# Acalabrutinib (Capsules) Monotherapy

**Note:**

- **There are two formulations of acalabrutinib available, acalabrutinib tablets and capsules**
  - **From 1st July 2023, all new prescriptions should specify the tablet formulation (see regimen NCCP 00840 Acalabrutinib (Tablets) Monotherapy)**

- **This regimen is for treatment with acalabrutinib capsules only**
- **Acalabrutinib capsules should not be co-administered with certain gastric acid reducing products since uptake of acalabrutinib may be impaired. See Drug Interaction section for further information**

## INDICATIONS FOR USE:

| INDICATION | ICD10 | Regimen Code | 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 | 00656a | CDS 01/10/2021 |
| 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 | 00656b | CDS 01/10/2021 |

## 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.<br>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.<br>The capsules should be swallowed whole with water at approximately the same time each day, with or without food. The capsules should not be chewed, dissolved or opened. | | | |

## ELIGIBILITY:

- Indications as above
- ECOG 0-2
- Chronic Lymphocytic Leukaemia requiring treatment
- Adequate haematological, hepatic and renal function
  - Estimated creatinine clearance of ≥ 30 mL/min

## EXCLUSIONS:

- Prolymphocytic leukaemia and Richter's syndrome
- Known CNS lymphoma or leukaemia.
- Any active clinically significant infection requiring therapy

## USE WITH CAUTION:

- Caution is required when prescribing for patients with significant cardiovascular disease

## 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: Patients should be tested for both HBsAg and HBcoreAb as per local policy
- 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 |
|---|---|
| No dose adjustment is needed for patients with mild or moderate renal impairment. Acalabrutinib should be administered to patients with severe renal impairment only if the benefit outweighs the risk and these patients should be monitored closely for signs of toxicity. | No dose adjustment is recommended in patients with mild or moderate hepatic impairment. However, patients with moderate hepatic impairment should be closely monitored for signs of toxicity.<br>Treatment is not recommended in patients with severe hepatic impairment. |

## Management of adverse events:

**Table 2: Dose Modifications of Acalabrutinib for Adverse Events**

| Adverse reaction | Adversereaction occurrence | Dose modification (Starting dose = 100mg approximately every 12 hours) |
|---|---|---|
| Grade 3 thrombocytopenia with bleeding,<br>Grade 4 thrombocytopenia<br>Or<br>Grade 4 neutropenia lasting longer than 7 days | First and second occurrence | Interrupt acalabrutinib.<br>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.<br>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:** Minimal to low (**Refer to local policy).**

**PREMEDICATIONS:** None required

**OTHER SUPPORTIVE CARE:** None required

## ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS:

*The adverse effects listed are not exhaustive. Please refer to the relevant Summary of Product Characteristics for full details*.

- **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.
- **Infections:** Serious infections (bacterial, viral or fungal), including fatal events have occurred in patients with haematologic malignancies treated with acalabrutinib monotherapy and in combination with obinutuzumab. These infections predominantly occurred in the absence of Grade 3 or 4 neutropenia, with neutropenic infection reported in 1.9% of all patients. Infections due to hepatitis B virus (HBV) and herpes zoster virus (HZV) reactivation, aspergillosis and progressive multifocal leukoencephalopathy (PML) have occurred.
- **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.
- **Cytopenias:** Treatment-emergent Grade 3 or 4 cytopenias, including neutropenia, anaemia and thrombocytopenia, occurred in patients with haematologic malignancies treated with acalabrutinib monotherapy and in combination with obinutuzumab. Monitor complete blood counts as medically indicated.
- **Second primary malignancies:** Second primary malignancies, including skin and non-skin cancers, occurred in patients with haematologic malignancies treated with acalabrutinib monotherapy and in combination with obinutuzumab. Skin cancers were commonly reported. Monitor patients for the appearance of skin cancers and advise protection from sun exposure.
- **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.
- **Pregnancy:** Acalabrutinib should not be used during pregnancy unless the clinical condition of the woman requires acalabrutinib
- **Breast feeding:** Do not breast feed during treatment with acalabrutinib and for 2 days after receiving the last dose

## DRUG INTERACTIONS:

- Current drug interaction databases should be consulted for more information.
- Co-administration of strong CYP3A inhibitors with acalabrutinib may lead to increased acalabrutinib exposure and consequently a higher risk for toxicity. Concomitant use should therefore be avoided. If these inhibitors will be used short term (such as anti-infectives for up to seven days), treatment with acalabrutinib should be interrupted. Patients should be closely monitored for signs of toxicity if a moderate CYP3A inhibitor is used.
- On the contrary, co-administration of strong CYP3A inducers may lead to decreased acalabrutinib exposure and consequently a risk for lack of efficacy. Concomitant use should therefore be avoided.
- Avoid concomitant use with proton pump inhibitors.
- If taking a H2-receptor antagonist, acalabrutinib must be taken either 2 hours before or 10 hours afterwards.
- If taking antacids, the interval between taking the medicinal products should be at least 2 hours.

## 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. NCCP Classification Document for Systemic Anti-Cancer Therapy (SACT) Induced Nausea and Vomiting. V5 20223 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
3. Acalabrutinib (Calquence®) 100mg capsules Summary of Product Characteristics. Accessed June 2023. Available at: https://www.ema.europa.eu/en/documents/product-information/calquence-epar-product-information_en.pdf


| Version | Date | Amendment | Approved By |
|---|---|---|---|
| 1 | 1/10/2021 | | NCCP Lymphoid Clinical Advisory Group |
| 2 | 15/10/2021 | Removal of "Prior exposure to a BCL-2 inhibitor or B-cell receptor inhibitor" from exclusion criteria | NCCP Lymphoid Clinical Advisory Group |
| 3 | 01/11/2023 | Reviewed. Updated adverse events section and dose modifications for hepatic impairment. | NCCP Lymphoid Clinical Advisory Group |

Comments and feedback welcome at oncologydrugs@cancercontrol.ie.