Alectinib Monotherapy

INDICATIONS FOR USE:

INDICATION	ICD10	Regimen Code	Reimbursement status*
Treatment of adult patients with anaplastic lymphoma kinase (ALK)-positive advanced non-small cell lung cancer (NSCLC) previously treated with crizotinib.	C34	00401a	CDS 01/11/2017
As monotherapy is indicated for the first-line treatment of adult patients with anaplastic lymphoma kinase (ALK)-positive advanced non-small cell lung cancer (NSCLC).	C34	00401b	CDS 01/06/2019
As monotherapy is indicated as adjuvant treatment following complete tumour resection for adult patients with anaplastic lymphoma kinase (ALK) -positive NSCLC at high risk of recurrence.	C34	00401c	N/A

*This is 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.

Alectinib is taken orally twice daily.

For adjuvant treatment of NSCLC, the maximum treatment duration with alectinib is 24 months (2 years) whichever occurs first.

For all other indications alectinib is administered until disease progression or unacceptable toxicity develops.

Ensure a minimum 7 day washout after crizotinib prior to starting alectinib (indication 00401a)

Drug	Dose	Route	Cycle
Alectinib	600mg BD	PO	Continuous
Alectinib capsules should be swallowed whole and must not be opened or dissolved. They must be taken with food.			
Delayed or Missed Doses: If a planned dose of alectinib is missed, patients can make up that dose unless the next dose is due within 6 hours. Patients should not take two doses at the same time to make up for a missed dose. **Vomiting:** If vomiting occurs after taking a dose of alectinib, patients should take the next dose at the scheduled time.			

ELIGIBILITY:

- Indications as above
- Adequate organ function

Treatment of advanced NSCLC:

- Histologically confirmed, advanced NSCLC with an *ALK* rearrangement by an approved and validated test method

Adjuvant NSCLC treatment:

- Histologically confirmed stage IB (tumour ≥ 4cm) to stage IIIA NSCLC with an *ALK* rearrangement by an approved and validated test method
- ECOG 0-1

EXCLUSIONS:

- Hypersensitivity to alectinib or to any of the excipients

PRESCRIPTIVE AUTHORITY:

The treatment plan must be initiated by a Consultant Medical Oncologist.

TESTS:

Baseline tests:

- Baseline confirmation that the patient's NSCLC tumour is *ALK* positive by an accurate and validated test method
- FBC, renal and liver profile
- Creatinine phosphokinase (CPK)
- Blood pressure
- ECG

Regular tests:

- Liver profile every 2 weeks during the first 3 months of treatment and every 4 weeks thereafter or as clinically indicated
- FBC and renal profile every 4 weeks
- CPK every 2 weeks for first month and then as clinically indicated
- Blood pressure as clinically indicated
- ECG prior to cycle 2, then as clinically 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
- Management of adverse events may require dose reduction, temporary interruption, or discontinuation of treatment with alectinib
- The dose of alectinib should be reduced in steps of 150 mg twice daily based on tolerability (Table 1)
- Alectinib treatment should be permanently discontinued if patients are unable to tolerate the 300 mg twice daily dose

Table 1: Dose reduction schedule for alectinib

Dose Reduction Schedule	Dose Level
Starting dose	600mg twice daily
First dose reduction	450mg twice daily
Second dose reduction	300mg twice daily

Renal and Hepatic Impairment:

Table 2: Dose modification of alectinib in renal and hepatic impairment

Renal Impairment		Hepatic Impairment	
CrCl	**Dose**	**Impairment**	**Dose**
≥30 mL/min	No dose adjustment is needed	Child-Pugh A/B	No dose adjustment is needed
<30 mL/min	No need for dose adjustment is expected	Child-Pugh C	75% of the original dose (450mg BID)
Haemodialysis	No need for dose adjustment is expected		
Renal and hepatic – Giraud et al 2023			

Management of adverse events:

Table 3: Dose modification schedule based on adverse events

CTCAE Grade	Dose Modification
ILD/pneumonitis of any severity grade	Immediately interrupt and permanently discontinue alectinib if no other potential causes of ILD/pneumonitis have been identified.
ALT or AST elevation of > 5 times ULN with total bilirubin ≤ 2 times ULN	Temporarily withhold until recovery to baseline or ≤ 3 times ULN, then resume at reduced dose (see Table 1).
ALT or AST elevation of > 3 times ULN with total bilirubin elevation > 2 times ULN in the absence of cholestasis or haemolysis	Permanently discontinue alectinib.
Bradycardia[a] Grade 2 or Grade 3 (symptomatic, may be severe and medically significant, medical intervention indicated)	Temporarily withhold until recovery to ≤ Grade 1 (asymptomatic) bradycardia or to a heart rate of ≥ 60 bpm. Evaluate concomitant medicinal products known to cause bradycardia, as well as anti-hypertensive medicinal products. • If a contributing concomitant medicinal product is identified and discontinued, or its dose is adjusted, resume at previous dose upon recovery to ≤ Grade 1 (asymptomatic) bradycardia or to a heart rate of ≥ 60 bpm. • If no contributing concomitant medicinal product is identified, or if contributing concomitant medicinal products are not discontinued or dose modified, resume at

