Gefitinib Monotherapy

INDICATION FOR USE:

INDICATION	ICD10	Regimen Code	Reimbursement Status
Treatment of adult patients with locally advanced or metastatic non-small cell lung cancer (NSCLC) with activating mutations of EGFR-TK	C34	00220a	CDS

TREATMENT:

The starting dose of the drugs detailed below may be adjusted downward by the prescribing clinician, using their independent medical judgement, to consider each patients individual clinical circumstances.

Gefitinib is administered once daily until disease progression or unacceptable toxicity develops.

Drug	Dose	Route	Cycle
Gefitinib	250mg daily	PO with or without food at the same time each day. Tablet may be swallowed whole or may be dispersed* in water (non-carbonated)	Continuous Therapy
To prepare dispersion the whole 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 naso-gastric or gastrostomy tube.			
If a dose is missed it should be taken as soon as the patient remembers. If it is <12hrs to the next dose the patient should not take the missed dose. Patients should not take a double dose (two doses at the same time) to make up for a forgotten dose. If a patient vomits within a few hours of taking the drug do not repeat the dose			

ELIGIBILTY:

- Indications as above
- EGFR activating mutation positive tumour as demonstrated by a validated test method
- ECOG status 0-2

EXCLUSIONS:

- Hypersensitivity to gefitinib or any of the excipients
- Breast feeding

PRESCRIPTIVE AUTHORITY:

The treatment plan must be initiated by a Consultant Medical Oncologist.

TESTS:

Baseline tests:

- FBC, renal and liver profile
- Chest X-ray and CT scan.

Regular tests:

- FBC, renal and liver profile*every 60 days.

*See Adverse Effects/Regimen Specific Complications

Disease monitoring:

Disease monitoring should be in line with the patient's treatment plan and any other test/s as directed by the supervising Consultant.

DOSE MODIFICATIONS:

- Any dose modification should be discussed with a Consultant.
- For patients unable to tolerate treatment after a therapy interruption, gefitinib should be discontinued and an alternative treatment should be considered.

Renal and Hepatic Impairment:

Table 1: Dose modification of gefitinib in renal and hepatic impairment

Renal Impairment		Hepatic Impairment
CrCl (ml/min)	**Dose**	Patients with moderate to severe hepatic impairment due to cirrhosis have increased plasma levels of gefitinib. These patients should be closely monitored. Plasma concentrations were not increased in patients with elevated aspartate transaminase (AST), alkaline phosphatase or bilirubin due to liver metastases.
>20	No dose modification required	
≤20	Limited data available. Caution advised	

Management of adverse events:

Table 2: Dose modification schedule for gefitinib for adverse events. Refer to local policies for the management of EGFR-inhibitor adverse skin reactions and diarrhoea.

Adverse reactions	Recommended dose modification
Grade ≥ 3 or Grade 1-2 failing to respond to initial symptomatic treatment	Interrupt therapy for up to 14 days until toxicity resolved to grade 1 or less and then treatment may be reinitiated at 250mg daily If symptoms reoccur consider stopping treatment
Worsening of respiratory symptoms (e.g. cough, dyspnoea)	Interrupt therapy and clinically evaluate for ILD.
Interstitial lung disease (ILD)	Discontinue

SUPPORTIVE CARE:

EMETOGENIC POTENTIAL: Minimal-Low(**Refer to local policy).**

PREMEDICATIONS: Not usually required

OTHER SUPPORTIVE CARE:

- Medication may be required for management of diarrhoea, e.g. loperamide (4mg at first onset followed by 2mg after each loose stool (max 16 mg /day) or see local policy.
- See local skin care policy for the prevention and treatment of EGFR-inhibitor adverse reactions.
- Patients should be advised to seek medical advice immediately if they experience severe or persistent diarrhoea, nausea, vomiting or anorexia as these may indirectly lead to dehydration.

- During treatment with gefitinib, asthenia has been reported. Therefore, patients who experience this symptom should be cautious when driving or using machines.

ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS

The adverse effects listed are not exhaustive. Please refer to the relevant Summary of Product Characteristics for full details.

- **Interstitial Lung Disease (ILD):** If patients experience worsening of respiratory symptoms such as dyspnoea, cough and fever, treatment should be interrupted and the patient should be promptly investigated. If ILD is confirmed, gefitinib should be permanently discontinued and the patient treated appropriately.
- **Hepatitis, hepatic failure:** Gefitinib should be used cautiously in the presence of mild to moderate changes in liver function. Discontinuation should be considered if changes are severe. Impaired liver function due to cirrhosis has been shown to lead to increased plasma concentrations of gefitinib.
- **Gastrointestinal perforation:** In most cases this is associated with other known risk factors, including concomitant medications such as steroids or NSAIDS, underlying history of GI ulceration, age, smoking or bowel metastases at sites of perforation.
- **Ocular disorders:** 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 should be interrupted, and if symptoms do not resolve, or if symptoms recur on reintroduction of gefitinib, permanent discontinuation should be considered.

DRUG INTERACTIONS:

- Potent inducers of CYP3A4 may reduce the efficacy of gefitinib
- Potent inhibitors of CYP3A4 may lead to increased toxicity of gefitinib. Patients should also be counselled with regard to consumption of grapefruit and grapefruit juice.
- INR elevations and/or bleeding events have been reported in some patients taking warfarin together with gefitinib. Patients taking warfarin and gefitinib concomitantly should be monitored regularly for changes in prothrombin time (PT) or INR.
- Concomitant treatment with substances that increase gastric pH (i.e. proton pump inhibitors, H2 antagonists and antacids) should be avoided, as the bioavailability of gefitinib may be reduced. If the use of antacids is considered necessary during treatment with gefitinib, they should be taken at least 4 hours before or 2 hours after the daily dose of gefitinib.
- Current drug interaction databases should be consulted for more information.

ATC CODE:

Gefitinib - L01XE02

REFERENCES:

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2. Maemondo M, Inoue A et al. Gefitinib or Chemotherapy for Non-Small Cell Lung Cancer with Mutated EGFR. NEJM. 2010 Jun 24; 362(25):2380-2388.
3. Mitsudomi T. Mitsudomi T. et al. Gefitinib versus cisplatin plus docetaxel in patients with non-small-cell lung cancer harbouring mutations of the epidermal growth factor receptor (WJTOG3405): an open label, randomised phase 3 trial. Lancet Oncol. 2010 11(2):121-8

4. Gefitinib (IRESSA®) Summary of Product Characteristics Last updated: 28/05/2019. Accessed April 2020. Available at https://www.ema.europa.eu/en/documents/product-information/iressa-epar-product-information_en.pdf
5. NCCP Classification Document for Systemic AntiCancer Therapy (SACT) Induced Nausea and Vomiting. V2 2019. Available at: https://www.hse.ie/eng/services/list/5/cancer/profinfo/chemoprotocols/nccp-classification-document-for-systemic-anti-cancer-therapy-sact-induced-nausea-and-vomiting.pdf

Version	Date	Amendment	Approved By
1	05/04/2014		Prof Maccon Keane
2	25/03/2016	Inclusion of standard wording re treatment	Prof Maccon Keane
3	18/04/2018	Updated with new NCCP Regimen Template and updated emetogenic status	Prof Maccon Keane
4	29/04/2020	Reviewed.	Prof Maccon Keane

Comments and feedback welcome at oncologydrugs@cancercontrol.ie.