Indication	First-line treatment of adult patients with anaplastic lymphoma kinase (ALK)-positive advanced non-small cell lung cancer (NSCLC). (ie no previous cytotoxic except when this has been given as neoadjuvant or adjuvant therapy or concurrently with radiotherapy). NB: In cases of intolerance to alectinib, either ceritinib or crizotinib is to be used only if the patient has not had progressive disease whilst on alectinib.
Treatment Intent	Palliative
Frequency and number of cycles	Every 28 days Until disease progression, unacceptable toxicity or patient choice.
Monitoring parameters pre-treatment	• FBC & U&Es every 4 weeks. If neutrophils <0.5 or platelets <50 d/w consultant • LFTs at baseline then every 2 weeks for the first three months, then monthly, or as clinically indicated. • CPK levels should be assessed every two weeks for the first month of treatment and then as clinically indicated. • Heart rate and blood pressure should be monitored monthly. • Hepatic impairment: No starting dose adjustment is required in patients with mild or moderate (Child-Pugh A or B) hepatic impairment. Patients with severe hepatic impairment (Child-Pugh C) should receive a starting dose of 450 mg taken twice daily (total daily dose of 900 mg). • Renal impairment: No dose adjustment is required in patients with mild, moderate or severe renal impairment. • If a dose of alectinib is missed and the next dose is due within 6 hours patients should not take the missed dose. If vomiting occurs after taking a dose of alectinib, patients should take the next dose at the scheduled time. • Dose adjustments & management of adverse events: Management of adverse events may require dose reduction, temporary interruption, or discontinuation of treatment with alectinib (see table below). Dose modification advice is provided in Tables below. Dose reduction levels: 1st dose reduction level 450mg po bd, 2nd dose reduction level 300mg po bd. Alectinib treatment should be permanently discontinued if patients are unable to tolerate the 300 mg twice daily dose. Patients should be monitored for pulmonary symptoms indicative of pneumonitis. Alectinib should be immediately interrupted in patients diagnosed with ILD/pneumonitis and should be permanently discontinued if no other potential causes of ILD/pneumonitis have been identified. Severe myalgia and elevations in CPK have been reported with alectinib. Patients should be advised to report any unexplained muscle pain, tenderness, or weakness. Symptomatic bradycardia can occur with alectinib.

	• Patients should be advised to avoid prolonged sun exposure and use sun screen while taking alectinib, and for at least 7 days after discontinuation of treatment. • The recommended daily dose (1200 mg) of alectinib contains 2.1 mmol (or 48 mg) sodium. • Drug interactions: Appropriate monitoring is recommended for patients taking concomitant strong CYP3A inducers which may reduce alectinib levels (e.g carbamazepine, phenobarbital, phenytoin, rifabutin, rifampicin and St. John's Wort) or strong CYP3A inhibitors which may increase alectinib levels (e.g ritonavir, saquinavir, telithromycin, ketoconazole, itraconazole, voriconazole, posaconazole nefazodone, grapefruit or Seville oranges). Co-administration with P-gp substrates (e.g. digoxin, dabigatran etexilate, topotecan, sirolimus, everolimus, nilotinib and lapatinib) or BCRP substrates (e.g. methotrexate, mitoxantrone, topotecan and lapatinib) require monitoring, as plasma concentration of the P-gp substrate or BCRP substrate may be increased. • Alectinib has a minor influence on the ability to drive and use machines. Caution should be exercised when driving or operating machines as patients may experience symptomatic bradycardia (e.g syncope, dizziness, hypotension) or vision disorders while taking alectinib.
Reference(s)	SmPC accessed on line 2/7/18

Dose modification advice for specified Adverse Drug Reactions

CTCAE grade	Alectinib treatment
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 Grade ≥ 3 (> 5 times ULN) with total bilirubin ≤ 2 times ULN	Temporarily withhold until recovery to baseline or ≤ Grade 1 (≤ 3 times ULN), then resume at reduced dose.
ALT or AST elevation of Grade ≥ 2 (> 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 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 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.

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

Repeat every 28 days

TTO	Drug	Dose	Route	Directions
Day 1	Alectinib	600mg	po	bd swallowed whole with food
	Metoclopramide	10mg	po	up to 3 times a day as required. Do not take for more than 5 days continuously.