**Chemotherapy Protocol**

## Chronic Myeloid Leukaemia

# DASATINIB (chronic phase)

**Funding may be required for specific indications**

## Regimen

- CML – Dasatinib (chronic phase)

## Indication

- As a treatment option for patients with accelerated phase Philadelphia-chromosome-positive CML who are refractory to imatinib or who have developed a significant intolerance to either imatinib or nilotinib (grade 3 or 4 adverse reaction).

## Toxicity

| Drug | Adverse Effect |
|---|---|
| Dasatinib | Pulmonary arterial hypertension (PAH), pleural effusion, dyspnoea, headache, haemorrhage, nausea and vomiting, diarrhoea, skin rash, musculoskeletal pain, oedema, fatigue. |

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

## Monitoring

### *Drugs*

- An ECG should be performed at baseline for all patients presenting with symptoms of cardiac disease and for all other patients who present with risk factors for cardiac or pulmonary disease.
- FBC, U&Es and LFTs prior to starting dasatinib therapy.
- All patients should be tested for hepatitis B virus (HBV) before initiating dasatinib treatment as reactivation of HBV in patients who are chronic carriers of this virus has occurred after these patients received BCR-ABL tyrosine kinase inhibitors. Those patients who test positive for HBV serology should be discussed with a consultant specialist in HBV before starting dasatinib therapy.
- FBC weekly for the first two months and then monthly thereafter, or as clinically indicated. U&Es and LFTs 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 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 dasatinib, this occurs earlier and with increased frequency in patients in the accelerated phase of CML.

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

**Chronic phase CML** (starting dose 100mg)

| **Neutrophils ($x10^9$/L)** | **Dose Modifications** |
|---|---|
| Less than 0.5 | Stop treatment until neutrophils are greater than $1x10^9$/L,<br>1st occurrence – resume treatment at the original starting dose.<br>2nd occurrence – resume treatment at a reduced dose of 80mg once daily.<br>3rd occurrence – resume treatment at a reduced dose of 50mg once a day (for newly diagnosed patients) or discontinue dasatinib (for patients resistant or intolerant to prior therapy). |
| **Platelets ($x10^9$/L)** | **Dose Modifications** |
| Less than 50 | Stop treatment until platelets are greater than or equal to $50x10^9$/L.<br>1st occurrence – resume treatment at the original starting dose.<br>2nd occurrence – if platelets are less than $25x10^9$/L and/or neutrophils less than 0.5 for more than 7 days, resume treatment at a reduced dose of 80mg once a day.<br>3rd occurrence – resume treatment at a reduced dose of 50mg once a day (for newly diagnosed patients) or discontinue dasatinib (for patients resistant or intolerant to prior therapy). |

### *Hepatic Impairment*

Patients with mild, moderate or severe hepatic impairment may receive the starting doses of dasatinib. However, dasatinib should be used with caution in patients with hepatic impairment particularly during dose escalation.

### *Renal Impairment*

No studies have been done with dasatinib in renal impairment, but due to the low renal excretion, there is unlikely to be a reduction in clearance.

### *Pleural effusion*

If a pleural effusion is diagnosed, dasatinib should be interrupted until patient is asymptomatic or has returned to baseline. If the episode does not improve within approximately one week, a course of diuretics or corticosteroids or both concurrently should be considered.

Following resolution of the first episode, reintroduction of dasatinib at the same dose level should be considered. Following resolution of a subsequent episode, dasatinib at one dose level reduction should be reintroduced. Following resolution of a severe (grade 3 or 4) episode, treatment can be resumed as appropriate at a reduced dose depending on the initial severity of the adverse reaction or consider switching to an alternative tyrosine kinase inhibitor.

## Regimen

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

**Chronic Phase**

| Drug | Dose | Days | Administration |
|---|---|---|---|
| Dasatinib | 100mg once a day | 1-28 (inclusive) | Oral |

In clinical studies in adult CML and Ph+ ALL patients, dose escalation to 140 mg once daily (chronic phase CML) was allowed in patients who did not achieve a haematologic or cytogenetic response at the recommended starting dose.

## Dose Information

- Dasatinib is available as 20mg, 50mg, 80mg,100mg and 140mg tablets.

## Administration Information

- Dasatinib should be swallowed whole, either with or without a meal, consistently at the same time each day either in the morning or in the evening. The film-coated tablets must not be crushed or cut in order to minimize the risk of dermal exposure.

## Additional Information

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

- It must be made clear to all staff, including those in the community, that dasatinib should only be prescribed under the supervision of an oncologist/haematologist.

- Dasatinib is an inhibitor and a substrate for cytochrome P450 (CYP) 3A4, therefore there is a potential for interaction with many other medicinal products particularly those that are metabolized primarily by or modulate the activity of CYP3A4. Care should be exercised when prescribing other medicines concomitantly with dasatinib, always check for drug interactions.

## Coding

- Procurement – X71.5

- Delivery – X73.1

References


1. Bristol Myers-Squibb Pharmaceutical Limited. (2016). Sprycel 20mg, 50mg, 80mg, 100mg, 140mg film-coated tablets Summary of Product Characteristics. Electronic Medicines Compendium. Online at http://www.medicines.org.uk/emc/medicine/26080, accessed 1 September 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 18 October 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. NHS England (2016). Cancer Drugs Fund List. Online at https://www.england.nhs.uk/cancer/cdf/cancer-drugs-fund-list/, accessed 28 November 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.**

## Dasatinib (chronic phase)

### Cycle 1 onwards

### Day 1-28

1. Dasatinib 100mg once a day oral
   Administration Information
   Oral chemotherapy

   Swallow whole, either with or without food, at the same time each day.

   Please supply the nearest original 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.