

Lung Pathway Group – Erlotinib in Non-Small Cell Lung Cancer (NSCLC)

Indication:

NICE TA258

Locally advanced or metastatic NSCLC as a first line treatment option
Positive test for epidermal growth factor receptor tyrosine kinase (EGFR-TK) mutation

NICE TA162

Alternative to docetaxel as a second line treatment option in locally advanced or metastatic NSCLC

3rd and subsequent line treatment of locally advanced or metastatic stage III or IV NSCLC in patients who have previously not received erlotinib.

Performance status ECOG \leq 2

Eligible for patients able to tolerate and comply with oral dosage forms.

Regimen details:

Erlotinib 150mg PO Once daily continuously

Administration:

Erlotinib available as available as 25mg, 100mg and 150mg film coated tablets.

Tablets to be swallowed whole with water, on an empty stomach – at least an hour before or 2 hours after food.

Drugs that alter the pH of the upper GI tract, like proton pump inhibitors, H2 antagonists and antacids, may alter the solubility and bioavailability of erlotinib and should be avoided. Increasing the dose of erlotinib when co-administered with such agents is not likely to compensate for the loss of exposure. If required, antacids should be taken at least 4 hours before or 2 hours after the dose of erlotinib.

Version: 1.0 Supersedes: all other versions	Approved by LCA Lung Pathway Chemotherapy Lead: Dr Rohit Lal	
Reason for Update: LCA Protocol Development	Approved by LCA Joint Delivery Subgroup Co-Chairs: Pauline McCalla & Rebecca Johl	
Prepared by: Lisa Yuen	Approved by LCA Medicines & Chemotherapy Steering Group Chair: Jamie Ferguson	
Second check by: Laura Cameron	Date prepared: November 2014	Review Date: November 2016
<p>Disclaimer: The Joint Delivery Chemotherapy Nurse/Oncology Pharmacist Group is a sub-group of the Medicines & Chemotherapy Steering Group (MCSG) working within the London Cancer Alliance Integrated Cancer System (LCA). The output of the LCA MCSG includes documentation that can be adopted by healthcare organisations at their discretion. It is the responsibility of each individual organisation to ensure that appropriate governance and safety clearance procedures within their own clinical service have been followed prior to implementation of any such pieces of work. LCA assume no responsibility for this process within individual organisations, and no responsibility for the clinical management of individual patients or patient groups. Any clinical queries regarding individual patients or documentation should be directed to the relevant clinical team within the most appropriate healthcare organisation.</p> <p>©LCA Copyright 2014</p>		

Lung Pathway Group – Erlotinib in Non-Small Cell Lung Cancer (NSCLC)

Frequency: Dosing is continuous, until disease progression or unacceptable toxicity

Pre-medication: Not routinely required

Anti- emetics: Minimal emetogenicity
Follow local anti-emetic policy

Supportive medication: Diarrhoea can be managed with loperamide
Mouthcare as per local policy
Various approaches may be considered to deal with skin reactions including rash, acne type reactions, erythema/ pruritus, dryness or blistering (topical emollients, cleansers or possibly anti-infective creams). Urea containing creams may be beneficial to treat dry skin. Support use of non-deodorant, non-fragrance products. Consider products with anti-itch additions in pruritus, and exfoliating products in hyperkeratosis. Anti-dandruff shampoo may help in management of itchy scalp. Analgesia may help but a 1-2 week dose interruption may be necessary for painful and severe symptoms. Rashes usually resolve rapidly upon cessation of treatment.

Extravasation: Not applicable

Regular investigations: Prior to Cycle 1:
EGFR mutation analysis
FBC Day 1 (within 14 days)
LFTs Day 1 (within 14 days)
U&Es Day 1 (within 14 days)
Imaging Baseline

Cycle 1, Day 14
Consider LFTs and clinical toxicity review (as per local practice)

Post cycle 2*:
FBC Every 2 - 3 months
LFTs Every 2 - 3 months
U&Es Every 2 - 3 months
Imaging Every 3 months

Regular clinical assessments and grading of diarrhoea, adverse skin reaction and tolerance of treatment. Monitor for signs and symptoms of dehydration.

