor of ribonucleotide reductase.

Dose and Route of Administration

Hydroxycarbamide is available as 500mg capsules.

Starting doses are typically 500mg or 1g daily and subsequent dosing is determined by the FBC, typically ranging from 500mg – 2g daily. It is common for the dose to vary according to the day of the week e.g. 1g daily Monday to Friday, 1.5g on days Saturday &Sunday or 500mg on days Monday, Wednesday and Friday.

Most patients require several dose adjustments in the first months of treatment and then fewer adjustments subsequently.

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Adverse Effects

Very common (≥ 1 in 10)
Azoospermia, oligospermia

Common (≥ 1 in 100 and < 1 in 10)
Bone marrow depression, leucopenia
Megaloblastosis (raised mean corpuscular volume, MCV); an isolated macrocytosis without cytopenias can be ignored.
Diarrhoea, constipation

Uncommon (≥ 1 in 1000 and < 1 in 100)
Thrombocytopenia, anaemia
Maculopapular rash
Anorexia
Peripheral neuropathy
Pancreatitis, nausea, vomiting, stomatitis
Raised liver enzymes
Raised blood urea / creatinine
Drug fever, chills, malaise

Rare (≥ 1 in 10000 and < 1 in 1000)
Hypersensitivity reaction
Tumour lysis syndrome
Hallucinations
Neurological disturbances
Acute pulmonary reactions
Alopecia
Dysuria
Skin reactions (e.g. skin hyperpigmentation / atrophy, nail pigmentation / atrophy, skin / mouth ulcers, skin cancers, cutaneous vasculitis). Leg ulcers generally require cessation of therapy, often permanently.
In patients receiving long-term treatment with hydroxycarbamide for MPNs, secondary leukemia may develop. Although some researchers have raised the suggestion that hydroxycarbamide increases this risk, this remains unsubstantiated and is refuted by a number of large clinical studies.
Further information can be found in the Summary of Product Characteristics (SPC)
https://www.medicines.org.uk/emc/medicine/18928

Cautions

Myelosuppression (leucopenia, thrombocytopenia or severe anaemia).
Experience is limited in patients with impaired renal and/or liver function. Therefore special care should be taken in the treatment of these patients, especially at the beginning of therapy.
Further information can be found in the SPC https://www.medicines.org.uk/emc/medicine/18928

Contraindications

Severe bone marrow depression, leucopenia (white cell count <2.5 x 10^9/l), thrombocytopenia (platelets <100 x 10^9/l), severe anaemia. Patients on therapy who are found to have cytopenias should be discussed with a haematologist prior to discontinuation of therapy or dose reduction (see below).
Hypersensitivity to the active substance of to any of the excipients listed in the SPC.
Female patients should be advised not to conceive whilst receiving hydroxycarbamide. A reliable form of contraception should be used by men and women whilst on hydroxycarbamide and for at least 3 months afterwards.
Patients should not breastfeed whilst receiving hydroxycarbamide.

Live vaccines should be avoided by patients receiving hydroxycarbamide.
Further information can be found in the SPC https://www.medicines.org.uk/emc/medicine/18928

Interactions

Hydroxycarbamide may enhance the antiretroviral activity of nucleoside reverse transcriptase inhibitors like didanosine and stavudine. Hydroxycarbamide may also enhance potential side effects of these drugs such as hepatotoxicity, pancreatitis and peripheral neuropathy.
There is an increased risk of bone marrow depression, gastric irritation and mucositis in patients taking hydroxycarbamide with previous or concomitant radiotherapy or cytotoxic therapy.
Further information can be found in the SPC https://www.medicines.org.uk/emc/medicine/18928

Monitoring

During the initiation phase of treatment, when the dose is being optimised, the FBC may be monitored at intervals of 1-12 weeks. During the maintenance phase, the FBC will be monitored a minimum of 4-monthly.
If dose adjustments are made the Specialist will advise the GP on the plan for frequency of monitoring FBC.

