# AFATINIB

A first-line option for locally advanced or metastatic NSCLC, in patients with EGFR-TK mutation
NICE approved April 2014

Only for the sub-group of patients with an exon 19 mutation, afatinib is the only EGFR inhibitor to demonstrate an OS benefit versus chemotherapy[1]

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| Drug/Dosage: | **Afatinib** | initiate at 40mg po once daily as continuous therapy<br><br>(any dose escalation to the maximum daily dose of 50mg/day is a Consultant only decision) |

Administration: Afatinib is available as 50mg, 40mg, 30mg and 20mg tablets.
The daily dose should be swallowed whole with water once daily at least one hour before, and at least **three** hours after, any food.

For patients who cannot swallow tablets, the dose may be dispersed in approx 100ml of noncarbonated drinking water (no other liquids should be used). The tablet should be dropped into the water without crushing it, and stirred occasionally for up to 15 min until it is broken up into very small particles. The dispersion should be consumed immediately. The glass should be rinsed with approximately 100 ml of water which should also be consumed. The dispersion can also be administered through a gastric tube.

Frequency: Continuous therapy until progression or unacceptable toxicity.
Toxicity review 2 weeks after starting

Main Toxicities: rash; diarrhoea; stomatitis; paronychia

Anti- emetics: none usually needed, but some patients may have nausea

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| Regular: | FBC | monthly |
| Investigations: | LFTs & U&Es | monthly |
| | CT scan | every 3 months |

Comments: Loperamide should be routinely prescribed with the first supply of afatinib, and patients should be encouraged to use loperamide promptly and pro-actively at the first sign of any diarrhoea.

Encourage routine use of a moisturiser at the start of afatinib treatment to prevent and minimise problems with skin dryness. Aveeno colloidal oatmeal lotion is our recommended moisturiser. This is a moisturiser with anti-inflammatory properties that has been shown in small studies to have good efficacy and no toxicity[2, 3]. However, if the patient prefers, they may use a moisturiser of their choice.

Interactions: Concomitant use of strong P-gp inducers (e.g. rifampicin, carbamazepine, phenytoin, phenobarbital, St. John's wort) may decrease exposure to afatinib, and so increase the risk of therapeutic failure.

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| Reason for Update: N/A | Approved by Consultant: Dr V Ezhil |
| Version: 1 | Approved by Lead Chemotherapy Nurse: P Deery |
| Supersedes: None | Date: 12.2.15 |
| Prepared by: S Taylor | Checked by: C Tucker |

It is recommended to administer any strong P-gp inhibitors (e.g. ritonavir, cyclosporine A, itraconazole, erythromycin, verapamil, quinidine, tacrolimus, nelfinavir, saquinavir, amiodarone) using staggered dosing, preferably 12 hours apart from afatinib (for once daily drugs) or 6 hours apart from afatinib (for twice daily drugs).
The patient needs to be closely monitored for afatinib adverse reactions.

**Dose Modifications**

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| Haematological Toxicity: | Afatinib is not myelosuppressive. Patients may continue afatinib during periods of mild myelosuppression. Discuss with doctor if concerned. |
| Primary Rash: | Ensure moisturiser is being used regularly. The recommended frequency of application for Aveeno colloidal oatmeal lotion is three times daily.<br>Consider using topical hydrocortisone 1% early in patients with mild rash, but use cautiously, especially for severe rash, as efficacy may be limited by inability to penetrate skin. Analgesia may be of benefit.<br>In the event of a Grade 2 + rash (papular eruption with or without pruritis, covering 10 - 30% of BSA) of > 7 days, afatinib should be interrupted until rash resolved. Afatinib may then be re-started with a 10mg dose reduction (40mg → 30mg; 30mg → 20mg).<br>If a patient cannot tolerate 20mg/day, permanent discontinuation of afatinib should be considered.<br>Topical acne medications are **not** recommended. |
| Infected Rash: | If a pustular component, consider a short course of oral doxycycline or flucloxacillin. Use of topical antibiotics is not encouraged, and needs to be discussed with Microbiology first. |
| Diarrhoea: | Mild to moderate diarrhoea may be managed with loperamide. Afatinib therapy may continue.<br>In the event of an increase of ≥ 4 – 6 stools/day over baseline for > 48 hours, afatinib should be interrupted until diarrhoea resolved. Afatinib may then be re-started with a 10mg dose reduction (40mg → 30mg; 30mg → 20mg).<br>If a patient cannot tolerate 20mg/day, permanent discontinuation of afatinib should be considered. |
| Hepatic Impairment: | No start dose adjustment is required in patients with mild or moderate hepatic impairment. Use of afatinib in patients with severe (Child Pugh C) hepatic impairment is not recommended.<br>Raised transaminases may occur after starting treatment. Generally these elevations are transient and do not require interruption of afatinib. |
| Renal Impairment: | No start dose adjustment is required in patients with CrCl > 30 ml/min. Use of afatinib in patients with CrCl < 30ml/min is not recommended. |
| References: | [1]Sequist, L et al ; JCO 2013 ; 31 (27) : 3327 - 3334<br>Rash advice adapted from HER1/EGFR Inhibitor Rash Management Forum, 2005<br>[2]Alexandrescu, D et al; Clinical and Experimental Dermatology 2006; 32: 71 – 74<br>[3]Talsania, T et al; Clinical and Experimental Dermatology 2008; 33 (1): 108 |