Version: 1.0 Supersedes: all other versions	Approved by LCA Lung Pathway Chemotherapy Lead: Dr Rohit Lal
Reason for Update: LCA Protocol Development	Approved by LCA Joint Delivery Subgroup Co-Chairs: Pauline McCalla & Rebecca Johl
Prepared by: Lisa Yuen	Approved by LCA Medicines & Chemotherapy Steering Group Chair: Jamie Ferguson
Second check by: Laura Cameron	Date prepared: November 2014 Review Date: November 2016
<p>Disclaimer: The Joint Delivery Chemotherapy Nurse/Oncology Pharmacist Group is a sub-group of the Medicines & Chemotherapy Steering Group (MCSG) working within the London Cancer Alliance Integrated Cancer System (LCA). The output of the LCA MCSG includes documentation that can be adopted by healthcare organisations at their discretion. It is the responsibility of each individual organisation to ensure that appropriate governance and safety clearance procedures within their own clinical service have been followed prior to implementation of any such pieces of work. LCA assume no responsibility for this process within individual organisations, and no responsibility for the clinical management of individual patients or patient groups. Any clinical queries regarding individual patients or documentation should be directed to the relevant clinical team within the most appropriate healthcare organisation.</p> <p>©LCA Copyright 2014</p>	

*Repeat supply of erlotinib does not require blood monitoring parameters to be accessible on the day. The medical team will set up treatment pathways to ensure continuous trend monitoring and timely clinical review when needed.

Toxicities: Diarrhoea, skin reactions, nail changes, mucositis, elevated liver enzymes, ocular disorders, neutropenia, anaemia, asthenia, headache, gastrointestinal bleeding and perforation, interstitial lung disease.

DOSE MODIFICATIONS

Haematological Toxicity No dose modifications are required for haematological toxicity

Non-haematological Toxicities

Renal Impairment

The safety and efficacy of erlotinib has not been studied in patients with renal impairment (serum creatinine concentration >1.5 times the upper normal limit). Based on pharmacokinetic data no dose adjustments appear necessary in patients with mild or moderate renal impairment. No data is available for patients with creatinine clearance <15 ml/min and is not recommended.

Hepatic Impairment

Erlotinib undergoes hepatic metabolism and biliary excretion; use with caution with hepatic impairment. In population pharmacokinetic analysis, increased serum concentrations of total bilirubin were associated with a slower rate of erlotinib clearance. The safety and efficacy of erlotinib has not been studied in patients with severe hepatic dysfunction (AST/ALT> 5 x ULN). Consider dose interruption and/or reduction if severe adverse effects occur – discuss with consultant.

Dose modifications for other toxicities as appropriate

Diarrhoea and Rash

Diarrhoea can usually be managed with loperamide. Patients with severe diarrhoea who are unresponsive to loperamide or who become dehydrated may require dose reduction or temporary interruption of erlotinib therapy.

Patients with severe skin reactions require aggressive treatment that may include oral steroids and antibiotics; discuss with the Consultant. In general, dose interruptions should be avoided in the first instance. (Note: the rash usually subsides despite continued therapy by week 4 in some patients).

When dose reduction is necessary, erlotinib should be reduced in 50mg decrements.

Version: 1.0 Supersedes: all other versions	Approved by LCA Lung Pathway Chemotherapy Lead: Dr Rohit Lal	
Reason for Update: LCA Protocol Development	Approved by LCA Joint Delivery Subgroup Co-Chairs: Pauline McCalla & Rebecca Johl	
Prepared by: Lisa Yuen	Approved by LCA Medicines & Chemotherapy Steering Group Chair: Jamie Ferguson	
Second check by: Laura Cameron	Date prepared: November 2014	Review Date: November 2016
<p>Disclaimer: The Joint Delivery Chemotherapy Nurse/Oncology Pharmacist Group is a sub-group of the Medicines & Chemotherapy Steering Group (MCSG) working within the London Cancer Alliance Integrated Cancer System (LCA). The output of the LCA MCSG includes documentation that can be adopted by healthcare organisations at their discretion. It is the responsibility of each individual organisation to ensure that appropriate governance and safety clearance procedures within their own clinical service have been followed prior to implementation of any such pieces of work. LCA assume no responsibility for this process within individual organisations, and no responsibility for the clinical management of individual patients or patient groups. Any clinical queries regarding individual patients or documentation should be directed to the relevant clinical team within the most appropriate healthcare organisation.</p> <p>©LCA Copyright 2014</p>		

Interstitial Lung Disease (ILD):

Erlotinib should be discontinued in patients who develop an acute onset of new progressive pulmonary symptoms, such as dyspnoea, cough or fever. If ILD is diagnosed, erlotinib should be discontinued and appropriate treatment instituted.

Note that in most cases pulmonary symptoms are associated with contributing factors such as prior chemotherapy/radiotherapy, lung disease or pulmonary infections.

