PROTOCOL

The Clatterbridge Cancer Centre NHS Foundation Trust

Systemic Anti Cancer Therapy Protocol

ASCIMINIB
CHRONIC MYELOID LEUKAEMIA

PROTOCOL REF: MPHAACML
(Version No. 1.1)

Approved for use in:

- Chronic phase, Philadelphia positive chronic myeloid Leukaemia (CML) patients after 2 or more tyrosine kinase inhibitors.
- They must *not* have a T315l mutation.

A blueteq application is required

Dosage:

Drug	Dose	Route	Frequency
Asciminib	**40mg**	Oral	Twice daily (continuous treatment)
OR			
Asciminib	**80mg**	Oral	Once daily (continuous treatment)

Continuous treatment until progression or unacceptable toxicity

Administration:

- Asciminib should be taken on an empty stomach: - i.e. avoid food for at least 2 hours before the dose is taken and for at least 1 hour after the dose is taken. Water is permitted during this period.
- Asciminib should be taken with approximately 240 mL of water.

- Asciminib should be swallowed whole and not chewed or crushed.
- If vomiting occurs within the first hour after taking the drug, re-dosing is allowed before the next scheduled dose
- For the 40mg twice daily regimen: If the patient does not take asciminib within 6 hours after the approximate time of the usual dosing time, that dose should be skipped and treatment should continue with the next daily dose at the prescribed level
- For the 80mg once daily regimen: If the patient does not take asciminib within 12 hours after the approximate time of the usual dosing time, that dose should be skipped and treatment should continue with the next daily dose at the prescribed level
- Asciminib *may* have phototoxic properties so patients should avoid prolonged exposure to sunlight and sunbeds and to use sunscreen (phototoxicity was seen in mice at doses much higher than the doses licensed for humans)
- Patients changing from 40 mg twice daily to 80 mg once daily should start taking asciminib 80 mg once daily approximately 12 hours after the last 40 mg twice daily dose, and then continue at 80 mg once daily.
- Patients changing from 80 mg once daily to 40 mg twice daily should start taking asciminib 40 mg twice daily approximately 24 hours after the last 80 mg once daily dose and then continue at 40 mg twice-daily at approximately 12 hour intervals.
- Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose--galactose malabsorption should not take this medicine.

Emetogenic risk:

Mildly emetogenic.

Supportive treatments:

None required

Interactions:

Strong CYP3A4 inducers

Caution should be exercised during concomitant administration of asciminib with strong CYP3A inducers, including, but not limited to, carbamazepine, phenobarbital, phenytoin or St. John's wort (Hypericum perforatum) because these agents may decrease the plasma concentration of asciminib. Dose adjustment of asciminib is not required**.**

CYP3A4 substrates with narrow therapeutic index

Caution should be exercised during concomitant administration of asciminib with CYP3A4 substrates known to have a narrow therapeutic index, including, but not limited to, the CYP3A4 substrates fentanyl, alfentanil, dihydroergotamine or ergotamine because there is a risk of increased plasma concentrations of these agents. Dose adjustment of asciminib is not required.

CYP2C9 substrates

Caution should be exercised during concomitant administration of asciminib with CYP2C9 substrates known to have a narrow therapeutic index, including, but not limited to, phenytoin or warfarin because there is a risk of increased plasma concentrations of these agents. Dose adjustment of asciminib is not required.

P-gp substrates

Caution should be exercised during concomitant use of asciminib and P-gp substrates with narrow therapeutic index (e.g dabigatran or digoxin). Asciminib is expected to be a weak to moderate inhibitor of P-gp and therefore there is a risk of increased plasma concentrations of P-gp substrates with narrow therapeutic index.

QT prolonging agents

Caution should be exercised during concomitant administration of asciminib and medicinal products known to cause torsades de pointes, including, but not limited to, bepridil, chloroquine, clarithromycin, halofantrine, haloperidol, methadone, moxifloxacin or pimozide.

A list of drugs associated with QT prolongation and/or Torsades de Pointes is available online at www.crediblemeds.org/.

