Afatinib (NSCLC)

Indication

Treatment of locally advanced or metastatic non-small-cell lung cancer (NSCLC) for patients who test positive for the epidermal growth factor receptor tyrosine kinase (EGFR-TK) mutation and have not had previous treatment with an EGFR-TK inhibitor.

(NICE TA310)

ICD-10 codes

Codes with a prefix C34

Regimen details

Day	Drug	Dose	Route
1-28	Afatinib	40mg *OD	PO

* doses may be escalated to 50mg OD in patients who tolerate 40mg OD without adverse reactions in the first 3 weeks (consultant decision)

Cycle frequency

Continuously until disease progression or unacceptable toxicity.

Number of cycles

As above

Administration

Afatinib is available as 50mg, 40mg, 30mg and 20mg tablets.

The dose should be taken once daily at least one hour before and at least three hours after food.

If patients cannot swallow the tablets they may be dispersed in 100mL non-carbonated water. The tablet should be dropped into the water (not crushed) and stirred until it has dispersed into very small particles. The dispersion should be drunk immediately. Patients should be advised to then rinse the glass in approximately 100mL of water and also consume this. Afatinib may also be administered via a gastric tube following this method.

Pre-medication

Nil

Emetogenicity

This regimen has low emetic potential (no routine antiemetics required)

Additional supportive medication

Patients should be supplied with loperamide on commencing treatment. They should be advised to use loperamide immediately at the first sign of diarrhoea and continue for persistent diarrhoea until loose movements cease.

Patients should be advised to use a regular moisturiser from the start of afatinib treatment to prevent and minimise problems with skin dryness.

Extravasation

N/A

Investigations – pre first cycle

Investigation	**Validity period** (or as per local practice)
FBC	14 days
U+E (including creatinine)	14 days
LFTs	14 days

Investigations – pre subsequent cycles

Clinical review is recommended after 2 weeks, and then at a maximum of 4 week intervals until stabilisation of toxicities. Once this is achieved this period may be extended.

Investigation	**Validity period** (or as per local practice)
FBC	Monthly
U+E (including creatinine)	Monthly
LFTs	Monthly

Standard limits for administration to go ahead

If blood results not within range, authorisation to administer **must** be given by prescriber/ consultant

Investigation	**Limit**
Neutrophils*	≥ 1.0 x 10^9/L
Platelets*	≥ 100 x 10^9/L
Creatinine clearance (CrCl)	≥ 30mL/min
AST/ALT	< 5 x ULN
Bilirubin	< 3 x ULN

* see haematological toxicity below

Dose modifications

- **Haematological toxicity**

Afatinib is not myelosuppressive. Patients may continue to take afatinib during periods of mild myelosuppression.

- **Renal impairment**

Afatinib has not been studied in patients with renal impairment. Treatment is not recommended in patients with CrCl < 30mL/min.

- **Hepatic impairment**

In mild to moderate hepatic impairment, no starting dose adjustment is required. In severe hepatic impairment (Childs Pugh C) afatinib is not recommended.

After starting treatment patients may experience raised transaminsases. Usually this is transient and does not require interruption of treatment.

- **Other toxicities**

Toxicity	Definition	Dose adjustment
Diarrhoea	Grade 1-2	Continue with 100% dose
	Grade 2 for > 48 hours Grade ≥ 3	Interrupt treatment until ≤ grade 1 Interrupt treatment until ≤ grade 1 and then resume with 10mg dose reduction
Rash	Grade 1-2	Continue with 100% dose
	Grade 2 for > 7 days Grade ≥ 3	Interrupt treatment until ≤ grade 1 Interrupt treatment until ≤ grade 1 and then resume with 10mg dose reduction

If patients cannot tolerate 20mg OD treatment should be discontinued.

Interstitial Lung Disease (ILD) should be considered if a patient develops acute or worsening of respiratory symptoms. Treatment should be interrupted pending evaluation. If ILD is diagnosed, treatment should be permanently discontinued.

Adverse effects - for full details consult product literature/ reference texts

- **Serious side effects**

Stevens-Johnson syndrome/toxic epidermal necrosis
Interstitial lung disease
Left ventricular dysfunction

- **Frequently occurring side effects**

Diarrhoea – may be severe
Rash
Stomatitis
Epistaxis
Anorexia
Fatigue
Elevated LFTs

- **Other side effects**

Keratitis
Nail infections

Significant drug interactions – for full details consult product literature/ reference texts

P-gp inducers (e.g. rifampicin, carbamazepine, phenytoin, phenobarbital, St. John's wort) may decrease exposure to afatinib. Increased risk of therapeutic failure. Avoid co-administration.

Strong P-gp inhibitors (e.g. ritonavir, cyclosporine A, itraconazole, erythromycin, verapamil, quinidine, tacrolimus, nelfinavir, saquinavir, amiodarone): use staggered dosing, preferably 12 hours apart from afatinib (for once daily drugs) or 6 hours apart from afatinib (for twice daily drugs).

BCRP: afatinib is a substrate and an inhibitor of the transporter BCRP. Afatinib may increase the bioavailability of orally administered BCRP substrates (e.g. rosuvastatin and sulfasalazine).

Additional comments

This medicinal product contains lactose. Patients with rare hereditary conditions of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicinal product.

References

- National Institute for Health and Clinical Excellence. NICE Technology Appraisal Guidance 310 accessed 1 July 2015 via www.nice.org.uk
- Summary of Product Characteristics Afatinib (Boehringer Ingelheim) accessed 1 July 2015 via www.medicines.org.uk
- Sequist, L et al; Phase III Study of Afatinib or Cisplatin Plus Pemetrexed in Patients With Metastatic Lung Adenocarcinoma With EGFR Mutations JCO 2013 ; 31 (27) : 3327 - 3334

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