Chemotherapy Protocol

LUNG CANCER – NON-SMALL CELL (NSCLC)

CRIZOTINIB

This protocol may require funding

Regimen

- NSCLC - Crizotinib

Indication

- The treatment of ALK+ve advanced or metastatic non-small cell lung cancer as second or subsequent line treatment post first line combination chemotherapy

Toxicity

Drug	Adverse Effects
Crizotinib	Diarrhoea, constipation, rash, interstitial lung disease, GI perforation, eye disorders, QT interval prolongation

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

Monitoring

- Current CT scan (ideally within 1 month) before starting crizotinib and repeat within 3 months of starting treatment, or earlier if necessary
- Chest x-ray should be performed before starting treatment and every 4 weeks
- LFT every two weeks for two months then monthly
- FBC, U&Es every four weeks

Dose Modifications

If dose modifications are required then the dose of crizotinib should be reduced to 200mg twice a day. If a second dose reduction is necessary then prescribe 250mg once a day.

Haematological

Any haematological toxicity (except lymphopenia)	Dose Modification Algorithms
NCI-CTC Grade 1 or 2	Continue treatment at same dose; monitor as clinically indicated.
NCI-CTC Grade 3	**Step 1.** Interrupt treatment until toxicity reduced to NCI-CTC grade 2 or below **Step 2.** Restart treatment at same dose.
NCI-CTC Grade 4 (first and second occurence)	**Step 1.** Interrupt treatment until toxicity reduced to NCI-CTC grade 2 or below **Step 2**. Restart treatment with lower dose
NCI-CTC Grade 4 (further recurrence)	Discontinue permanently

Hepatic Impairment

Drug	Dose
Crizotinib	Crizotinib has not been studied in patients with hepatic impairment. Crizotinib should be used with extra caution in patients with mild or moderate hepatic impairment, and is not recommended in patients with severe hepatic impairment.

Crizotinib can also cause liver abnormalities, adjust doses according to the table below.

Liver	Dose Modification Algorithms
AST or ALT greater than 5xULN, and bilirubin greater than 1.5 x ULN	**Step 1.** Interrupt treatment until toxicity reduced to NCI-CTC grade 1 or baseline. **Step 2.** Restart treatment with lower dose. If recurrence of toxicity, discontinue. **Step 3.** In 3rd recurrence, discontinue permanently
AST or ALT greater than 3xULN, and bilirubin greater than 1.5xULN (in the absence of cholestasis or hemolysis)	Discontinue permanently

Renal Impairment

Drug	Dose
Crizotinib	No starting dose adjustment is required in patients with CrCl equal to or greater than 30ml/min. No data is available in patients with creatinine clearance of less than 30ml/min so no dosing recommendation can be made for these patients.

Other

Cardiac

QTc prolongation has been observed, which may lead to an increased risk for ventricular tachyarrhythmias (e.g., Torsade de Pointes) or sudden death. The risk of QTc prolongation may be increased in patients concomitantly taking antiarrhythmics and in patients with relevant pre-existing cardiac disease, bradycardia, or electrolyte disturbances (e.g., secondary to diarrhoea or vomiting). Crizotinib should be administered with caution to patients who have a history of or predisposition for QTc prolongation, or who are taking medicinal products that are known to prolong the QT interval.

Cardiac	Dose Modification Algorithms
NCI-CTC grade 3 QTc prolongation	**Step 1.** Interrupt treatment until toxicity reduced to NCI-CTC grade 1 or below **Step 2.** Restart treatment with lower dose.
NCI-CTC grade 4	Discontinue permanently

Pneumonitis

Crizotinib has been associated with severe, life-threatening, or fatal treatment-related pneumonitis in clinical trials. All of these cases occurred within two months after the initiation of treatment. Patients with pulmonary symptoms indicative of pneumonitis should be monitored and treatment withheld if pneumonitis is suspected. Other causes of pneumonitis should be excluded, and crizotinib should be permanently discontinued in patients diagnosed with treatment-related pneumonitis.

Regimen

Continuous (28 day cycle)

Drug	Dose	Days	Administration
Crizotinib	250mg twice a day	Continuous	Oral

Dose Information

- Crizotinib is available as 200mg and 250mg capsules
- Swallow whole, do not chew or crush.

Additional Therapy

- Loperamide 4mg oral stat after the first loose stool and then 2-4mg when required for the relief of diarrhoea (maximum 16mg/24 hours)
- Metoclopramide 10mg oral three times a day when required for the relief of nausea and vomiting

Additional Information

- Crizotinib interacts with a number of other medications
- The National Patient Safety Alert on oral chemotherapy (NPSA/2008/RRR001) must be followed in relation to crizotinib

Coding

- Procurement – X70.8
- Delivery – X72.9

References
1.Shaw AT, Kim DW, Nakagawa K et al. Crizotinib versus chemotherapy in advanced ALK positive lung cancer. N Engl J Med 2013; 368 (25): 2385-2394.

REGIMEN SUMMARY

Crizotinib

Day One

1. Crizotinib 250mg twice a day continuous oral
   Administration Instructions
   Swallow whole, do not crush or chew

DOCUMENT CONTROL

Version	Date	Amendment	Written By	Approved By
1	June 2015	None	Dr Deborah Wright Pharmacist	Dr Andrew Bates Consultant Clinical 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 NHS Foundation Trust
University Hospital Southampton NHS Foundation Trust
Western Sussex Hospitals NHS Trust

All actions have been taken to ensure these protocols are correct. However, no responsibility can be taken for errors which occur as a result of following these guidelines.