

## Chemotherapy Protocol

### LUNG CANCER – NON-SMALL CELL (NSCLC)

#### ALECTINIB

##### Regimen

- NSCLC - ALEctinib

##### Indication

- Alectinib (as monotherapy) is indicated for first-line treatment of adult patients with anaplastic lymphoma kinase (ALK)-positive advanced NSCLC where;
  - the patient has a histologically or cytologically confirmed diagnosis of stage IIIB or IV non small cell lung cancer that carries an anaplastic lymphoma kinase (ALK) rearrangement
  - The patient has received no previous ALK-targeted therapy
  - the patient has received no previous cytotoxic chemotherapy for locally advanced or metastatic non small cell lung cancer ie no previous systemic treatment except when this has been given as neoadjuvant or adjuvant therapy or concurrently with radiotherapy
  - alectinib will be used only as single-agent therapy
  - the patient either has no brain metastases or, if the patient has brain metastases, the patient is symptomatically stable prior to starting alectinib
  - the patient will be treated until loss of clinical benefit or excessive toxicity or patient choice to discontinue treatment, whichever is the sooner
  - treatment breaks of up to 6 weeks are allowed but solely to allow toxicities to settle
  - 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. Neither ceritinib nor crizotinib are to be used following disease progression on alectinib as there is no current clear evidence to support treatment with ceritinib or crizotinib after disease progression on alectinib. Alectinib cannot be used in any line other than 1st line as the manufacturer chose not to make a submission to NICE for its licensed indication for use after crizotinib
  - WHO performance status 0, 1, 2

### Toxicity

Drug	Adverse Effect
Alectinib	Anaemia, gastrointestinal disturbances, hepatobiliary disorders, myalgia, nausea, oedema, skin rash, weight gain, interstitial lung disease, pneumonitis, bradycardia, photosensitivity, constipation, oedema, nausea, vomiting, diarrhoea, visual disorders

The adverse effects listed are not exhaustive. Please refer to the relevant Summary of Product Characteristics for full details.

### Monitoring

- FBC, LFTs and U&Es prior to day one of treatment. These should be monitored every two weeks for the first twelve weeks of treatment and then on day 1 thereafter. However, in some centres it is practice to monitor on days 1 and 14 of the first cycle and then on day 1 of the cycle thereafter.
- Creatinine phosphokinase levels, heart rate and blood pressure on day 1 one of the cycle
- ALK status prior to starting treatment

### Dose Modifications

The dose modifications listed are for haematological, liver and renal function and drug specific toxicities only. Dose adjustments may be necessary for other toxicities as well. The toxicities below should be read in conjunction with the relevant Summary of Product Characteristics ([www.medicines.org.uk](http://www.medicines.org.uk)).

In principle all dose reductions due to adverse drug reactions should not be re-escalated in subsequent cycles without consultant approval. It is also a general rule for chemotherapy that if a third dose reduction is necessary treatment should be stopped.

Management of adverse events may require dose reduction, temporary interruption, or discontinuation of treatment (see table below). Alectinib should be permanently discontinued if patients are unable to tolerate the 300mg twice a day dose.

Dose reductions	Dose
Starting dose	600mg twice daily
First dose reduction	450mg twice daily
Second dose reduction	300mg twice daily

### Haematological

Alectinib is not considered myelotoxic therefore dose adjustment for haematological parameters is not required.

Consider blood transfusion if patient symptomatic of anaemia or has a haemoglobin of less than 8g/dL (80mg/L).

### Hepatic impairment

No starting dose adjustment is required in patients with underlying mild (Child-Pugh A) or moderate (Child-Pugh B) hepatic impairment. Patients with underlying severe hepatic impairment (Child-Pugh C) should receive a starting dose of 450 mg taken twice a day (total dose of 900mg). For all patients with hepatic impairment, appropriate monitoring is advised.

