**Regimen Monograph**



## A - Regimen Name

# ALEC Regimen

**Alectinib**

**Disease Site**

Lung
Non-Small Cell

**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**

- First-line treatment of patients with anaplastic lymphoma kinase (ALK)-positive, locally advanced (not amenable to curative therapy) or metastatic non-small cell lung cancer (NSCLC).
- Monotherapy for the treatment of patients with (ALK)-positive, locally advanced (not amenable to curative therapy) or metastatic NSCLC who have progressed on or are intolerant to crizotinib.

**Supplementary Public Funding**

**alectinib**
Exceptional Access Program (alectinib - Treatment of non-small cell lung cancer, according to specific criteria)

back to top

## B - Drug Regimen

Patients must have documented ALK-positive status, based on a validated ALK assay, prior to starting treatment with alectinib.

| | | | |
|---|---|---|---|
| **alectinib** | 600 mg | PO | BID |

back to top

## C - Cycle Frequency

**CONTINUOUS TREATMENT**

Until disease progression or unacceptable toxicity.

back to top

## D - Premedication and Supportive Measures

**Antiemetic Regimen:** Low – 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:**

- Patients must avoid sun exposure while on treatment and for at least 7 days after the last dose, and must use UVA/B sunscreen and lip balm (at least SPF 50).

back to top

## E - Dose Modifications

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

**Dosage with toxicity**

| Dose level | Dose (mg) BID |
|---|---|
| Starting Dose | 600 |
| - 1 | 450 |
| - 2 | 300 |
| -3 | Discontinue |

| Toxicity | Action |
|---|---|
| GI perforation | Discontinue. |
| ILD/pneumonitis of any Grade | Hold; if confirmed, discontinue. |
| Grade 3 Renal Impairment | Hold until serum creatinine recovers to baseline or ≤ Grade 1, then resume at 1 dose level ↓. |
| Grade 4 Renal Impairment | Discontinue. |
| ≥ Grade 3 ALT or AST elevation (> 5 x ULN)<br>**and**<br>Total bilirubin ≤ 2 x ULN | Hold until recovery to baseline or ≤ Grade 1;<br><br>Resume at 1 dose level ↓. |
| ≥ Grade 2 ALT or AST elevation (> 3 x ULN)<br>**and**<br>Total bilirubin ≥ 2 x ULN (in absence of cholestasis or hemolysis) | Discontinue. |
| Grade 2 to 3 Bradycardia (HR < 60 bpm) (symptomatic) | Hold until recovery to ≤ Grade 1 (asymptomatic) bradycardia or HR of ≥ 60 bpm.<br><br>Evaluate concomitant medications; if contributing, discontinue or reduce dose of concomitant drug. Resume at previous dose.<br><br>If no concomitant medication contributing, or contributing medication not stopped/reduced: resume at 1 dose level ↓ |

| | |
|---|---|
| Grade 4 Bradycardia (HR < 60 bpm) (life-threatening consequences, urgent intervention required) | Discontinue if no contributing concomitant medication.<br><br>If contributing concomitant medication is discontinued or reduced: Hold until recovery to ≤ Grade 1 (asymptomatic) bradycardia or HR of ≥ 60 bpm, with frequent monitoring. Resume at 1 dose level ↓.<br><br>If recurs: discontinue. |
| CPK elevation > 5 x ULN | Hold until recovery to baseline or ≤ 2.5 x ULN; resume at same dose. |
| CPK elevation > 10 x ULN **or** 2nd Occurrence of CPK elevation > 5 x ULN | Hold until recovery to baseline or ≤ 2.5 x ULN; resume at 1 dose level ↓. |
| Hemolytic anemia with hemoglobin of < 100 g/L (≥ Grade 2) | Hold until recovery, then resume at 1 dose level ↓.<br>OR<br>Discontinue. |

## Hepatic Impairment

| Pre-existing Hepatic Impairment | Alectinib Dose |
|---|---|
| Mild or Moderate | No dose adjustment required. |
| Severe | 450 mg twice daily. |

## Renal Impairment

| Renal Impairment | Alectinib Dose |
|---|---|
| Mild or Moderate (CrCl ≥ 30 mL/min) | No dose adjustment required. |
| Severe (CrCl < 30 mL/min) | Has not been studied. |

## Dosage in the Elderly

No dose adjustment required. Fatal adverse events and adverse events leading to treatment withdrawal were more common in patients 65 years or older compared to younger patients.