Other toxicities

Gastrointestinal bleeding and perforation has been reported, some associated with concomitant warfarin administration or NSAID administration. Regular monitoring of prothrombin time or INR is advised with warfarin (or other coumarin-derived agents). Patients with history of peptic ulceration or diverticular disease are at increased risk.

Mucositis, hyperbilirubinemia, ocular disorders, neutropenia, and anaemia have been reported. Seek further advice if these occur.

Headache has been reported within hours of an oral dose in some patients; responding well to non-opioid analgesics.

Location of regimen delivery:

Outpatient setting

Comments:

To be supplied to the patient for oral self-administration. Ensure that the patient has an information pack and the treatment plan. Adequate contraceptive methods should be used during therapy, and for at least 2 weeks after completing therapy.

Drug interactions:

CYP3A4 inducers (e.g. phenytoin, carbamazepine, rifampicin, barbiturates, St John’s Wort) can decrease erlotinib plasma concentration and reduce efficacy.
 CYP3A4 and P-gp inhibitors (e.g. ketoconazole, erythromycin, clarythromycin, cyclosporine, verapamil, grape fruit juice) can increase erlotinib plasma concentration and increase toxicity.
 Coumarin-derived agent (e.g. warfarin) - anticoagulant effect can be enhanced.
 Statins - increased risk of myopathy.
 Tobacco smoking decreases serum levels of erlotinib.

References:

NICE TA258, TA162
 Roche products Ltd. 2013. Summary of product characteristics : Tarceva (erlotinib). Available at www.medicines.org.uk [accessed 21/01/2014]
 Hidalgo M et al (2001); JCO,19(13):3267-3279.

Version: 1.0 Supersedes: all other versions	Approved by LCA Lung Pathway Chemotherapy Lead: Dr Rohit Lal	
Reason for Update: LCA Protocol Development	Approved by LCA Joint Delivery Subgroup Co-Chairs: Pauline McCalla & Rebecca Johl	
Prepared by: Lisa Yuen	Approved by LCA Medicines & Chemotherapy Steering Group Chair: Jamie Ferguson	
Second check by: Laura Cameron	Date prepared: November 2014	Review Date: November 2016
<p>Disclaimer: The Joint Delivery Chemotherapy Nurse/Oncology Pharmacist Group is a sub-group of the Medicines & Chemotherapy Steering Group (MCSG) working within the London Cancer Alliance Integrated Cancer System (LCA). The output of the LCA MCSG includes documentation that can be adopted by healthcare organisations at their discretion. It is the responsibility of each individual organisation to ensure that appropriate governance and safety clearance procedures within their own clinical service have been followed prior to implementation of any such pieces of work. LCA assume no responsibility for this process within individual organisations, and no responsibility for the clinical management of individual patients or patient groups. Any clinical queries regarding individual patients or documentation should be directed to the relevant clinical team within the most appropriate healthcare organisation.</p> <p>©LCA Copyright 2014</p>		

Lung Pathway Group – Erlotinib in Non-Small Cell Lung Cancer (NSCLC)

Shepherd F et al (2005); NEJM,352(2):123-132.

Perez-Soler R et al (2004); JCO,22:3238.

Tsao MS et al (2005); NEJM,353(2):133-144.

Version: 1.0 Supersedes: all other versions	Approved by LCA Lung Pathway Chemotherapy Lead: Dr Rohit Lal
Reason for Update: LCA Protocol Development	Approved by LCA Joint Delivery Subgroup Co-Chairs: Pauline McCalla & Rebecca Johl
Prepared by: Lisa Yuen	Approved by LCA Medicines & Chemotherapy Steering Group Chair: Jamie Ferguson
Second check by: Laura Cameron	Date prepared: November 2014 Review Date: November 2016
<p>Disclaimer: The Joint Delivery Chemotherapy Nurse/Oncology Pharmacist Group is a sub-group of the Medicines & Chemotherapy Steering Group (MCSG) working within the London Cancer Alliance Integrated Cancer System (LCA). The output of the LCA MCSG includes documentation that can be adopted by healthcare organisations at their discretion. It is the responsibility of each individual organisation to ensure that appropriate governance and safety clearance procedures within their own clinical service have been followed prior to implementation of any such pieces of work. LCA assume no responsibility for this process within individual organisations, and no responsibility for the clinical management of individual patients or patient groups. Any clinical queries regarding individual patients or documentation should be directed to the relevant clinical team within the most appropriate healthcare organisation.</p> <p>©LCA Copyright 2014</p>	