Most patients on treatment are expected to have blood counts in the target range, as below. In the event of an unexpectedly low or high count, the following guidance is suggested:

Haemoglobin	< 80 g/l 80-109 g/l with symptoms	80-109 g/l, no symptoms	≥ 110 g/l
Haematocrit	≥0.50 0.45-0.50 with symptoms	0.45-0.50, no symptoms	< 0.45
Neutrophil count	< 1.5 x 10^9/l	1.5-1.9 x 10^9/l	≥ 2.0 x 10^9/l
Platelet count	< 100x10^9/l > 1000 x 10^9/l	100-150 x 10^9/l 450-1000x10^9/l	150-450 x 10^9/l
Action	Discuss with Specialist within 72 hours at the latest	Can be reviewed at next haematology consultation (should be within 2 weeks if abnormalities are new)	Satisfactory: no action

Patients who are found to have unexpectedly high blood counts (haematocrit >0.50 or platelet count >1000 x 10^9/l) or new symptoms should be discussed with the hospital Specialist team.
Side effects that require immediate discussion with the hospital Specialist team include severe bone marrow suppression (neutrophil count <1.5 x 10^9/l, platelet count <100 x 10^9/l or haemoglobin <80 g/l), severe mouth ulcers or leg ulcers. Patients presenting with symptoms that may reflect cytopenias (e.g. fever, sore throat, bleeding, bruising, symptoms of anaemia) should also have a full blood count checked urgently.
U&E, creatinine and liver function tests will be monitored a minimum of 4-monthly.
If creatinine clearance <45ml/min discuss with Specialist
If >3 fold increase in ALT / AST discuss with Specialist

References

Summary of Product Characteristics – Hydroxycarbamide Medac Brand
http://www.medicines.org.uk/emc/medicine/18928 -

West Essex Shared Care Agreements http://westessexccg.nhs.uk/your-health/medicines-optimisation/shared-care-medicines

Therapeutic indications
Treatment of patients with essential thrombocythemia or polycythemia vera with a high risk for thromboembolic complications.
British National Formulary- latest edition www.medicinescomplete.com
J.T.Reilly , M McMullin, P Beer et al. Guideline for the Diagnosis and Management of Myelofibrosis
British Journal of Haematology 2012 Vol 158 P 453-471

"Hydroxycarbamide is the most widely used agent despite limited published data supporting its efficacy" http://onlinelibrary.wiley.com/doi/10.1111/j.1365-2141.2012.09179.x/full BHS Guideline Harrison et al Guidelines for investigation and management of adults and children presenting with a thrombocytosis
British Journal of Haematology 2010 Vol 149 P 352-375
http://onlinelibrary.wiley.com/doi/10.1111/j.1365-2141.2010.08122.x/full BHS Guideline

GP response to Shared Care Agreement

(only complete & send if NOT participating in shared care)

This shared care agreement has been approved by the Medicines Management Optimisation Programme Board

Shared Care Agreement

HYDROXYCARBAMIDE – MYELOPROLIFERATIVE NEOPLASMS

Patient Name:	NHS No:
Consultant:	Medicine requested for shared care: **Hydroxycarbamide**

I will **NOT** be undertaking the GP responsibilities as described in the agreed shared care agreement. My clinical reasons for declining shared care for this patient are listed in the box below:

Yours sincerely

{GP name}

{Surgery}

Please send a copy of this response to:
1. The Specialist/consultant requesting shared care
2. **ANONYMISED COPY OF THIS FORM ONLY** to the E-MAIL: **tpa-tr.ClinicalPharmacy@nhs.net**

(sending a copy of this form to the PAH pharmacy will help to identify any inappropriate requests for shared care e.g. indication not covered, hospital monitoring requirements not fulfilled. It will also help to inform the CCG Medicines Optimisation Team of the reasons shared care is not being undertaken by GPs allowing for changes to be made in future updates to improve patient safety)

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The Prlncess Alexandra Hospltal NHS
NHS Trust

Hamstel Road
Harlow, Essex
CM20 1QX

Tel: 01279 444455

Information for patients:

SHARED CARE: Agreement information and confirmation

Patient name:

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Medicine:

.....

