Afatinib Monotherapy

INDICATIONS FOR USE:

INDICATION	ICD10	Regimen Code	HSE approved Reimbursement Status*
Treatment of Epidermal Growth Factor Receptor (EGFR) TKI- naïve adult patients with locally advanced or metastatic non-small cell lung cancer (NSCLC) with activating EGFR mutation(s).	C34	00221a	CDS

*This applies to post 2012 indications.

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 patient's individual clinical circumstances.

Afatinib is administered orally on a continuous basis once daily until disease progression or unacceptable toxicity develops.

Drug	Dose	Route	Cycle
Afatinib	40mg daily*	PO without food at the same time each day. Tablet may be swallowed whole with water *Food should not be consumed for at least 3 hours before and at least 1 hour after taking this medicinal product.	Continuous
*DOSE ESCALATION: To a maximum of 50mg/day may be considered in patients who tolerate a 40mg/day dose (i.e. absence of diarrhoea, skin rash, stomatitis, and other Grade > 1 adverse reactions) in the first 3 weeks. The dose should not be escalated in any patients with a prior dose reduction. The maximum daily dose is 50mg.			
If swallowing of whole tablets is not possible, these can be dispersed in approximately 100 mL 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 minutes 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.			
If a dose is missed it should be taken as soon as the patient remembers. However, if the next scheduled dose is due within 8 hours then the missed dose must be skipped. 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.			

ELIGIBILITY:

- Indications as above
- EGFR activating mutation status as demonstrated by a validated test method

CAUTIONS:

- Underlying history of gastrointestinal ulceration.
- Underlying history of keratitis, ulcerative keratitis, severe dry eye

EXCLUSIONS:

- Hypersensitivity to afatinib or any of the excipients
- Known pre-existing interstitial lung disease (ILD)
  Pregnancy or breastfeeding

PRESCRIPTIVE AUTHORITY:

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

TESTS:

Baseline tests:

- FBC, renal and liver profile
- Cardiac function (LVEF using ECHO, MUGA scan) if clinically indicated

Regular tests:

- FBC, renal and liver profile monthly
- Cardiac function (MUGA or ECHO) if clinically indicated

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
- DOSE ESCALATION**: see treatment table above for information regarding dose escalation**

Renal and Hepatic Impairment:

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

Renal Impairment		**Hepatic Impairment**	
CrCl (mL/min)	**Dose**		**Dose**
≥15	No dose adjustment is needed	**Child Pugh A and B**	No dose adjustment is needed.
		Child Pugh C	No need for dose adjustment is expected
<15	No need for dose adjustment is expected		
Haemodialysis	No need for dose adjustment is expected		
Renal and hepatic as per Giraud et al.			

Management of adverse events:

Table 2: Dose Modification of afatinib for Adverse Events

Adverse reactions	Recommended dose modification
Grade 1 or 2	No interruption[a] or dose adjustment
Grade 2 (prolonged[b] or intolerable) or Grade ≥3	Interrupt until reaction has resolved to Grade 0 or 1[a]. Resume with dose reduction by 10mg decrements[c].
Interstitial Lung Disease	Discontinue

[a]In case of diarrhoea, anti-diarrhoeal medicinal products (e.g. loperamide) should be taken immediately and continued for persistent diarrhoea until loose bowel movements cease.
[b]> 48 hours of diarrhoea and/or > 7 days of rash.
[c]If patient cannot tolerate 20 mg/day, permanent discontinuation of afatinib should be considered.
Refer to local policy for prevention and treatment of EGFR-inhibitor adverse skin reactions.

SUPPORTIVE CARE:

EMETOGENIC POTENTIAL:

- As outlined in NCCP Classification Document for Systemic Anti-Cancer Therapy (SACT) Induced Nausea and Vomiting - Available on the NCCP website

Afatinib: Minimal to Low (**Refer to local policy).**

For information:
Within NCIS regimens, antiemetics have been standardised by the Medical Oncologists and Haemato-oncologists. Information is available in the following documents:

- NCCP Supportive Care Antiemetic Medicines for Inclusion in NCIS (Medical Oncology) - Available on the NCCP website
- NCCP Supportive Care Antiemetic Medicines for Inclusion in NCIS (Haemato-oncology) - Available on the NCCP website

PREMEDICATIONS: Not usually required

OTHER SUPPORTIVE CARE:

- Emollients may be required to prevent dry skin **(Refer to local policy)**
- Counsel patient that they may they experience ocular adverse reactions (conjunctivitis, dry eye, keratitis) which may affect patients ability to drive or use machines
- Adequate hydration and medication may be required for management of diarrhoea Antidiarrhoeals (e.g. loperamide) should be initiated at first signs of diarrhoea and continued until loose bowel movements cease for 12 hours. If necessary their dose should be escalated to the highest recommended approved dose. **(Refer to local policy)**

ADVERSE EFFECTS

- Please refer to the relevant Summary of Product Characteristics (SmPC) for details**.**

DRUG INTERACTIONS:

- Current SmPC and drug interaction databases should be consulted for information.

REFERENCES:

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2. Sequist LV, Yang JC, Yamamoto N, et al. Phase III Study of Afatinib or CISplatin Plus PEMEtrexed in Patients With Metastatic Lung Adenocarcinoma With EGFR Mutations. J Clin Oncol. 2013;31(27):3327-34.
3. Yang JC, Hirsh V, Schuler M, et al. Symptom Control and Quality of Life in LUX-Lung 3: A Phase III Study of Afatinib or CISplatin/PEMEtrexed in Patients With Advanced Lung Adenocarcinoma With EGFR Mutations. J Clin. Oncol 2013;31(27):3342-50.
4. Giraud E L, Lijster B D, et al. Dose recommendations for anticancer drugs in patients with renal or hepatic impairment: an update. Accessed 04/03/2025. Available at: https://pubmed.ncbi.nlm.nih.gov/37269847/
5. NCCP Classification Document for Systemic Anti-Cancer Therapy (SACT) Induced Nausea and Vomiting. V6 2025. 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
6. Afatinib (GIOTRIF®) Summary of Product Characteristics. Last updated: 26/02/2025. Accessed 27/02/2025. Available at: https://www.ema.europa.eu/en/documents/product-information/giotrif-epar-product-information_en.pdf

Version	Date	Amendment	Approved By
1	20/12/2013	Initial Draft	Dr Linda Coate
2	01/02/2016	Updated Adverse Events/Regimen specific complications	Dr Linda Coate
3	22/02/2018	Updated emetogenic status, dosing in renal and hepatic impairment and adverse effects as per SmPC. Updated with new NCCP regimen template	Prof Maccon Keane
4	26/02/2020	Reviewed. Update of emetogenic potential. adverse events.	Prof Maccon Keane
5	21/03/2025	Regimen Reviewed. Updated treatment table. Added caution section, updated exclusion section and testing requirements. Updated renal and hepatic impairment recommendations to align with Giraud et al. Adverse effects and drug interaction section amended as per NCCP standardisation.	Prof Maccon Keane

Comments and feedback welcome at oncologydrugs@cancercontrol.ie.