LONDON CANCER ALLIANCE West and South

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

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| Indication: | |
| **NICE TA192** | First line treatment option in locally advanced or metastatic NSCLC<br>Positive test for epidermal growth factor receptor tyrosine kinase (EGFR-TK) mutation<br><br>Eligible for patients able to tolerate and comply with oral dosage forms |
| Regimen details: | Gefitinib 250mg PO once daily continuously |
| Administration: | Gefinitib available as 250mg film coated tablets.<br><br>If dosing of whole tablets is not possible, tablets may be administered as a dispersion in water (non-carbonated). No other liquids should be used. Without crushing it, the tablet should be dropped in half a glass of drinking water. The glass should be swirled occasionally, until the tablet is dispersed (this may take up to 20 minutes). The dispersion should be drunk immediately after dispersion is complete (i.e. within 60 minutes). The glass should be rinsed with half a glass of water, which should also be drunk. The dispersion can also be administered through a nasogastric or gastrostomy tube. |
| Frequency: | Dosing is continuous, until disease progression or unacceptable toxicity |
| Pre-medication: | Not routinely required |
| Anti- emetics: | Minimal emetogenicity<br>Follow local anti-emetic policy |

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| 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 |

Supportive medication:

Diarrhoea can be managed with loperamide.
Mouthcare as per local policy.
Various approaches may be considered to deal with the 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

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| 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*

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| 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.

* Repeat supply of gefitinib 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:

Nutrition disorders, GI effects, elevated liver enzymes, skin reactions, nail changes, asthenia, pyrexia, vascular disorders, respiratory disorders, mucositis, eye disorders. Less common but may be life-

threatening: QT interval prolongation, Interstitial lung disease, haemorrhage

## DOSE MODIFICATIONS

**Haematological Toxicity** No dose modifications are required for haematological toxicity

**Non-haematological Toxicities**

**Renal Impairment**

| Creatinine Clearance (ml/min) | Gefitinib Dose |
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| ≥ 20 | Give 100% dose |
| < 20 | Caution – limited data available, discuss with Consultant |

**Hepatic Impairment**

Plasma concentrations were not increased in patients with elevated aspartate transaminase, alkaline phosphatase or bilirubin due to liver metastases, and therefore no dose reductions are required in this clinical situation.

Patients with moderate to severe hepatic impairment (Child Pugh B or C) due to cirrhosis have increased plasma concentrations of gefitinib. These patients should be closely monitored for adverse events.

**Dose modifications for other toxicities as appropriate**

Diarrhoea and Rash

Patients with poorly tolerated diarrhoea or skin adverse reactions despite maximal supportive medications may be successfully managed by providing a brief (up to 14 days) therapy interruption followed by reinstatement of the 250 mg dose. It is advisable to allow the toxicity to resolve to grade 1 level before re-starting the therapy.

For patients unable to tolerate treatment after a therapy interruption, gefitinib should be discontinued and an alternative treatment should be considered.

Interstitial lung disease (ILD)

ILD, which may be acute in onset, has been observed in 1.3 % of patients, and some cases have been fatal. If patients experience worsening of respiratory symptoms such as dyspnoea, cough and fever, gefitinib should be interrupted and the patient should be promptly investigated. If ILD is confirmed, gefitinib should be discontinued and the patient treated appropriately.

Location of regimen delivery: Outpatient setting

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| Comments: | To be supplied to the patient for oral self-administration.<br>Ensure that the patient has an information pack and the treatment plan.<br>Adequate contraceptive methods should be used during therapy, and for at least 2 weeks after completing therapy.<br><br>Local pathways set up to accommodate gefitinib patient access scheme. |
| Drug interactions: | Concurrent use of CYP3A4 inducers (e.g. phenytoin, carbamazepine, rifampicin, barbiturates, dexamethasone, St John's Wort) can decrease gefitinib plasma concentration and reduce efficacy.<br>Concurrent use of CYP3A4 inhibitors (e.g. ketoconazole, itraconazole, erythromycin, clarithromycin, grape fruit juice) in individual patients with CYP2D6 poor metaboliser genotypecan can increase gefitinib plasma concentration and increase toxicity. Monitor closely for any adverse reactions.<br>Concurrent use of a coumarin-derived agent (e.g. warfarin) can enhance their anticoagulant effect. Monitor INR carefully.<br>Medicinal products that cause significant sustained elevation in gastric pH, such as protonpump inhibitors and h2antagonists may reduce bioavailability and plasma concentrations of gefitinib.<br>Antacids if taken regularly close in time to administration of gefitinib may have a similar effect<br>Vinorelbine - exacerbated neutropenic effect with concomitant gefitinib |
| References: | NICE TA192<br>Mok T.S. *et al* (2009); NEJM, 361:947-57 |



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