back to top

## F - Adverse Effects

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

| Common (25-49%) | Less common (10-24%) | Uncommon (< 10%),<br><br>but may be severe or life-threatening |
|---|---|---|
| • Constipation<br>• Fatigue | • Musculoskeletal pain<br>• Edema<br>• ↑ LFTs (may be severe)<br>• Anemia<br>• Rash<br>• Nausea, vomiting<br>• Diarrhea<br>• Bradycardia | • Photosensitivity<br>• Visual disorders<br>• Venous thromboembolism<br>• Atrioventricular block<br>• QT interval prolonged<br>• GI perforation<br>• Pneumonitis/eosinophilic pneumonia<br>• Nephrotoxicity<br>• ↑ CPK<br>• Drug-induced liver injury<br>• Hemolytic anemia |

back to top

## G - Interactions

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

- Caution with strong CYP3A inducers, strong CYP3A inhibitors, and CYP2C8 substrates; monitor closely.
- Caution with BCRP and P-glycoprotein substrates with a narrow therapeutic index (in vitro increases in substrate concentration).
- Avoid concomitant use of drugs that lower the heart rate, if possible, due to additive effects. If clinically important bradycardia occurs, discontinue or adjust dosage of the concomitant drug, if possible.

back to top

## H - Drug Administration and Special Precautions

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

### Administration

- Alectinib should be taken with food (fasted state decreases exposure three fold).
- Capsules should not be opened or dissolved.
- If a dose is missed the next dose should be taken at the next scheduled time.
- If vomiting occurs, a repeat dose should not be taken; the next dose should be taken at the next scheduled time.
- Avoid grapefruit, grapefruit juice, products with grapefruit extract, star fruit, Seville oranges, pomegranate, and other similar fruits that inhibit CYP3A4 during alectinib treatment due to risk for increased toxicity.
- Store between 15-30ºC in the original package.

### Contraindications

- Patients who have a hypersensitivity to this drug or any of its components

### Warnings/Precautions

- Use with caution in patients who are at risk for gastrointestinal perforation (eg. concomitant use of medications with GI perforation risk, history of diverticulitis, metastases to the GI tract).
- Use with caution in patients with hepatic impairment or renal impairment.
- Use with caution in patients who have bradycardia at baseline (< 60 bpm), a history of syncope or arrhythmia, sick sinus syndrome, sinoatrial block, AV block, ischemic heart disease, CHF or who are on medications that lower HR.
- Vision disorders, asthenia, fatigue and dizziness have been reported. Patients with these symptoms should use caution when driving or operating machines.
- Contains lactose; carefully consider use in patients with hereditary galactose intolerance, severe lactase deficiency or glucose-galactose malabsorption.

**Pregnancy/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 this treatment and after the last treatment dose. Refer to the drug monograph(s) for recommendations after the last treatment dose (if available).
- Effects on fertility: Unknown

back to top

## 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

- Liver function tests; Baseline, every 2 weeks during the first 3 months of treatment, then at each visit or as clinically indicated; more frequent with abnormal LFTs.
- Blood CPK levels; Every 2 weeks for the first month, and as clinically indicated
- Renal function tests; Baseline, at each visit, and as clinically indicated
- Electrolytes, including serum calcium and potassium; Baseline, at each visit, and as clinically indicated
- Blood pressure and heart rate; Baseline, at each visit, and as clinically indicated.
- ECG; Baseline and as required to evaluate QTc, AV block.
- CBC; Baseline and as clinically indicated, or if hemolytic anemia suspected
- Clinical toxicity assessment for photosensitivity, rash, edema, fatigue, myalgia, dizziness, headache, visual disorders, respiratory and GI effects; At each visit.
- Grade toxicity using the current NCI-CTCAE (Common Terminology Criteria for Adverse Events) version

back to top

## J - Administrative Information

Outpatient prescription for home administration

back to top

## K - References

Alectinib drug monograph, Ontario Health (Cancer Care Ontario).

Ou SI, Ahn JS, De Petris L, et al: Alectinib in Crizotinib-Refractory ALK-Rearranged Non-Small-Cell Lung Cancer: A Phase II Global Study. J Clin Oncol, 2015.

Shaw AT, Gandhi L, Gadgeel S, et al: Alectinib in ALK-positive, crizotinib-resistant, non-small-cell lung cancer: a single-group, multicentre, phase 2 trial. Lancet Oncol 17:234-42, 2016.

**PEBC Advice Documents or Guidelines**

- Therapy for Stage IV Non-Small-Cell Lung Cancer With Driver Alterations: ASCO and OH(CCO) Joint Guideline Update

**April 2024** Updated pregnancy/breastfeeding section

back to top

## 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.*

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***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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back to top