Chemotherapy Protocol

Chronic Myeloid Leukaemia

Asciminib

Regimen

- Asciminib

Indication

- Patients with chronic phase Philadelphia chromosome-positive chronic myeloid Leukaemia previously treated with two or more tyrosine kinase inhibitors where the following criteria are met:
    - A test for T315I mutation has been done and is negative
    - The patient has received treatment with 2 or more TKIs for CML
    - The patient has an ECOG performance status of 0 or 1.
    - The patient has not received prior treatment with asciminib unless the patient was started via the EAMS scheme or via the Novartis compassionate use scheme and all other treatment criteria are fulfilled.
    - Asciminib will be given until the development of disease resistance or patient intolerance or withdrawal of patient consent.

Toxicity

Drug	Adverse Effect
Asciminib	Upper respiratory tract infection, thrombocytopenia, neutropenia, anaemia, Dyslipidaemia, headache, dizziness, cough, pancreatitis, vomiting, diarrhoea, nausea, abdominal pain, hepatic enzyme increased, rash, muscoskeletal pain, arthraligia, fatigue, pruritus, hypertension, QT prolongation, pleural effusion

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 at baseline, prior to starting asciminib therapy.
- FBC, LFTs and U&Es every two weeks for the first three months then monthly thereafter, or as clinically indicated.
- Hepatitis B and C and HIV status should be checked prior to starting asciminib therapy. Patients who are carriers of either hepatitis B or C and those with active disease should be discussed with a consultant hepatologist prior to starting bosutinib therapy.
- Magnesium and potassium levels at baseline, then periodically throughout therapy. If abnormal at baseline these should be corrected before starting asciminib therapy.

- A baseline ECG prior to starting asciminib is advised for all patients. Those patients with a prolonged QTc interval, and those at high risk for developing a prolonged QTc interval, should be treated with extreme caution and may require regular ECG surveillance during asciminib therapy.

- Amylase and lipase should be monitored prior to starting treatment, then monthly for 3 months, then as clinically indicated. More frequent monitoring may be required in patients with a history of pancreatitis.

- Blood pressure should be monitored prior to starting treatment and then monthly thereafter or as clinically indicated.

- Annually BNP

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.

Recommended dose modifications

Starting dose	Reduced dose	Resumed dose
80mg once daily	40mg once daily	80mg once daily
40mg twice daily	20mg twice daily	40mg twice daily

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 bosutinib.

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

Neutrophils ($x10^9$/L)	**Dose Modifications**
Less than 1	1. Withhold asciminib until resolved to ANC ≥1 x109/L 2. If resolved within 2 weeks, resume at starting dose. 3. If resolved after more than 2 weeks, resume at reduced dose. 4. For recurrent severe neutropenia withhold asciminib until resolved to ANC ≥1x109/L, then resume at reduced dose.
Platelets ($x10^9$/L)	**Dose Modifications**
Less than 50	1. Withhold asciminib until resolved to ≥50x109/L 2. If resolved within 2 weeks, resume at starting dose.

	3. If resolved after more than 2 weeks, resume at reduced dose. 4. For recurrent severe thrombocytopenia withhold asciminib until resolved to ≥50x109/L, then resume at reduced dose.

Hepatic Impairment

No dose adjustment is required in patients with mild, moderate, or severe hepatic impairment. Since there is no data available in patients with moderate or severe hepatic impairment, caution should be exercised in these patients.

Renal Impairment

No dose adjustment is required in patients with mild, moderate or severe renal impairment.

Asymptomatic amylase and/or lipase elevation

If increase of amylase and/or lipase is >2xULN withhold asciminib until resolved to <1.5xULN. If resolved resume at a reduced dose. If events reoccur at reduced dose, permanently discontinue. If not resolved permanently discontinue and perform diagnostic tests to exclude pancreatitis.

Patients should be monitored for pancreatic toxicity. If serum lipase and amylase elevation are accompanied by abdominal symptoms, treatment should be temporarily withheld and appropriate diagnostic tests should be considered to exclude pancreatitis.

Non-haematological adverse reactions

If adverse reaction grade 3 or higher withhold asciminib until resolved to grade 1 or lower. If resolved resume at a reduced dose. If not resolved permanently discontinue.

Regimen

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

Drug	Dose	Days	Administration
Asciminib	80mg once a day	1-28 (inclusive)	Oral

Dose Information

- Asciminib is available as 20mg and 40mg film-coated tablets.

Administration Information

- Asciminib can be taken either as 80mg once a day at approximately the same time each day or as 40mg twice a day at approximately 12 hour intervals.
- Patients changing from 40mg twice daily to 80mg once daily should start taking asciminib once daily approximately 12 hours after the last twice-daily dose and then continue at 80mg once daily.

- Patients changing from 80 mg once daily to 40 mg twice daily should start taking asciminib twice daily approximately 24 hours after the last once-daily dose and then continue at 40 mg twice daily at approximately 12-hour intervals.

- Once-daily dosage regimen: If a dose is missed by more than approximately 12 hours, it should be skipped and the next dose should be taken as scheduled.

- Twice-daily dosage regimen: If a dose is missed by more than approximately 6 hours, it should be skipped and the next dose should be taken as scheduled.

- The tablets should be taken orally without food. Food consumption should be avoided for at least 2 hours before and 1 hour after taking asciminib.

- Tablets should be swallowed whole with a glass of water and should not be broken, crushed or chewed.

- Asciminib has no or negligible influence on the ability to drive and use machines. However, it is recommended that patients experiencing dizziness, fatigue or other undesirable effects with a potential impact on the ability to drive or use machines safely should refrain from these activities as long as the undesirable effects persist.

Additional Information

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

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

- Asciminib interacts with many other agents. Always check for drug interactions.

References

1. Novartis. Scemblix 40mg film-coated tablets summary for product characteristics. Available from: www.medicines.org.uk/emc/profuct/13818/smpc. Last updated 15/06/2022.

REGIMEN SUMMARY

Asciminib

Cycle 1

Day 1-28

1. Asciminib 80mg once a day for 28 days oral
   Administration Information
   Oral SACT
   Take on an empty stomach. Food consumption should be avoided for at least 2 hours before and 1 hour after taking asciminib. Swallow whole.

DOCUMENT CONTROL

Version	Date	Amendment	Written By	Approved By
1	September 2022	None	Alexandra Pritchard Pharmacist	Dr Edward Belsham 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.