Chemotherapy Protocol

Chronic Myeloid Leukaemia (CML)

Hydroxycarbamide

Regimen

- CML - Hydroxycarbamide

Indication

- Chronic or accelerated phase chronic myeloid leukaemia in those who are intolerant or refractory to a tyrosine kinase inhititor.

Toxicity

Drug	Adverse Effect
Hydroxycarbamide	Bone marrow suppression, anorexia, pancreatitis, gastrointestinal disturbance, abdominal pain, hepatotoxicity, cholestasis, cutaneous vasculitis, dermatomyositis, alopecia, skin rash pyrexia, dysuria, leg ulcers

The adverse effects listed are not exhaustive. Please refer to the relevant Summary of Product Characteristics for full details.

Monitoring

Drugs

- FBC, U&Es and LFTs prior to initiating hydroxycarbamide, then two weekly initially. This may be increased to 3 monthly in stable, responding patients, or as clinically indicated.

Dose Modifications

The dose modifications listed are for haematological, liver and renal function and drug specific toxicities only. Dose adjustments may be necessary for other toxicities as well.

Please discuss all dose reductions / delays with the relevant consultant before prescribing, if appropriate. The approach may be different depending on the clinical circumstances.

Haematological

Dose modifications for haematological toxicity are for general guidance only. Always refer to the responsible consultant as any dose reductions or delays will be dependent on clinical circumstances and treatment intent.

In CML hydroxycarbamide is given at an initial dose of 40 mg/kg daily, dependent on the white cell count. The dose should be reduced by 50% to 20 mg/kg daily when the WBC has dropped below $20x10^9$/L. The dose should then be individually adjusted to keep the white cell count between 5-$10x10^9$/L. The hydroxycarbamide dose should be reduced if the WBC falls below $5x10^9$/L and increased if WBC becomes elevated to more than $10x10^9$/L.

If the WBC falls below $2.5x10^9$/L, or the platelet count below $100x10^9$/L, therapy should be interrupted in order to determine whether the cytopenia is treatment or disease related. If disease related, treatment may resume at the discretion of the consultant haematologist.

Hepatic Impairment

Dose reductions are probably not necessary in patients with hepatic impairment. However, due to a lack of information, this remains a clinical decision. Frequency of monitoring may need to be increased.

Renal Impairment

GFR (mL/min)	Dose (% of original dose)
More than 60	85% and titrate to response
45 - 60	80% and titrate to response
30 - 45	75% and titrate to response
10 – 30	50% and titrate to response
Less than 10	20% and titrate to response

Other

Hydroxycarbamide syndrome is a rare syndrome consisting of fever, hepatitis and pneumonitis occurring within four weeks of commencing therapy. It has a high mortality. The hydroxycarbamide should be stopped immediately on suspicion of this condition and not re-started.

Regimen

28 day cycle until disease progression or intolerance (6 cycles will be set in Aria)

Initial response to treatment should be determined after 6 weeks. If there is a significant clinical response, treatment may continue indefinitely.

Drug	Dose	Days	Administration
Hydroxycarbamide	40mg/kg once a day*	1 -28 (inclusive)	Oral

* The dose should be calculated on the patient's actual or ideal body weight, whichever is less.

The dose may require adjustment in response to changes in the white cell and platelet count.

Dose Information

- Hydroxycarbamide is only available as a 500mg hard capsule (a 100mg and 1000mg tablet are available but are only licensed for sickle cell disease. They are not in routine use). Doses are rounded up or down to the nearest number of capsules. For more accurate dosing, a variable dose scheme may need to be utilised. Doses will be rounded to the nearest 250mg on ARIA, this may need to be adjusted on an individual patient basis.

Administration Information

- Hydroxycarbamide capsules should be swallowed whole once a day.

- In those with swallowing difficulties an unlicensed liquid preparation is available. Alternatively the contents of the capsule can be dispersed in a glass of water, immediately prior to administration. The contents of the capsule must not be inhaled or be allowed to come into contact with the skin or mucous membranes. Spillages must be wiped immediately. The patient must be informed of safe handling procedures for oral chemotherapy. Nursing staff must also follow such procedures during administration to patients unless this practice is prohibited in your local Trust. Please refer to your local institutional guidelines on oral chemotherapy administration.

