Acalabrutinib (Tablets) Monotherapy

NOTE:

- **This regimen relates to acalabrutinib tablets only.**
- **Acalabrutinib tablets may be co-administered with gastric acid reducing products.**

INDICATIONS FOR USE:

INDICATION	ICD10	Regimen Code	HSE approved reimbursement status*
As monotherapy is indicated for the treatment of adult patients with chronic lymphocytic leukaemia (CLL) who have received at least one prior therapy	C91	00840a	CDS 01/07/2023
As monotherapy for the treatment of previously untreated CLL in the presence of 17p deletion or TP53 mutation in adult patients unsuitable for chemoimmunotherapy	C91	00840b	CDS 01/07/2023

*For post 2012 indications only

TREATMENT:

The starting dose of the drugs detailed below may be adjusted downward by the prescribing clinician, using their independent medical judgement, to consider each patients individual clinical circumstances.

Treatment with acalabrutinib should be continued until disease progression or unacceptable toxicity develops.

Drug	Dose	Route	Cycle
Acalabrutinib	100mg twice daily	PO	Continuous
The dose interval is approximately 12 hours. If a patient misses a dose of acalabrutinib by more than 3 hours, the patient should be instructed to take the next dose at its regularly scheduled time. A double dose of acalabrutinib should not be taken to make up for a missed dose. The tablets should be swallowed whole with water at approximately the same time each day, with or without food. The tablets should not be chewed, crushed, dissolved or divided.			

ELIGIBILITY:

- Indications as above
- ECOG 0-2
- Chronic Lymphocytic Leukaemia requiring treatment
- Adequate haematological, hepatic and renal function

EXCLUSIONS:

- Hypersensitivity to acalabrutinib or to any of the excipients

USE WITH CAUTION:

- Caution is required when prescribing for patients with significant cardiovascular disease
- Any active clinically significant infection requiring therapy

PRESCRIPTIVE AUTHORITY:

- The treatment plan must be initiated by a Consultant Haematologist working in the area of haematological malignancies

TESTS:

Baseline tests:

- FBC, renal and liver profile
- Virology screen - Hepatitis B (HBsAg, HBcoreAb), Hepatitis C, HIV
  *(**Reference Regimen Specific Complications for information on Hepatitis B reactivation)**
- ECG

Regular tests:

- FBC, renal and liver profile minimum 4 monthly
- ECG as indicated

Disease monitoring:

Disease monitoring should be in line with the patient's treatment plan and any other test/s as directed by the supervising Consultant.

DOSE MODIFICATIONS:

- Any dose modification should be discussed with a Consultant

Renal and Hepatic Impairment:

Table 1: Dose Modifications of Acalabrutinib in Renal and Hepatic Impairment

Renal Impairment		Hepatic Impairment	
CrCl (mL/minute)	**Dose**	**Level**	**Dose**
≥ 30	No dose adjustment is needed	Child-Pugh A/B or mild/moderate	No dose adjustment is needed
< 30	No dose adjustment is expected	Child-Pugh C or severe	Not recommended
Haemodialysis	No need for dose adjustment is expected		
Dose modifications for renal and hepatic impairment from Giraud et al, 2023.			

Management of adverse events:

Table 2: Dose Modifications of Acalabrutinib for Adverse Events

Adverse reaction	**Adverse reaction occurrence**	**Dose modification** (Starting dose = 100mg approximately every 12 hours)
Grade 3 thrombocytopenia with bleeding, Grade 4 thrombocytopenia Or Grade 4 neutropenia lasting longer than 7 days	First and second occurrence	Interrupt acalabrutinib. Once toxicity has resolved to Grade 1 or baseline, acalabrutinib may be resumed at 100mg approximately every 12 hours.
Grade 3 or greater non-haematological toxicities	Third occurrence	Interrupt acalabrutinib. Once toxicity has resolved to Grade 1 or baseline, acalabrutinib may be resumed at a reduced frequency of 100mg once daily.
	Fourth occurrence	Discontinue acalabrutinib.

*Adverse reactions graded by the National Cancer Institute Common Terminology Criteria for Adverse Events (NCI CTCAE) version 4.03.