	reduced dose (see Table 1) upon recovery to ≤ Grade 1 (asymptomatic) bradycardia or to a heart rate of ≥ 60 bpm
Bradycardia[a] Grade 4 (life-threatening consequences, urgent intervention indicated)	• Permanently discontinue if no contributing concomitant medicinal product is identified • If a contributing concomitant medicinal product is identified and discontinued, or its dose is adjusted, resume at reduced dose (see Table 1) upon recovery to ≤ Grade 1 (asymptomatic) bradycardia or to a heart rate of ≥ 60 bpm, with frequent monitoring as clinically indicated • Permanently discontinue in case of recurrence
CPK elevation > 5 times ULN	Temporarily withhold until recovery to baseline or to ≤ 2.5 times ULN, then resume at the same dose.
CPK elevation > 10 times ULN or second occurrence of CPK elevation of > 5 times ULN	Temporarily withhold until recovery to baseline or to ≤ 2.5 times ULN, then resume at reduced dose as per Table 1.
Haemolytic anaemia with haemoglobin of < 10 g/dL (Grade ≥ 2)	Temporarily withhold until resolution, then resume at reduced dose (see Table 1).

ALT = alanine aminotransferase; AST = aspartate aminotransferase; CPK = creatine phosphokinase; CTCAE = NCI Common Terminology Criteria for Adverse Events; ILD = interstitial lung disease; ULN = upper limit of normal

[a] Heart rate less than 60 beats per minute (bpm).

SUPPORTIVE CARE:

EMETOGENIC POTENTIAL:

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

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

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

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

PREMEDICATIONS: Not required

OTHER SUPPORTIVE CARE: No specific recommendations

ADVERSE EFFECTS

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

DRUG INTERACTIONS:

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

REFERENCES:

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3. Yang et al. Pooled Systemic Efficacy and Safety Data from the Pivotal Phase II Studies (NP28673 and NP28761) of Alectinib in ALK-positive Non-Small Cell Lung Cancer. J Thoracic Oncology 2017;
4. Peters et al. Alectinib versus Crizotinib in Untreated ALK-Positive Non Small-Cell Lung Cancer. NEJM 2017; 377(19) 829-838.
5. Wu YL, ALINA Investigators, et al. Alectinib in Resected ALK-Positive Non-Small-Cell Lung Cancer. N Engl J Med. 2024 Apr 11; 390(14):1265-1276. doi: 10.1056/NEJMoa2310532. PMID: 38598794
6. 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://www.thelancet.com/journals/lanonc/article/PIIS1470-2045(23)00216-4/fulltext
7. NCCP Classification Document for Systemic Anti-Cancer Therapy (SACT) Induced Nausea and Vomiting. V6 2025. 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
8. Alecesa® Summary of Product Characteristics. EMA. Last updated: 12/11/2024. Accessed Dec 2024. Available at: https://www.ema.europa.eu/en/documents/product-information/alecensa-epar-product-information_en.pdf

Version	Date	Amendment	Approved By
1	26/09/17		Dr. Deirdre O'Mahony
2	01/11/2017	Updated reimbursement status	
3	21/01/2019	Updated hepatic impairment dose modifications as per SmPC update. Adverse Events: Updated wording on sodium content as per SmPC update	Dr. Deirdre O'Mahony
4	13/06/2019	Inclusion of indication for 1L treatment	Dr Dearbhaile Collins
5	06/01/2021	Amended emetogenic potential	Prof. Maccon Keane
6	13/05/2025	Inclusion of indication for adjuvant treatment. Updated text above and within treatment table. Updated eligibility criteria for adjuvant indication. Updated Testing section. Updated recommendations for renal and hepatic impairment line with Giraud et al 2023. Updated Table 3 in line with SmPC update. Emetogenic potential amended as per NCCP standard wording. Adverse effects removed and regimen specific complications amended as per NCCP standard wording. Drug interactions sections removed.	Prof Maccon Keane

Comments and feedback welcome at oncologydrugs@cancercontrol.ie.