

## Acalabrutinib (Tablets) Monotherapy

**NOTE:**

- From 1st July 2023, all new prescriptions for acalabrutinib should specify the tablet formulation. Acalabrutinib capsules are no longer available.
- 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	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

**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
  - Estimated creatinine clearance of  $\geq 30$  mL/min

NCCP Regimen: Acalabrutinib (Tablets) Monotherapy	Published: 01/11/2023 Review: 01/11/2024	Version number: 1a
Tumour Group: Leukaemia NCCP Regimen Code: 00840	IHS Contributor: Prof Elisabeth Vandenberghe	Page 1 of 5

The information contained in this document is a statement of consensus of NCCP and ISMO or IHS professionals regarding their views of currently accepted approaches to treatment. Any clinician seeking to apply or consult these documents is expected to use independent medical judgement in the context of individual clinical circumstances to determine any patient's care or treatment. Use of these documents is the responsibility of the prescribing clinician and is subject to HSE's terms of use available at <http://www.hse.ie/eng/Disclaimer>

*This information is valid only on the day of printing, for any updates please check [www.hse.ie/NCCPchemoregimens](http://www.hse.ie/NCCPchemoregimens)*

## EXCLUSIONS:

- Polymphocytic 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

NCCP Regimen: Acalabrutinib (Tablets) Monotherapy	Published: 01/11/2023 Review: 01/11/2024	Version number: 1a
Tumour Group: Leukaemia NCCP Regimen Code: 00840	IHS Contributor: Prof Elisabeth Vandenberghe	Page 2 of 5

The information contained in this document is a statement of consensus of NCCP and ISMO or IHS professionals regarding their views of currently accepted approaches to treatment. Any clinician seeking to apply or consult these documents is expected to use independent medical judgement in the context of individual clinical circumstances to determine any patient's care or treatment. Use of these documents is the responsibility of the prescribing clinician and is subject to HSE's terms of use available at <http://www.hse.ie/eng/Disclaimer>

*This information is valid only on the day of printing, for any updates please check [www.hse.ie/NCCPchemoregimens](http://www.hse.ie/NCCPchemoregimens)*

## 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. 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	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  Grade 3 or greater non-haematological toxicities	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
	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:** Minimal to low (Refer to local policy).

**PREMEDICATIONS:** None required

**OTHER SUPPORTIVE CARE:** None required

NCCP Regimen: Acalabrutinib (Tablets) Monotherapy	Published: 01/11/2023 Review: 01/11/2024	Version number: 1a
Tumour Group: Leukaemia NCCP Regimen Code: 00840	IHS Contributor: Prof Elisabeth Vandenberghe	Page 3 of 5

The information contained in this document is a statement of consensus of NCCP and ISMO or IHS professionals regarding their views of currently accepted approaches to treatment. Any clinician seeking to apply or consult these documents is expected to use independent medical judgement in the context of individual clinical circumstances to determine any patient's care or treatment. Use of these documents is the responsibility of the prescribing clinician and is subject to HSE's terms of use available at <http://www.hse.ie/eng/Disclaimer>

*This information is valid only on the day of printing, for any updates please check [www.hse.ie/NCCPchemoregimens](http://www.hse.ie/NCCPchemoregimens)*

## 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

NCCP Regimen: Acalabrutinib (Tablets) Monotherapy	Published: 01/11/2023 Review: 01/11/2024	Version number: 1a
Tumour Group: Leukaemia NCCP Regimen Code: 00840	IHS Contributor: Prof Elisabeth Vandenberghe	Page 4 of 5

The information contained in this document is a statement of consensus of NCCP and ISMO or IHS professionals regarding their views of currently accepted approaches to treatment. Any clinician seeking to apply or consult these documents is expected to use independent medical judgement in the context of individual clinical circumstances to determine any patient's care or treatment. Use of these documents is the responsibility of the prescribing clinician and is subject to HSE's terms of use available at <http://www.hse.ie/eng/Disclaimer>

*This information is valid only on the day of printing, for any updates please check [www.hse.ie/NCCPchemoregimens](http://www.hse.ie/NCCPchemoregimens)*

## 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.

## 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 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>
3. Acalabrutinib (Calquence®) Summary of Product Characteristics. Accessed June 2023. Available at: [https://www.ema.europa.eu/en/documents/product-information/calquence-epar-product-information\\_en.pdf](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

Comments and feedback welcome at [oncologydrugs@cancercontrol.ie](mailto:oncologydrugs@cancercontrol.ie).

NCCP Regimen: Acalabrutinib (Tablets) Monotherapy	Published: 01/11/2023 Review: 01/11/2024	Version number: 1a
Tumour Group: Leukaemia NCCP Regimen Code: 00840	IHS Contributor: Prof Elisabeth Vandenberghe	Page 5 of 5

The information contained in this document is a statement of consensus of NCCP and ISMO or IHS professionals regarding their views of currently accepted approaches to treatment. Any clinician seeking to apply or consult these documents is expected to use independent medical judgement in the context of individual clinical circumstances to determine any patient's care or treatment. Use of these documents is the responsibility of the prescribing clinician and is subject to HSE's terms of use available at <http://www.hse.ie/eng/Disclaimer>

*This information is valid only on the day of printing, for any updates please check [www.hse.ie/NCCPchemoregimens](http://www.hse.ie/NCCPchemoregimens)*