Additional Treatment

- Allopurinol 300mg once a day until the white cell count is less than $10x10^9$/L.

Additional Information

- The National Patient Safety Alert on oral chemotherapy (NPSA/2008/RRR001) must be followed in relation to hydroxycarbamide.

- It must be made clear to all staff, including those in the community, that hydroxycarbamide should be prescribed under the supervision of a consultant haematologist, or a trust approved shared care agreement.

- The concomitant use of hydroxycarbamide and didanosine, with or without stavudine, is contraindicated due to an increased risk of fatal and non-fatal hepatotoxicity. Other drug interactions may occur, always check for interactions when initiating new drugs.

Coding

- Procurement – X70.1

- Delivery – X73.1

References

1. Medac GmbH (2016). Hydroxycarbamide medac 500 mg capsule, hard Summary of Product Characteristics. Online at http://www.medicines.org.uk/emc/medicine/18928, accessed 28 November 2016.
2. University College London Hospitals NHS Foundation Trust (2009). Dosage Adjustment for Cytotoxics in Renal Impairment (Version 3). Online at http://www.londoncancer.org/media/65600/renal-impairment-dosage-adjustment-for-cytotoxics.pdf, accessed 1 November 2016.
3. University College London Hospitals NHS Foundation Trust (2009). Dosage Adjustments for Cytotoxics in Hepatic Impairment (Version 3). Online at http://www.londoncancer.org/media/65594/hepatic-impairment-dosage-adjustments-for-cytotoxics.pdf, accessed 1 November 2016.
4. Chronic Myeloid Leukemia Trialists Collaborative Group. Hydroxyurea versus busulphan for chronic myeloid leukemia: an individual patient data meta-analysis of three randomized trials. Br J Haem 2000; 110 (3):573-576.

REGIMEN SUMMARY

Hydroxycarbamide

Cycle 1

Day 1-28

1. Hydroxycarbamide 40mg/kg once a day oral
   Administration Information
   Oral chemotherapy

   The capsules can be swallowed whole, or the contents dispersed in a glass of water, immediately prior to administration. The contents of the capsule must not be inhaled or be allowed to come into contact with the skin or mucous membranes. Spillages must be wiped immediately. The patient must be informed of safe handling procedures. Nursing staff must also follow such procedures during administration to patients unless this practice is prohibited in your local Trust. Please refer to your local institutional guidelines on oral chemotherapy administration.

   Hydroxycarbamide is available as 500mg capsules. A variable dose given on alternate days may be necessary to achieve the correct dose.

2. Allopurinol 300mg once a day for 28 days oral

Cycle 2 onwards

Day 1-28

1. Hydroxycarbamide 40mg/kg once a day oral
   Administration Information
   Oral chemotherapy

   The capsules can be swallowed whole, or the contents dispersed in a glass of water, immediately prior to administration. The contents of the capsule must not be inhaled or be allowed to come into contact with the skin or mucous membranes. Spillages must be wiped immediately. The patient must be informed of safe handling procedures. Nursing staff must also follow such procedures during administration to patients unless this practice is prohibited in your local Trust. Please refer to your local institutional guidelines on oral chemotherapy administration.

   Hydroxycarbamide is available as 500mg capsules. A variable dose given on alternate days may be necessary to achieve the correct dose.

DOCUMENT CONTROL

Version	Date	Amendment	Written By	Approved By
1	January 2017	None	Eleanor Taylor Pharmacist	Dr Andrew Duncombe Consultant Haematologist

This chemotherapy protocol has been developed as part of the chemotherapy electronic prescribing project. This was and remains a collaborative project that originated from the former CSCCN. These documents have been approved on behalf of the following Trusts;

Hampshire Hospitals NHS Foundation Trust
NHS Isle of Wight
Portsmouth Hospitals NHS Trust
Salisbury NHS Foundation Trust
University Hospital Southampton NHS Foundation Trust
Western Sussex Hospitals NHS Foundation Trust

All actions have been taken to ensure these protocols are correct. However, no responsibility can be taken for errors that occur as a result of following these guidelines.