Asciminib (CML)

Indication
Chronic-phase Philadelphia chromosome-positive chronic myeloid leukaemia without a T3151 mutation after 2 or more tyrosine kinase inhibitors.

(NICE TA813)

ICD-10 codes
C92.1

Regimen details

Drug	Dose	Route
Asciminib	40mg BD* (or 80mg OD if BD not tolerated)	Oral

* Or 80mg OD if BD not tolerated

Cycle frequency
Continuous

Number of cycles
Until loss of clinical benefit or unacceptable toxicity occurs.

Administration
Asciminib is available as 40mg and 20mg film-coated tablets. Asciminib should be swallowed whole with a glass of water and should not be broken, crushed or chewed. Food should be avoided for at least 2 hours before and 1 hour after taking asciminib.

For patients on the twice daily regimen, if a dose is missed by more than approximately 6 hours, it should be omittedand the next dose taken as scheduled. For patients on the once daily regimen, if a dose is missed by more than approximately 12 hours it should be omitted and the next dose taken as scheduled.

Pre-medication
Nil

Emetogenicity
This regimen has low emetic potential – refer to local policy

Additional supportive medication
Not usually required

Extravasation
N/A

Investigations – pre first cycle

Investigation	Validity period
FBC	14 days
U&Es* (including creatinine)	14 days
LFTs	14 days
Magnesium*	14 days
Lipase/Amylase	14 days
ECG (for QTc interval)	Baseline
Blood pressure	Baseline

* Hypokalaemia and hypomagnesaemia should be corrected prior to asciminib administration

Other investigations prior to commencing treatment:
Confirm the presence of t (9;22) and/or BCR-ABL transcript (or other TKI sensitive target)
Hepatitis B (HBV) serology
Coagulation screen
Blood glucose, HbA1c
Fasting cholesterol and lipid profile
QRISK3 score

Investigations – pre subsequent cycles

Investigation	Validity period
FBC	Every 2 weeks for the first 2 months, then monthly
U&Es (including creatinine)	Monthly
LFTs	Monthly
Magnesium	Monthly
Lipase/Amylase	Monthly
ECG (for QTc interval)	After treatment initiation then as clinically indicated
Blood pressure	Monthly

Fasting cholesterol and lipid profile should also be reviewed annually.

Standard limits for administration to go ahead

If blood results not within range, authorisation to administer **must** be given by prescriber/ consultant

Investigation	Limit
Neutrophils	≥ 1.0 x 10^9/L
Platelets	≥ 50 x 10^9/L
Bilirubin	< 3 x ULN
AST/ALT	< 5 x ULN
Lipase/Amylase	< 2 x ULN

Dose modifications

For management of adverse reactions, asciminib dose may be reduced as below, depending on original dosing regimen.

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

Asciminib should be permanently discontinued if a total daily dose of 40mg is not tolerated.

- **Haematological toxicity**

Neutrophil count		Platelet count	Management
< 1.0 x 10^9/L	and/or	< 50 x 10^9/L	Withhold asciminib until resolved to ANC ≥ 1 x 10^9/L and platelets ≥ 50 x 10^9/L If resolved *within 2 weeks*: resume at same dose If *>2 weeks to resolve*, resume at reduced dose. For recurrent severe thrombocytopenia/ neutropenia withhold asciminib until resolved then resume at reduced dose.

- **Renal impairment**

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

- **Hepatic impairment**

No dose adjustment is required in mild, moderate or severe hepatic impairment. There is however no data in moderate or severe hepatic impairment so caution is advised.

- **Other toxicities**

Toxicity	Definition	Action/Dose adjustment
Asymptomatic pancreatic enzyme elevation (amylase/lipase)	> 2 x ULN	Withhold asciminib until resolved to <1.5 x ULN then resume at reduced dose. If does not resolved or recurrence of elevation permanently discontinue treatment.
Pancreatitis	Symptomatic radiologic pancreatitis (Grade 2)	Withhold treatment until recovery, if resolved restart at reduced dose If reoccurs at reduced dose, permanently discontinue
	≥ Grade 3	Permanently discontinue
Any other non-haematological adverse reaction	≥ Grade 3 adverse reaction	Withhold asciminib until resolved to ≤ Grade 1 If resolved, resume at reduced dose If the toxicity does not resolve, permanently discontinue treatment.

Hypertension

Hypertension should be monitored and managed using standard antihypertensive therapy during treatment with asciminib as clinically indicated.

Adverse effects - for full details consult product literature/ reference texts

- **Serious side effects**

Myelosuppression
Pancreatitis
Hypertension
Hepatitis B reactivation
QT prolongation

- **Frequently occurring side effects**

Myelosuppression
Nausea, vomiting
Diarrhoea
Anorexia
Cough, dyspnoea
Pleural effusion
Palpitations
Oedema
Hyperbilirubinaemia
Hyperlipasaemia
Dyslipidaemia
Myalgia, arthralgia
Headache
Rash
Dry eye
Blurred vision
Dizziness
Asthenia
Fever
Fatigue

- **Other side effects**

Blood creatine phosphokinase increased

Significant drug interactions – for full details consult product literature/ reference texts

Strong CYP3A4 inducers e.g. carbamazepine, phenobarbital, rifampicin, phenytoin, St John's Wort: dose adjustment is not required but caution is advised due to potential to reduce asciminib exposure.
CYP3A4 substrates with a narrow therapeutic index e.g. fentanyl, alfentanil, ergotamine: asciminib may increase plasma concentrations of the substrate.
CYP2C9 substrates e.g. warfarin, phenytoin: asciminib may increase plasma concentrations of the substrate
P-gp substrates e.g. digoxin: asciminib may cause clinically relevant increase in plasma concentrations of the substrate
Drugs that cause QT prolongation e.g. chloroquine, clarithromycin, haloperidol, methadone, moxifloxacin: increased risk of torsades de pointes with coadministration
Medicinal products containing hydroxypropyl-β-cyclodextrin as an excipient e.g. itraconazole oral solution: use with caution as reduces bioavailability of asciminib

Additional comments

Patients with rare hereditary problems of galactose intolerance, total lactose deficiency or glucose-galactose malabsorption should not take this medicine.

There is no data on the effect of asciminib on human fertility. It is not recommended for use during pregnancy and women of child bearing potential should be advised to use effective contraception during treatment and for at least 3 days after stopping treatment.

References

- Summary of Product Characteristics – Asciminib (Novartis) accessed 14th September 2023 via www.medicines.org.uk
- National Institute for Health and Care Excellence (TA813) accessed 14th September 2023 via www.nice.org.uk
- Mauro M. *et al*. Efficacy and Safety Results from ASCEMBL, a multicenter, Open-Label, Phase 3 Study of Asciminib, a First-in-Class STAMP inhibitor, vs Bosutinib in Patients with Chronic Myeloid Leukaemia in Chronic Phase after ≥2 prior Tyrosine Kinase Inhibitors: Update after 48 Weeks. Blood (2021);138(Supplement 1):310

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