SUPPORTIVE CARE:

EMETOGENIC POTENTIAL

- As outlined in NCCP Classification Document for Systemic Anti-Cancer Therapy (SACT) Induced Nausea and Vomiting - Available on the NCCP website

Acalabrutinib : Minimal to low (**Refer to local policy).**

For information:
Within NCIS regimens, antiemetics have been standardised by the Medical Oncologists and Haemato-oncologists. Information is available in the following documents:

- NCCP Supportive Care Antiemetic Medicines for **Inclusion in NCIS** (Medical Oncology) - Available on the NCCP website
- NCCP Supportive Care Antiemetic Medicines for **Inclusion in NCIS** (Haemato-oncology) - Available on the NCCP website

PREMEDICATIONS: None required

OTHER SUPPORTIVE CARE: None required

ADVERSE EFFECTS:

- Please refer to the relevant Summary of Product Characteristics (SmPC) for details.

This medicinal product is subject to additional monitoring. Healthcare professionals are asked to report any suspected adverse reactions.

REGIMEN SPECIFIC COMPLICATIONS:

- **Haemorrhage:** Major haemorrhagic events including central nervous system and gastrointestinal haemorrhage, some with fatal outcome, have occurred in patients with haematologic malignancies treated with acalabrutinib monotherapy and in combination with obinutuzumab. These events have occurred in patients both with and without thrombocytopenia. Overall, the bleeding events were less severe events including bruising and petechiae. The mechanism for the bleeding events is not well understood. Patients receiving antithrombotic agents may be at increased risk of haemorrhage. Use caution with antithrombotic agents and consider additional monitoring for signs of bleeding when concomitant use is medically necessary. **Warfarin or other vitamin K antagonists should not be administered concomitantly with acalabrutinib**. Consider the benefit-risk of withholding acalabrutinib for at least 3 days pre- and post-surgery.
- **Hepatitis B Reactivation:** Patients should be tested for both HBsAg and HBcoreAb as per local policy. If either test is positive, such patients should be treated with anti-viral therapy **(Refer to local infectious disease policy).** These patients should be considered for assessment by hepatology.
- **Atrial fibrillation:** Atrial fibrillation/flutter occurred in patients with haematologic malignancies treated with acalabrutinib monotherapy and in combination with obinutuzumab. Monitor for symptoms (e.g., palpitations, dizziness, syncope, chest pain, dyspnoea) of atrial fibrillation and atrial flutter and obtain an ECG as medically indicated. In patients who develop atrial fibrillation on therapy with acalabrutinib, a thorough assessment of the risk for thromboembolic disease should be

undertaken. In patients at high risk for thromboembolic disease, tightly controlled treatment with anticoagulants and alternative treatment options to acalabrutinib should be considered.

DRUG INTERACTIONS:

- Current SmPC and drug interaction databases should be consulted for information.

REFERENCES:

1. Ghia P, Pluta A, Wach M, et al. ASCEND: Phase III randomised trial of acalabrutinib versus idelalisib plus rituximab or bendamustine plus rituximab in relapsed or refractory chronic lymphocytic leukemia. Journal Clin Onc 2020 38:25, 2849-2861
2. Giraud E L, Lijster B D, et al. Dose recommendations for anticancer drugs in patients with renal or hepatic impairment: an update. Available at: https://pubmed.ncbi.nlm.nih.gov/37269847
3. NCCP Classification Document for Systemic Anti-Cancer Therapy (SACT) Induced Nausea and Vomiting. V5 2023. Available at: https://www.hse.ie/eng/services/list/5/cancer/profinfo/chemoprotocols/nccp-classification-document-for-systemic-anti-cancer-therapy-sact-induced-nausea-and-vomiting.pdf
4. Acalabrutinib (Calquence®) Summary of Product Characteristics. Accessed October 2024. Last updated 19/02/2024. Available at: https://www.ema.europa.eu/en/documents/product-information/calquence-epar-product-information_en.pdf

Version	Date	Amendment	Approved By
1	01/11/2023		Prof Elisabeth Vandenberghe
1a	13/12/2023	Modified note under title of regimen to clarify that the capsule formulation is no longer available.	NCCP
2	03/12/2024	Reviewed. Modified note under regimen title. Updated Exclusions, Caution section, Baseline tests. Updated renal and hepatic dose modifications to align with Giraud et al 2023. Updated regimen in line with NCCP standardisation (emetogenic potential, adverse effects, regimen specific complications, adverse effects).	Prof Elisabeth Vandenberghe

Comments and feedback welcome at oncologydrugs@cancercontrol.ie.