Main toxicities:

Thrombocytopenia, neutropenia, anaemia, nausea, vomiting, diarrhoea, increased lipase, fatigue, QT prolongation, arthralgia, rash, headache, increased amylase, abdominal pain, pyrexia, URTIs, back pain, hypertension, cough, pruritus, pain in extremity, dyspnoea, bone pain, peripheral oedema, non-cardiac chest pain, pancreatitis, hepatitis B reactivation and insomnia.

Investigations and treatment plan:

	Pre	Cycle 1	Cycle 2+	Ongoing
Clinical Assessment	X			As clinically indicated or at the end of treatment
Informed Consent	X			
SACT Assessment (including performance status and toxicity assessment		X	X	
FBC	X	X	X	Every 2 weeks for the first three months and then monthly thereafter or as clinically indicated
U&E & LFTs & Magnesium, CK & **amylase**	X	X	X	
CrCl (Cockcroft and Gault)	X			
ECG (including QtcF measurement)	X			Repeat if clinically indicated
Hepatitis B/C screen	X			If clinically indicated
Blood pressure measurement	X			Repeat if clinically indicated
Respiratory Rate				If clinically indicated
Height	X	X	X	Every Cycle
Weight recorded	X	X	X	Every cycle
Pregnancy test	X			If appropriate
Blood glucose	X			Repeat if clinically indicated

Dose Modifications and Toxicity Management:

Starting Dose	Reduced dose	Resumed dose
80mg OD	40mg OD	80mg OD
40mg BD	20mg BD	40mg BD

Haematological toxicity:

Proceed if-

ANC ≥ 1.0 x 10^9/L	Plt ≥ 50 x 10^9/L

If ANC < 1.0 x 10^9/L and/or platelets < 50 x 10^9/L withhold asciminib until counts have resolved to ANC ≥1 x 10^9/L and/or platelets ≥50 x 10^9/L.

If resolved:

• Within 2 weeks: resume at starting dose.

• After more than 2 weeks: resume at reduced dose.

For *recurrent* severe thrombocytopenia and/or neutropenia, withhold asciminib until resolved to ANC ≥1 x 10^9/l and PLT ≥50 x 10^9/l, then resume at reduced dose.

These haematological guidelines assume that patients are well with good performance status, that other acute toxicities have resolved and the patient has not had a previous episode of neutropenic sepsis.

Non- Haematological toxicity:

Dosing in renal and hepatic impairment:

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

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

Asymptomatic amylase elevation	If level > 200 units/L (>2 ULN) withhold asciminib until resolved to < 1.5 x ULN (150 units/L) • If resolved: resume at reduced dose. If events reoccur at reduced dose, permanently discontinue. • If not resolved: permanently discontinue. Perform diagnostic tests to exclude pancreatitis.
Any other non-haem adverse effects	If ≥ grade 3 withhold asciminib until resolved (grade ≤1). • If resolved: resume at a reduced dose. • If not resolved: permanently discontinue.
Pancreatitis (radiologic findings)	Grade 2: Asymptomatic radiologic pancreatitis, withhold asciminib until recovery of the radiologic findings. If resolved: resume at reduced dose. If events reoccur at reduced dose, permanently discontinue If ≥ grade 3: permanently discontinue asciminib

References:

1. Summary of Product Characteristics. Asciminib (Scemblix). https://www.medicines.org.uk/emc. Revised 15/06/22. Accessed 04/08/22
2. Asciminib for treating chronic myeloid leukaemia after 2 or more tyrosine kinase inhibitors. NICE TA 813. Published 03/08/22.
3. Early Access to Medicines Scheme – Treatment protocol – Information for healthcare professionals. Asciminib. Version 1.0. 19/11/21.

Circulation/Dissemination

Date added into Q-Pulse	26th January 2023
Date document posted on the Intranet	N/A

Version History

Date	Version	Author name and designation	Summary of main changes
	1.0	**Aileen McCaughey** **Advanced HO Pharmacist**	New regimen protocol
	1.1	**Aileen McCaughey** **Advanced HO Pharmacist**	Updated to include CDF approval, remove mentions to EAMS scheme and update protocol to SPC specifications