We would be grateful if you would take time to read this information as it will help us work with you to manage your condition and ensure safe prescribing of the specific medicine listed above.

What is a Shared Care Agreement (SCA)?

A Shared Care Agreement (SCA) enables the care you have for a specific condition to be shared between the hospital and your GP.

The agreement means that the medicine the hospital has started, can be continued by your GP, so you won't have to visit the hospital to collect your medicine.

The SCA gives information on your medicine, guidance on the prescribing and monitoring responsibilities for your consultant (in the hospital), your GP and you. For an SCA, to work everyone involved must understand it and communicate effectively.

Your consultant and your GP will need to sign the agreement and if you agree to this approach, we would ask you to sign this letter, to indicate your agreement to have your care managed in this way.

How does shared care work?

Your consultant and GP share responsibility for your care.

The consultant is a specialist in your condition and will start prescribing your medicine, making sure it is suitable for you. There will come a point in your treatment when you may not need to be monitored by the consultant as often and this monitoring can be done by your GP.

Once your GP has agreed to the SCA, they will be able to prescribe the same medicine for you at the dose recommended by the consultant.

The organisation which regulates GPs, the General Medical Council, says that 'when a GP prescribes a medicine, the GP needs to satisfy themselves that the prescription is needed, appropriate for the patient and within the limits of their competence'.

So, your GP can only issue a prescription if the consultant and you keep to the responsibilities you have agreed (see below). If responsibilities are not kept or if the GP no longer feels it is safe to prescribe the medicine, he/she will explain the reasons to you and your consultant, then prescribing responsibilities will be transferred back to the hospital.

What do I need to do to ensure the SCA can continue?

- **Attend hospital outpatients**

You must still attend the hospital for regular reviews as directed by your consultant (these may be less frequent than before and you may be seen by a specialist pharmacist or a specialist nurse). If you do not attend your hospital appointments, your GP will not be able to continue issuing prescriptions for this medication.

- **Attend GP appointments**

You must attend any appointments you have with your GP in relation to this medicine, so they can look after you effectively

- **Have blood tests as you have been advised to:** Your consultant should have informed you if and how often you need to have blood monitoring tests. You can usually have your blood taken at an appropriate clinic and not need to go to the hospital.

- If you do not have the blood monitoring tests as advised by your consultant, your GP will no longer be able to issue you with prescriptions as it would not be safe to do so.

What do I do if I am having side-effects to the medicine?

Your consultant should have informed you of the common side-effects to expect and what to do if you experience them. If you think you may be having side-effects from a medicine report these directly to your consultant. Your GP may need to seek advice from your consultant before issuing you with another prescription; this is to ensure it is safe for you to continue on the medication.

What if my disease symptoms change or get worse?

Report any changes in disease symptoms or circumstances that could affect management of your disease to your consultant.

What about the other medicines I take?

Inform your GP and the consultant of all other medicines you are taking, including those you may have bought yourself. Do not take new medicines (including those you could buy) until you have discussed this with your pharmacist, GP or consultant.

If you would like to go ahead with a shared care agreement for the specific medication identified on page 1, please sign below to confirm that you:

- Understand the shared care agreement.

- Are happy to have your care for this aspect of your health managed by a shared care agreement.

- You agree to attend regular review appointments as requested.

- You agree to have blood tests as required.

What happens if I change GP Practice?

If you register at a new GP Practice a new agreement needs to be put in place between your new GP and the specialist team.

The specialist team can start this process if you provide them with information before you move to make sure there is a smooth handover.

Patient's signature .....

Date .....

Print name .....

If at any point in time you would like this shared care agreement to stop, please talk to your GP.