Acalabrutinib

Indication

Untreated chronic lymphocytic leukaemia (CLL) if:

- There is a 17p deletion or TP53 mutation
- There is no 17p deletion or TP53 mutation and FCR or R-bendamustine are unsuitable.

(NICE TA689)

Previously treated chronic lymphocytic leukaemia (CLL)
(NICE TA689)

ICD-10 codes

Codes with a prefix C91

Regimen details

Drug	Dose	Route
Acalabrutinib	100mg BD	PO

Cycle frequency

Continuous

Number of cycles

Continue until disease progression or unacceptable toxicity.

Administration

Acalabrutinib is available as 100mg tablets.

Tablets should be swallowed whole with water, with or without food and should be taken approximately every 12 hours. Tablets should not be chewed, dissolved, crushed or divided.

Pre-medication

Adequate hydration and allopurinol started 24 hours pre-treatment to prevent tumour lysis syndrome is recommended prior to initiation of acalabrutinib.

Emetogenicity

This regimen has low emetic potential (no routine anti-emetics required)

Additional supportive medication

Allopurinol 300mg OD to start 24 hours before first cycle to continue for 7 days (100mg OD if creatinine clearance <20ml/min).
Pneumocystis jirovecii pneumonia prophylaxis as per local policy during and for 3 months after treatment.
HSV prophylaxis as per local policy during and for 3 months after treatment.

Extravasation

N/A

Investigations – pre first cycle

Investigation	Validity period
FBC	14 days
U+E (including creatinine)	14 days
LFTs	14 days

Other assessments:
Hepatitis B core antibody and surface antigen, hepatitis C antibody, HIV viral screen.
Blood pressure measurement, ECG+/-echocardiogram (recommended for pre-existing AF, heart failure, diabetes, coronary artery disease and/or hypertension).

Investigations – pre subsequent cycles

Investigation	Validity period
FBC	Monthly (can be extended to 3 monthly in stable patients)
U+E (including creatinine)	Monthly (can be extended to 3 monthly in stable patients)
LFT	Monthly (can be extended to 3 monthly in stable patients)

Other recommended assessments:
Blood pressure should be measured at every clinic visit.
ECG 3-6 monthly in first year of treatment.

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	≥ 1.5 x 10^9/L
Platelets	≥ 75 x 10^9/L
Creatinine clearance	≥ 30ml/min
Bilirubin	< 3 x ULN
ALT	< 5 x ULN

Dose modifications

- **Haematological toxicity**

To commence treatment neutrophils should be ≥ 1.5 x 10^9/L and platelets should be ≥ 75 x 10^9/L. If counts fall during treatment follow the guidance in the table below:

Haematological event	Occurrence	Action
Platelets 25-49 x 10^9/L *and* bleeding OR Platelets <25 x 10^9/L OR Neutrophils <0.5 x 10^9/L for > 7 days (G-CSF could be considered)	First and second	Interrupt acalabrutinib Once resolved (platelets ≥ 75 x 10^9/L, neutrophils ≥ 1.5 x 10^9/L) or baseline, treatment may be resumed at starting dose.
	Third	Interrupt acalabrutinib. Once resolved (platelets ≥ 75 x 10^9/L, neutrophils ≥ 1.5 x 10^9/L) or baseline, treatment may be resumed at reduced dose of 100mg OD
	Fourth	Discontinue acalabrutinib

- **Renal impairment**

No modifications required for mild or moderate renal impairment.
The manufacturer recommends acalabrutinib should be administered to patients with severe renal impairment (<30ml/min) only if the benefit outweighs the risk and patients should be closely monitored for toxicity.

- **Hepatic impairment**

Bilirubin (x ULN)	Acalabrutinib dose
1.5-3	No dose modification required, monitor closely for toxicity
>3	Not recommended

- **Other toxicities**

Toxicity	Occurrence	Action
Grade ≥3 toxicity	First and second	Interrupt acalabrutinib Once resolved to ≤ Grade 1 or baseline, treatment may be resumed at same dose.
	Third	Interrupt acalabrutinib. Once resolved to ≤ Grade 1 or baseline, treatment may be resumed at reduced dose of 100mg OD
	Fourth	Discontinue acalabrutinib

Monitor for symptoms of arrhythmia (e.g. palpitations, dizziness, syncope, dyspnoea) and manage as appropriate. The risk of arrhythmia may be increased in patients with cardiac risk factors, hypertension, previous arrhythmias, and acute infection.

Progressive multifocal leukoencephalopathy (PML): PML has been reported in patients receiving acalabrutinib. Patients should be monitored for new or worsening neurological, cognitive or behavioural changes. All treatment should be held if PML is suspected and permanently discontinued if PML is confirmed.

For dose modifications due to concomitant drug use, see drug interaction section.

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

- **Serious side effects**

Myelosuppression
Haemorrhage
Serious and opportunistic infections
Secondary primary malignancies
Atrial fibrillation and flutter
Viral reactivation

- **Frequently occurring side effects**

Myelosuppression
Infection
Diarrhoea
Nausea
Rash
Headache and dizziness
Musculo-skeletal pain and arthralgia

- **Other side effects**

Fatigue
Constipation
Epistaxis

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

	Co- administered drugs	Action
CYP3A inhibitors	Strong CYP3a inhibitor	Avoid concomitant use. If use will be short-term (such as anti-infectives for up to 7 days) interrupt acalabrutinib
	Moderate CYP3a inhibitor	No dose adjustment. Monitor closely for adverse reactions.
	Moderate CYP3a inhibitor	No dose adjustment
CYP3A inducers	Strong CYP3A inducer	Avoid concomitant use

Haemorrhage: Use with caution with antithrombotic agents and consider additional monitoring for signs of bleeding when concomitant use is medically necessary. Consider withholding acalabrutinib for 3-7 days pre and post-surgery depending on the type of surgery and the risk of bleeding

Additional comments

Sun exposure: Monitor patients for skin cancers and counsel on protection from sun exposure.

Pregnancy and breastfeeding: There are no or limited amount of data of the use of acalabrutinib in pregnant or breast-feeding women. Acalabrutinib should not be used during pregnancy unless clinical condition requires. Breast-feeding mothers are advised not to breast feed during treatment with acalabrutinib and for 2 days after receiving the last dose.

References

- Summary of Product Characteristics: Acalabrutinib tablets (AstraZeneca) accessed 21/12/2023 via https://www.medicines.org.uk/
- National Cancer Drugs Fund (CDF) List accessed 17/02/2021 via https://www.england.nhs.uk/cancer/cdf/cancer-drugs-fund-list/
- Sharman JP, et al, ELEVATE-TN: Phase 3 Study of Acalabrutinib Combined with Obinutuzumab (O) or Alone Vs O Plus Chlorambucil (Clb) in Patients (Pts) with Treatment-Naive Chronic Lymphocytic Leukemia (CLL). *Blood 2019*; 134 (Supplement 1):31

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