Drug	Bilirubin $\mu\text{mol/L}$		ALT / AST units/L	Dose
Alectinib	Less than or equal to 1.5xULN	and	Greater than 5xULN	Temporarily withhold until recovery to baseline or ALT / AST is less than or equal to 3xULN, then resume at reduced dose.
	Greater than 2xULN	and	Greater than 3xULN	In the absence of cholestasis or haemolysis - permanently discontinue

### Renal Impairment

Drug	Renal impairment	Guidance
Alectinib	Mild / moderate	No dose adjustment required
	Severe	No information available. Although negligible drug is eliminated via the kidneys, therefore no dose adjustment required (monitor patient carefully)

### Other

Dose reductions or interruptions in therapy are not necessary for those toxicities that are considered unlikely to be serious or life threatening. For example, alopecia, altered taste or nail changes.

CTCAE grade	Guidance
Interstitial lung disease / pneumonitis (any grade)	Discontinue treatment (if no other causes can be identified)
Bradycardia (grade 2-3)	<p>Withhold until recovery to at least grade 1 (asymptomatic) bradycardia or to a heart rate of <math>\geq 60</math> bpm. Evaluate concomitant medicinal products known to cause bradycardia, as well as anti-hypertensive medicinal products.</p> <p>If a contributing concomitant medicinal product is identified and discontinued, or its dose is adjusted, resume at previous dose upon recovery to at least grade 1.</p> <p>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 above) upon recovery to at least grade 1.</p>
Bradycardia (grade 4)	<p>Permanently discontinue if no contributing concomitant medicinal product is identified.</p> <p>If a contributing concomitant medicinal product is identified and discontinued, or its dose is adjusted, resume at reduced dose (see table above) upon recovery to at least grade 1, with frequent monitoring as clinically indicated.</p> <p>Permanently discontinue in case of recurrence.</p>
CPK (5-10x ULN) 1 <sup>st</sup> occurrence	Temporarily withhold until recovery to baseline or to less than or equal to 2.5xULN, then resume at the same dose.
CPK (5-10x ULN) 2 <sup>nd</sup> occurrence	Temporarily withhold until recovery to baseline or to less than or equal to 2.5xULN, then resume at reduced dose (see table above).
CPK (greater than 10xULN)	

### [Regimen](#)

**28 day cycle until disease progression, unacceptable toxicity or patient chooses to stop treatment (12 cycles will be set in ARIA).**

Drug	Dose	Days	Administration
Alectinib	600mg twice a day	1-28 inclusive	Oral

### [Dose Information](#)

- Alectinib is available in 150mg hard capsules

### Administration Information

- Swallow whole, do not open or dissolve capsules
- Take with or after food
- 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.
- If vomiting occurs after taking a dose of alectinib, patients should take the next dose at the scheduled time.

### Additional Information

- The National Patient Safety Alert on oral chemotherapy (NPSA/2008/RRR001) must be followed in relation to alectinib.

### Coding

- Procurement – X71.5
- Delivery – X73.1

#### References

1. Peters S, Camidge DR, Shaw AT et al. Alectinib versus crizotinib in untreated ALK positive non-small cell lung cancer. N Engl J Med (2017); 377: 829-838.

## REGIMEN SUMMARY

ALECTinib

### Day One

1. Alectinib 600mg twice a day continuous oral  
Administration Instructions  
Take with or just after food. Swallow whole, do not crush or chew.  
  
Oral chemotherapy

## DOCUMENT CONTROL

Version	Date	Amendment	Written By	Approved By
1	August 2018	None	Stuart Martin Pharmacist  Dr Deborah Wright Pharmacist	Dr Luke Nolan Consultant Medical Oncologist

This chemotherapy protocol has been developed as part of the chemotherapy electronic prescribing project. This was and remains a collaborative project that originated from the former CSCCN. These documents have been approved on behalf of the following Trusts;

Hampshire Hospitals NHS Foundation Trust  
NHS Isle of Wight  
Portsmouth Hospitals NHS Trust  
Salisbury Hospitals NHS Foundation Trust  
University Hospital Southampton NHS Foundation Trust  
Western Sussex Hospitals NHS Foundation Trust

All actions have been taken to ensure these protocols are correct. However, no responsibility can be taken for errors that occur as a result of following these guidelines. These protocols should be used in conjunction with other references such as the Summary of Product Characteristics and relevant published papers.