Indication	For the treatment of Philadelphia chromosome-positive chronic myeloid leukaemia (CML) in the chronic phase without T315I mutation and previously treated with two or more tyrosine kinase inhibitors. NB no previous treatment with asciminib is permitted unless the patient started treatment via the EAMS scheme or via the Novartis compassionate use scheme.
Treatment Intent	Disease modification
Frequency and number of cycles	Repeat every 28 days Continuously until disease resistance, intolerable toxicity or patient's choice. A formal medical review will be scheduled by the end of the second cycle to establish tolerability and whether treatment should continue.
Monitoring Parameters pre-treatment	• Review TTOs and from cycle 2 prescribe hypromellose eye drops, allopurinol, metoclopramide and/or loperamide as required. • Virology status for HBV checked prior to cycle 1. • FBCs and U&Es should be taken weekly for the first cycle, then every 2 weeks for the second and third cycle and then at each cycle thereafter. • Hypokalaemia and hypomagnesaemia should be corrected prior to asciminib administration and monitored during treatment. • LFTs including amylase and lipase should be taken at each cycle or as clinically indicated. Patients with a history of pancreatitis should be closely monitored. • ECG baseline and as clinically indicated throughout treatment. • BP baseline and at each cycle. Hypertension should be medically controlled throughout treatment. • Patients with a history of cardiac disease or predisposition for QTc prolongation should be monitored closely. • **Renal impairment**: No recommended dose adjustment in mild, moderate or severe renal impairment. • **Hepatic impairment:** No recommended dose adjustment in mild, moderate or severe hepatic impairment. No data in moderate/severe hepatic impairment, use with caution. • **Management of adverse reactions and dose adjustments:** ○ Dose adjustment may be required for the management of adverse reactions see **table 1** for guidance. Asciminib should be permanently discontinued if a total daily dose of 40mg cannot be tolerated. ○ **Thrombocytopenia and /or neutropenia -** If ANC <1.0 x 10^9/l and/or PLT <50 x 10^9/l withhold asciminib until resolved to ANC >/= 1 x 10^9/l and/or PLT >/= 50 x 10^9/l. If recovery is within 2 weeks, resume at starting dose. If recovery time is > 2 weeks, resume at reduced dose. For recurrent severe thrombocytopenia and/or neutropenia, withhold asciminib until ANC >/= 1 x 10^9/l and PLT >/= 50 x 10^9/l, then resume at reduced dose. ○ **Asymptomatic amylase and/or lipase elevation –** If >2.0 x ULN withhold asciminib until recovery to <1.5 x UN and resume at reduced dose. If elevations reoccur or do not resolve permanently discontinue asciminib and exclude pancreatitis. ○ **Pancreatitis – Grade 2** (radiologic findings for pancreatitis) is asymptomatic, withhold asciminib until recovery of the radiologic findings, on resolution resume at reduced dose. If events reoccur at reduced dose, permanently discontinue. For **>/= Grade 3** pancreatitis permanently discontinue ○ **Non-haematological reactions >/= Grade 3 –** withhold until resolved to </= Grade 1 then resume at a reduced dose. If not permanently discontinue.

	• **<u>Common drug interactions</u>:** • Concomitant use of asciminib with oral products containing hydroxypropyl-β-cyclodextrin (e.g itraconazole oral solution) decreases the oral bioavailability of asciminib. • Caution with concomitant administration of asciminib with strong CYP3A inducers (e.g carbamazepine, phenobarbital, phenytoin or St. John's wort), avoid where possible. • Caution with co-administration of asciminib with substrates of CYP3A4, CYP2C9 and P-gp with a narrow therapeutic range (fentanyl, alfentanil, warfarin, dabigatran, phenytoin) • 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. • **Missed dose:** o 40 mg BD regimen - If a dose is missed by more than approximately 6 hours, it should be omitted and the next dose should be taken as scheduled. o 80mg OD regimen - If a dose is missed by more than approximately 12 hours, it should be omitted and the next dose should be taken as scheduled. • Patients may experience dizziness or fatigue, patients should be made aware and if affected advised not to drive or operate machinery. • For oral self-administration: refer to local Trust policy on oral anti-cancer medicines and supply Patient Information Leaflet.
References	KMCC protocol HAEM-CML -007 v1 blueteq form accessed online 08.08.2022 CDF list accessed online 08.08.2022 SPC accessed online 08.08.2022

NB For funding information, refer to CDF and NICE Drugs Funding List

Table 1 Asciminib Dose Adjustment

Starting Dose	**Reduced Dose**	**Resumed Dose**
80mg once daily	40mg once daily	80mg once daily
40mg twice daily	20mg twice daily	40mg twice daily

Repeat every 28 days

TTO	Drug	Dose	Route	Directions
	ASCIMINIB	**See directions**	PO	40mg BD at 12-hour intervals **or alternatively** 80mg OD (for patients unsuitable for BD administration) Swallow whole, do not crush or chew. Take at least 2 hours after food and do not eat for at least 1 hour after taking. Available as 20mg and 40mg tablets Dispense 30 days supply
	Hypromellose	0.3%	TOPICAL	One drop into each eye QDS. Dispense on cycle 1 only
	Allopurinol	300mg	PO	Once daily for 28 days Cycle 1 only Clinician to assess patient, and delete if not required.
	Metoclopramide	10mg	PO	TDS PRN Do not take for more than 5 days continuously. Dispense on cycle 1 only
	Loperamide	2mg-4mg	PO	Take 4mg initially then 2mg after each loose stool when required (max 16mg a day) Dispense on cycle 1 only