Chemotherapy Protocol

Chronic Myeloid Leukaemia

IMATINIB (accelerated phase)

Regimen

- CML - Imatinib (accelerated phase)

Indication

- As the preferred option for the treatment of people with Philadelphia-chromosome-positive CML who initially present in the accelerated phase or with blast crisis.

- As the preferred option for the treatment of people with Philadelphia-chromosome-positive CML who present in the chronic phase and then progress to the accelerated phase or blast crisis, if they have not received imatinib previously.

Toxicity

Drug	Adverse Effect
Imatinib	Oedema, fatigue, rash, nausea/vomiting, diarrhoea, cardiotoxicity, haemorrhage, muscle spasm/cramps, musculoskeletal pain, headache, periorbital oedema, raised liver enzymes, hepatitis, weight gain, renal impairment

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

Monitoring

Drugs

- FBC, LFTs and U&Es prior to starting treatment then fortnightly initially increasing to 3 monthly in stable, responding patients.

- Consider baseline evaluation of left ventricular ejection fraction in patients with known underlying heart disease or in elderly patients.

- Hepatitis B, C and HIV status should be checked prior to starting imatinib therapy. Patients who are carriers of HBV and those with active disease should be discussed with a consultant hepatologist prior to starting imatinib therapy.

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 in the table below 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.

Haematological toxicity usually presents within eight weeks of starting therapy with imatinib.

Consider blood transfusion if the patient is symptomatic of anaemia or has haemoglobin of less than 8g/dL (80g/L).

Accelerated Phase or Blast Crisis

Neutrophils ($x10^9$/L)		**Platelets ($x10^9$/L)**	**Dose Modifications**
Less than 0.5	And / or	Less than 10	Check whether the cytopenia is related to leukaemia (marrow aspirate or biopsy). If cytopenia is unrelated to leukaemia, reduce the dose to 400 mg. If cytopenia persists for 2 weeks, reduce the dose further to 300 mg. If cytopenia persists for 4 weeks and is still unrelated to leukaemia, stop imatinib until neutrophils are greater than or equal to 1 and platelets are greater than or equal to $20x10^9$/L, then resume treatment at 300 mg once a day.

Hepatic Impairment

Bilirubin µmol/L		**AST/ALT units**	**Dose (% of original dose)**
Greater than 3xULN	or	Greater than 5xULN	Withhold treatment until the bilirubin is less than 1.5xULN or ALT/AST are less than 2.5xULN, then resume treatment at a reduced dose. Reduce the 400mg dose to 300mg, 600mg dose to 400mg and 800mg dose to 600mg.

Renal Impairment

No dosage adjustment necessary. Long-term treatment with imatinib may be associated with a clinically significant decline in renal function. Renal function should be closely monitored during therapy particularly in those patients exhibiting risk factors for renal dysfunction. If renal dysfunction is observed, appropriate management and treatment should be prescribed in accordance with standard treatment guidelines.

Regimen

28 day cycle until disease progression or intolerance (12 cycles will be set in ARIA)

Accelerated Phase / Blast Crisis

Drug	**Dose**	**Days**	**Administration**
Imatinib	600mg once a day	1-28 (inclusive)	Oral

Starting doses may be increased from 600mg to a maximum of 800mg (given as 400mg twice daily) in patients with accelerated phase or blast crisis according to the European Haematology Association Guidelines.

Patients should be monitored closely following dose escalation given the potential for an increased incidence of adverse reactions at higher dosages.

Dose Information

- Imatinib is available as 400mg or 100mg tablets.

Administration Information

- Imatinib at doses of 600mg or below should be given once a day with plenty of water, with or after food. Doses of 800mg should be administered as 400mg twice a day

- For patients unable to swallow the film-coated tablets, the tablets may be dispersed in a glass of still water or apple juice. The required number of tablets should be placed in the appropriate volume of beverage (approximately 50 ml for a 100 mg tablet, and 200 ml for a 400 mg tablet) and stirred with a spoon. The suspension should be administered immediately after complete disintegration of the tablet(s).

Additional Information

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

- It must be made clear to all staff, including those in the community, that imatinib should only be prescribed under the supervision of a consultant haematologist.

- Imatinib is a substrate for the cytochrome p450 (CYP) 3A4 isoenzyme. Prescribing imatinib for co-administration with agents that are known to inhibit CYP3A4 should be undertaken with extreme caution. The concomitant use of agents that are strong CYP3A4 inducers should be avoided where possible. Imatinib has the potential to interact with many other agents. Always check for drug interactions.

Coding

- Procurement – X71.5

- Delivery – X73.1

References

1. National Institute for Health and Care Excellence. Dasatinib, nilotinib and standard-dose imatinib for the first-line treatment of chronic myeloid leukaemia [TA251]. London: National Institute for Health and Care Excellence.
2. Novartis Pharmacueticals UK Limited (2016). Glivec film-coated tablets Summary of Product Characteristics. Online at http://www.medicines.org.uk/emc/medicine/15014, accessed 1 September 2016.
3. 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 September 2016.

REGIMEN SUMMARY

Two regimens will be set up in Aria, one for the chronic phase and one for the accelerated phase of the disease.

Imatinib (accelerated phase)

Cycle 1 onwards

Day 1-28

1. Imatinib 600mg once a day oral
   Administration Information
   Oral chemotherapy

   Take with or just after food, or a meal. Take with a full glass of water. Imatinib at doses of 600mg or below should be given once a day. Doses of 800mg should be administered as 400mg twice a day.

   Please supply the nearest original whole pack according to local practice eg 30 tablets per 28 day cycle

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.