Regimen Monograph

A - Regimen Name

ACAL Regimen

Acalabrutinib

Disease Site

Hematologic
Leukemia - Chronic Lymphocytic (CLL)

Intent

Palliative

Regimen Category

Evidence-Informed :

Regimen is considered appropriate as part of the standard care of patients; meaningfully improves outcomes (survival, quality of life), tolerability or costs compared to alternatives (recommended by the Disease Site Team and national consensus body e.g. pan-Canadian Oncology Drug Review, pCODR). Recommendation is based on an appropriately conducted phase III clinical trial relevant to the Canadian context OR (where phase III trials are not feasible) an appropriately sized phase II trial. Regimens where one or more drugs are not approved by Health Canada for any indication will be identified under Rationale and Use.

Rationale and Uses

Monotherapy in patients with active CLL and good performance status, as:

- First-line treatment (previously untreated) in patients who present with one or more cytogenic markers†, OR
- Treatment in patients with relapsed or refractory disease, who have disease progression on at least one prior systemic treatment/regimen*

† Chromosome 17p deletion, OR TP53 mutation, OR unmutated immunoglobulin heavy chain variable region (IgHV)
* A prior line of therapy should include a fludarabine-based regimen in fit patients

Supplementary Public Funding	**acalabrutinib** Exceptional Access Program (acalabrutinib - For the treatment of adult patients with chronic lymphocytic leukemia (CLL), according to clinical criteria) (EAP Website)

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B - Drug Regimen

Acalabrutinib tablets and capsules are bioequivalent and have equivalent oral bioavailability **except** when co-administered with acid reducing agents. (Refer to Interactions section.)

acalabrutinib	100 mg	PO	BID

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C - Cycle Frequency

CONTINUOUS TREATMENT

Until disease progression or unacceptable toxicity

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D - Premedication and Supportive Measures

Antiemetic Regimen: Minimal – No routine prophylaxis; PRN recommended

- Also refer to CCO Antiemetic Recommendations.

Screen for hepatitis B virus in all cancer patients starting systemic treatment. Refer to the hepatitis B virus screening and management guideline.

Other Supportive Care:

- Consider prophylaxis for tumour lysis syndrome (TLS) in patients at higher risk of TLS.
- Consider prophylaxis in patients at increased risk for opportunistic infections (e.g. aspergillosis, fungal pneumonia, and Pneumocystis Jiroveci Pneumonia).

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E - Dose Modifications

Doses should be modified according to the protocol by which the patient is being treated.

Consider the benefit-risk analysis of withholding acalabrutinib for at least 3 days pre-and post-surgery due to bleeding risk.

Dosage with toxicity

Dose Level	Acalabrutinib Dose
0	100 mg BID
-1	100 mg Daily
-2	Discontinue

Toxicity	Occurrence	Action
Grade ≥ 3 non-hematologic toxicities OR Grade 3 thrombocytopenia with significant bleeding OR Grade 4 thrombocytopenia OR Grade 4 neutropenia lasting longer than 7 days	First and second	Hold until toxicity is Grade 1 or baseline. Resume at same dose.
	Third	Hold until toxicity is Grade 1 or baseline. Resume at 1 dose level ↓.
	Fourth	Discontinue.

Hepatic Impairment

Hepatic Impairment	Acalabrutinib Dose
Mild or Moderate (Child-Pugh class A, Child-Pugh class B, or total bilirubin 1.5-3 x ULN with any AST)	No dose adjustment required.
Severe (Child-Pugh class C, or total bilirubin > 3 x ULN with any AST)	Avoid use.

Renal Impairment

Approximate Creatinine Clearance* (mL/min)	Acalabrutinib Dose
≥ 30	No dose adjustment required.
< 30	No data available.

*Reported as eGFR in mL/min/1.73m^2, as estimated by MDRD.

Dosage in the Elderly

No dose adjustment is necessary due to age. Clinically relevant differences in safety or efficacy were not observed between those ≥ 65 years and < 65 years.

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F - Adverse Effects

Refer to acalabrutinib drug monograph(s) for additional details of adverse effects

Very common (≥ 50%)	Common (25-49%)	Less common (10-24%)	Uncommon (< 10%), but may be severe or life-threatening
• Infection (may be severe)	• Headache (generally mild) • Bleeding (may be severe) • Diarrhea (generally mild) • Fatigue	• Hyperuricemia • Musculoskeletal pain (generally mild) • ↑ LFTs • Cough, dyspnea • Nausea, vomiting • Rash • Constipation • Myelosuppression (may be severe) • Dizziness	• Secondary malignancy • Arrhythmia • Hypertension

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G - Interactions

Refer to acalabrutinib drug monograph(s) for additional details

- Avoid use with strong CYP3A inhibitors due to ↑ acalabrutinib toxicity. If co-administration with a strong CYP3A inhibitor is short-term, hold acalabrutinib.
- When co-administrated with a moderate CYP3A inhibitor, ↓ dose of acalabrutinib to 100 mg daily.
- Avoid use with strong CYP3A inducers due to ↓ efficacy of acalabrutinib.
- Avoid use of acalabrutinib **capsules** with proton pump inhibitors due to ↓ acalabrutinib absorption. Take acalabrutinib **capsules** 2 hours before taking a H2-receptor antagonist. Separate dosing by at least 2 hours with antacids.
- Acalabrutinib **tablets** can be co-administered with gastric acid reducing agents.

