Gefitinib

Indication
First line 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 TA192)

ICD-10 codes
Codes with a prefix C34

Regimen details

Day	Drug	Dose	Route
1-28	Gefitinib	250mg OD	PO

Cycle frequency
Continuously until disease progression or unacceptable toxicity.

Number of cycles
As above

Administration
Gefitinib is available as 250mg tablets.

The dose should be taken once daily, at the same time each day, either with or without food. If a dose is missed it should be taken as soon as possible, however if it is less than 12 hours until the next scheduled dose the missed should be omitted.

Tablets should be swallowed whole with water or they may be dispersed in non-carbonated water. The tablet should be dropped into half a glass of water (not crushed) and the glass swirled until the tablet has dispersed (this may take up to 20 minutes). The dispersion should be drunk immediately. Patients should be advised to then rinse the glass in approximately another half a glass of water and also consume this. Gefitinib 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 gefitinib 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)	≥ 20mL/min
AST/ALT	< 5 x ULN
Bilirubin	< 3 x ULN

Dose modifications

- **Haematological toxicity**

No dose modifications are required for haematological toxicity.

- **Renal impairment**

No dose adjustment is required if CrCl > 20mL/min. Caution is advised if CrCl ≤ 20mL/min.

- **Hepatic impairment**

Use with caution and close monitoring in moderate to severe hepatic impairment (Child Pugh B or C). Patients with moderate to severe hepatic impairment due to cirrhosis have shown increased plasma concentrations of gefitinib.

Liver function test abnormalities (including increases in ALT/AST and bilirubin) have been observed. Gefitinib should be used with caution in the presence of mild-moderate changes and should be discontinued if severe changes.

- **Other toxicities**

Patients with diarrhoea or skin adverse reactions may be managed by treatment interruption for up to 14 days, after which treatment may be recommenced at the same dose of 250mg OD. For patients unable to tolerate treatment after interruption, gefitinib should be discontinued.

Interstitial Lung Disease (ILD) should be considered if a patient develops acute or worsening of respiratory symptoms including cough, dyspnoea and fever. Treatment should be interrupted pending evaluation. If ILD is

diagnosed, treatment should be permanently discontinued.

Patients presenting with signs and symptoms suggestive of keratitis such as acute or worsening: eye inflammation, lacrimation, light sensitivity, blurred vision, eye pain and/or red eye should be referred promptly to an ophthalmology specialist. If a diagnosis of ulcerative keratitis is confirmed, treatment with gefitinib should be interrupted, and if symptoms do not resolve, or if symptoms recur on reintroduction of gefitinib, 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
GI perforation
Haemorrhage

- **Frequently occurring side effects**

Diarrhoea – may be severe
Nausea, vomiting
Rash
Stomatitis
Epistaxis
Anorexia
Elevated LFTs
Conjunctivitis, blepharitis

- **Other side effects**

Keratitis
Nail infections

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

CYP3A4 inducers (e.g. rifampicin, carbamazepine, phenytoin, St. John's wort) may decrease efficacy of gefitinib. Avoid co-administration.

CYP3A4 inhibitors may increase plasma levels of gefitinib. Closely monitor for adverse reactions.

Warfarin INR elevation and increased bleeding has been seen in patients taking warfarin and gefitinib. Close regular monitoring is recommended.

Medications that increase gastric pH (e.g. PPIs, H2 antagonists and antacids): may reduce bioavailability of gefitinib.

NSAIDs, steroids: increased risk of GI perforation.

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 192 accessed 11 Jan 2017 via www.nice.org.uk
- Summary of Product Characteristics Gefitinib (AstraZeneca) accessed 11 Jan 2017 via www.medicines.org.uk
- Mok T.C, Wu Y-L, Thongprasert S et al. Gefitinib or Carboplatin–Paclitaxel in Pulmonary Adenocarcinoma. N Engl J Med 2009; 361(10): 947-957.

Written/reviewed by: Dr A Cox (Consultant Oncologist, RUH Bath NHS Trust)

Checked by: Sarah Murdoch (Senior Oncology Pharmacist, SW Clinical Network)

Authorised by: Dr J Braybrooke (Consultant Oncologist, UHBristol NHS Trust, SW Clinical Network)

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