ALECTINIB (Alecensa)

INDICATION (ICD10) C34

Check the most recent Blueteq eligibility criteria before prescribing. Blueteq registration required. (www.england.nhs.uk/publication/national-cancer-drugs-fund-list/) (ALE1) (ALE2)

1. Monotherapy for anaplastic lymphoma kinase-positive locally advanced or metastatic non-small cell lung cancer (with no known brain metastases) previously untreated with an ALK inhibitor, and treatment-naïve to 1st line cytotoxic chemotherapy-containing systemic treatment for this locally advanced or metastatic NSCLC indication (the only previous cytotoxic treatment allowed for patients to be treated is adjuvant or neoadjuvant chemotherapy or chemotherapy given concurrently with radiotherapy). PS 0, 1 or 2. (TA536)
2. Alectinib monotherapy for adjuvant treatment in adults after complete tumour resection in patients with stage IB-IIIA non-small cell lung cancer whose tumours have an ALK gene rearrangement. Not received any pre-operative systemic therapy (cytotoxic chemotherapy, immunotherapy, ALK-targeted tyrosine kinase inhibitors), no prior treatment with an ALK-targeted drug or any pre-operative or post-operative radiation therapy for the NSCLC. No more than 12 weeks have elapsed since surgery. Does not have brain metastases on CT or MR imaging of the brain done either before surgery or prior to this application. PS 0 or 1. (TA1014)

REGIMEN

ALECTINIB 600mg orally twice daily continuously

CYCLE FREQUENCY AND NUMBER OF CYCLES

Adjuvant – for a maximum of 2 calendar years. A formal medical review to occur at least by the end of the first 8 weeks of treatment.

Advanced / metastatic - until disease progression. A formal medical review to occur at least by the end of the first 8 weeks of treatment. Review every 2-3 months by CT scan.

ADMINISTRATION

Available as 150mg capsules

Swallowed whole with food.

Grapefruit and grapefruit juice and Seville oranges should be avoided while on alectinib.

ANTI-EMETICS

Minimal risk

CONCURRENT MEDICATION REQUIRED

Alectinib	None required

EXTRAVASATION AND TYPE OF LINE / FILTERS

Not applicable

INVESTIGATIONS

Blood results required before SACT administration
FBC, U&E and LFTs every 2 weeks for 3 cycles then every cycle
Neutrophils x 10^9/L ≥1.0
Platelets x 10^9/L ≥100
Hb >100g/dl
Creatinine every cycle
Creatine phosphokinase every 1-2 cycles
ECG baseline
BP and heart rate baseline then as clinically indicated
Baseline weight and every cycle

MAIN TOXICITES AND ADVERSE REACTIONS

Alectinib	Constipation Photosensitivity Interstitial lung disease / pneumonitis Hepatotoxicity Bradycardia Severe myalgia

INTERACTIONS WHICH MAY REQUIRE DOSE MODIFICATIONS

(not exhaustive list check SPC/BNF/Stockleys)

Alectinib	Strong CYP3A inhibitors and inducers eg carbamazepine, phenobarbital, phenytoin, St John's Wort, rifampicin, ketoconazole, itraconazole, voriconazole, ritonavir. No dose reductions but monitor Potential to increase plasma concentrations of P-gp substrates eg digoxin, dabigatran, topotecan, sirolimus, everolimus and lapatinib). Monitor Risk of increased plasma concentrations of BRCP substrates (eg methotrexate, mitoxantrone). Monitor The effectiveness of concomitant administration of oral contraceptives may be reduced. Avoid grapefruit and seville oranges

DOSE MODIFICATIONS

Level	Alectinib dose
Starting dose	600mg twice daily
First dose reduction	450mg twice daily
Second dose reduction	300mg twice daily

Haematological

Alectinib

Haemolytic anaemia with haemoglobin <10g/dL (grade ≥2)	Temporarily withhold until resolution, then resume at reduced dose

Non-haematological

Alectinib

Any patient with a grade 3 or 4 toxicity not controlled by optimum supportive care will require a dose reduction.

Management of adverse events may require dose reduction, temporary interruption or discontinuation of treatment. Alectinib treatment should be permanently discontinued if patients are unable to tolerate the 300mg twice daily dose.

Alectinib should be withheld if pneumonitis is suspected, and must be permanently discontinued if treatment-related pneumonitis or interstitial lung disease is diagnosed.

Bradycardia

Grade 2 or 3 Pulse less than 60 beats per minute (bpm) Symptomatic, may be severe and medically significant, medical intervention indicated	Withhold alectinib until asymptomatic and heart rate ≥60bpm. Evaluate concomitant medications known to cause bradycardia, as well as anti-hypertensive medications. If contributing concomitant medication is identified and discontinued, or its dose is adjusted, resume alectinib at previous dose. If no contributing concomitant medication is identified, or if contributing concomitant medications are not discontinued or dose modified, resume alectinib at reduced dose upon recovery.
Grade 4 Pulse less than 60bpm Life-threatening consequences, urgent intervention indicated	Permanently discontinue alectinib if no contributing concomitant medication is identified. If contributing concomitant medication is identified and discontinued, or its dose is adjusted, resume alectinib at a reduced dose, with frequent monitoring, upon recovery and heart rate ≥60bpm. Permanently discontinue in case of recurrence.

Hepatotoxicity

ALT / AST >5xULN with Bilirubin ≤2xULN	Temporarily withhold alectinib until ALT / AST recovery to baseline or ≤3xULN. Then resume at reduced dose.
ALT / AST >3xULN with Bilirubin >2xULN in the absence of cholestasis or haemolysis	Permanently discontinue alectinib

Myalgia

CPK >5xULN	Temporarily withhold until recovery to baseline or to ≤2.5xULN, then resume at the same dose.
CPK >10xULN or 2nd occurrence of CPK >5xULN	Temporarily withhold until recovery to baseline or to ≤2.5xULN, then resume at reduced dose as table above.

Hepatic impairment
Alectinib
Patients with underlying severe hepatic impairment (Child-Pugh C) should start with a dose of 450mg twice daily.

Renal impairment
Alectinib
Alectinib elimination via the kidney is negligible, no dose adjustment is required in patients with severe renal impairment.

REFERENCES
1. Peters, S et al; NEJM 2017; 377: 829-838