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H - Drug Administration and Special Precautions

Refer to acalabrutinib drug monograph(s) for additional details.

Administration:

- Administer acalabrutinib with or without food.
- Tablets and capsules should be swallowed whole with a glass of **water** and not crushed, dissolved, opened or divided.
- Acidic beverages (i.e. orange juice or grapefruit juice) decrease absorption of acalabrutinib **capsules**.
- If a dose is missed, patient may take within 3 hours of missed dose. If more than 3 hours, the dose should be skipped and taken at the next planned time. Extra doses should not be taken to make up for missed dose.
- Grapefruit, starfruit, Seville oranges, their juices or products should be avoided during acalabrutinib treatment.
- Store at room temperature, in original bottle, and away from children or pets.

Contraindications:

- Patients who are hypersensitive to acalabrutinib or to any ingredient in the formulation or component of the container.

Warnings/Precautions:

- Avoid in patients with severe hepatic impairment (Child-Pugh C or total bilirubin > 3 times ULN, regardless of AST levels).
- Avoid concomitant use of strong CYP3A4 inhibitors.
- Use caution in patients at risk of bleeding, including those receiving concomitant antiplatelet or anticoagulant medications. Consider the benefits and risks of withholding acalabrutinib for at least 3 days pre-and post-surgery.
- Use caution in patients at risk of cardiac arrhythmias (e.g. history of atrial fibrillation or infection / pneumonia).
- Use caution when driving or operating a vehicle or potentially dangerous machinery due to fatigue and dizziness.

Pregnancy and Lactation:

- This regimen is not recommended for use in pregnancy. Adequate contraception should be used by patients and their partners while on treatment and after the last treatment dose. Recommended methods and duration of contraception may differ depending on the treatment. Refer to the drug monograph(s) for more information.
- Breastfeeding is not recommended during treatment and after the last treatment dose. Refer to the drug monograph(s) for recommendations after the last treatment dose (if available).
- Fertility effects: Unlikely

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I - Recommended Clinical Monitoring

Treating physicians may decide to monitor more or less frequently for individual patients but should always consider recommendations from the product monograph.

Refer to the hepatitis B virus screening and management guideline for monitoring during and after treatment.

Recommended Clinical Monitoring

- CBC; Baseline and at each visit
- Renal and liver function tests; Baseline and at each visit
- ECG; Baseline and as clinically indicated
- Clinical toxicity assessment for cardiac symptoms, skin cancers, infection, hyperuricemia, GI effects, pain and bleeding; At each visit
- Grade toxicity using the current NCI-CTCAE (Common Terminology Criteria for Adverse Events) version

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J - Administrative Information

Outpatient prescription for home administration.

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K - References

Acalabrutinib drug monograph. Ontario Health (Cancer Care Ontario).

Byrd JC et al. Acalabrutinib monotherapy in patients with relapsed/refractory chronic lymphocytic leukemia: updated phase 2 results. Blood. 2020;135(15):1204-1213.

Sharman JP, Egyed M, Jurczak W, et al. Acalabrutinib with or without obinutuzumab versus chlorambucil and obinutuzumab for treatment-naive chronic lymphocytic leukaemia (ELEVATE TN): a randomised, controlled, phase 3 trial. Lancet 2020; 395: 1278-91.

July 2024 Updated Hepatic Impairment section

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M - Disclaimer

Regimen Abstracts

A Regimen Abstract is an abbreviated version of a Regimen Monograph and contains only top level information on usage, dosing, schedule, cycle length and special notes (if available). It is intended for healthcare providers and is to be used for informational purposes only. It is not intended to constitute or be a substitute for medical advice, and all uses of the Regimen Abstract are subject to clinical judgment. Such information is provided on an "as-is" basis, without any representation, warranty, or condition, whether express, or implied, statutory or otherwise, as to the information's quality, accuracy, currency, completeness, or reliability, and Cancer Care Ontario disclaims all liability for the use of this information, and for any claims, actions, demands or suits that arise from such use.

Information in regimen abstracts is accurate to the extent of the ST-QBP regimen master listings, and has not undergone the full review process of a regimen monograph. Full regimen monographs will be published for each ST-QBP regimen as they are developed.

Regimen Monographs

Refer to the New Drug Funding Program or Ontario Public Drug Programs websites for the most up-to-date public funding information.

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last revision will be visible on each page of the monograph and regimen. Since standards of usage are constantly evolving, it is advised that the Formulary not be used as the sole source of information. It is strongly recommended that original references or product monograph be consulted prior to using a chemotherapy regimen for the first time.

Some Formulary documents, such as the medication information sheets, regimen information sheets and symptom management information (for patients), are intended for patients. Patients should always consult with their healthcare provider if they have questions regarding any information set out in the Formulary documents.

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