ErlotinibTherapy

INDICATIONS FOR USE:

INDICATION	ICD10	Regimen Code	Reimbursement Status
First-line treatment of patients with locally advanced or metastatic non-small cell lung cancer (NSCLC) with EGFR activating mutations.	C34	00219a	CDS
Switch maintenance treatment in patients with locally advanced or metastatic NSCLC with EGFR activating mutations and stable disease after first-line chemotherapy	C34	00219b	CDS
Treatment of patients with locally advanced or metastatic NSCLC after failure of at least one prior chemotherapy regimen.	C34	00219c	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.

Erlotinib is administered daily until disease progression or unacceptable toxicity develops.

Drug	Dose	Route	Diluent & Rate	Cycle
Erlotinib	150mg daily	PO[1]	N/A	Continuous
[1]1 hour before or two hours after the ingestion of food				
Missed doses should not be replaced. Normal dosing should be resumed at the next scheduled 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 as demonstrated by a validated test method.
- ECOG status 0-3.

EXCLUSIONS:

- Hypersensitivity to erlotinib or any of the excipients
- Severe hepatic impairment
- Severe renal impairment

PRESCRIPTIVE AUTHORITY:

The treatment plan must be initiated by a Consultant Medical Oncologist

TESTS:

Baseline tests:

- FBC, liver and renal profile

Regular tests:

- FBC, liver and renal 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
- **Any patient with a grade 3 or 4 toxicity not controlled by optimum supportive care will require a dose reduction as per table 1 below.**

Table 1: Dose reduction steps for erlotinib

Level	Erlotinib Dose
Starting Dose	150mg daily
1st Reduction	100mg daily
2nd Reduction	50mg daily

Renal and Hepatic Impairment:

Table 2: Dose modification of erlotinib in renal impairment

Renal Impairment	Hepatic Impairment
There is no data available to support use of erlotinib in patients with a CrCl< 15ml/min, therefore erlotinib should not be used if CrCl< 15ml/min	Erlotinib is eliminated by hepatic metabolism and biliary excretion. Dose reduction or interruption of treatment should be considered if severe adverse reactions occur. The safety and efficacy of erlotinib has not been studied in patients with severe hepatic dysfunction (AST/SGOT and ALT/SGPT> 5 x ULN). Use of erlotinib in patients with severe hepatic dysfunction is not recommended

Management of adverse events:

Table 3: Dose Modification of erlotinib for Adverse Events

Adverse reactions	Recommended dose modification
Skin reactions	
Grade 1-2	None*
Grade 3	Dose interruption may be required
Grade 4	• Dose interruption for 7 to 14 days may be required. • Dose reduction required in resuming treatment. • Discontinuation may be necessary
Diarrhoea	
Grade 3	If unresponsive to antidiarrhoeal medication for 24 hours then stop drug until resolution to grade <1 and then restart at next dose level down
Grade 4	If unresponsive to antidiarrhoeal agent for >24 hours then discontinue drug
Dehydration due to severe or persistent cases of diarrhoea.	Erlotinib treatment must be stopped and appropriate measures should be taken to intensively rehydrate the patients intravenously.
Acute onset of new and/or progressive unexplained pulmonary symptoms.	Discontinue erlotinib pending diagnostic evaluation.
Gastrointestinal Perforation	Discontinue permanently
Ulcerative keratitis	Interrupt treatment or discontinue

*Refer to local policy for the prevention and treatment of EGFR-inhibitor adverse skin reactions

SUPPORTIVE CARE:

EMETOGENIC POTENTIAL: Minimal to 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**
- Current smokers should be advised to stop smoking as plasma concentrations of erlotinib in smokers as compared to non-smokers are reduced.
- See local skin care policy for the prevention and treatment of EGFR-inhibitor adverse skin reactions.

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):** This has been reported in patients treated with EGFR inhibitors. In patients who develop acute onset of new and/or progressive unexplained pulmonary symptoms such as dyspnoea, cough and fever, erlotinib therapy should be interrupted pending diagnostic evaluation.
- **Diarrhoea, dehydration, electrolyte imbalance and renal failure:** Requires treatment and in some cases dose reduction may be necessary. In more severe or persistent cases of diarrhoea, or cases leading to dehydration, particularly in groups of patients with aggravating risk factors (especially concomitant chemotherapy and other medications, symptoms or diseases or other predisposing conditions including advanced age), therapy should be interrupted and appropriate measures should be taken to intensively rehydrate the patients intravenously. In addition, renal function and serum electrolytes including potassium should be monitored in patients at risk of dehydration.
- **Hepatitis, hepatic failure:** Rare cases of hepatic failure have been reported. For patients with pre-existing liver disease or concomitant hepatotoxic medications hepatic function should be closely monitored.
- **Gastrointestinal perforation:** Patients receiving concomitant anti-angiogenic agents, corticosteroids, NSAIDs, and/or taxane based chemotherapy, or who have prior history of peptic ulceration or diverticular disease are at increased risk of gastrointestinal perforation. Erlotinib should be permanently discontinued in patients who develop gastrointestinal perforation.
- **Bullous and exfoliative skin disorders:** Treatment should be interrupted or discontinued if the patient develops severe bullous, blistering or exfoliating conditions. Patients with bullous and exfoliative skin disorders should be tested for skin infection and treated according to local management guidelines.
- **Ocular disorders:** Ulcerative keratitis has been reported. Therapy should be interrupted or discontinued if patient presents with signs and symptoms suggestive of keratitis.

DRUG INTERACTIONS:

- Potent inducers of CYP3A4 may reduce the efficacy of erlotinib.
- Potent inhibitors of CYP3A4 may lead to increased toxicity of erlotinib. Patients should also be counselled with regard to consumption of grapefruit and grapefruit juice.
- Concomitant treatment with substances that increase gastric pH (i.e. Proton pump inhibitors, H2 antagonists and antacids) should be avoided, as erlotinib solubility and absorption may decrease. If the use of antacids or H2 antagonists is considered necessary during treatment with erlotinib, please refer to the Summary of Product Characteristics for information on staggered dosing.
- Current drug interaction databases should be consulted for more information.

REFERENCES:

1. Shepherd FA, Rodrigues Pereira J, Ciuleanu T, et al. Erlotinib in Previously Treated Non-small-cell Lung Cancer. N Engl J Med2005;353(2):123-32.
2. CappuzzoF,Ciuleanu T, et al. Erlotinib as maintenance treatment in advanced non-small cell lung cancer: a multicenter, randomized, placebo-controlled phase 3 study. Lancet Oncol 2010;11(6): 521-9.
3. Zhou C, Wu YL et al. Erlotinib versus chemotherapy as first-line treatment for patients with advanced EGFR mutation-positive non-small-cell lung cancer (OPTIMAL, CTONG-0802): a multicentre, open-label, randomised, phase 3 study. Lancet Oncol. 2011;(8):735-42.
4. Tarceva®Summary of Product Characteristics Accessed Feb 2021. Available at: https://www.ema.europa.eu/en/documents/product-information/tarceva-epar-product-information_en.pdf
5. NCCP Classification Document for Systemic Anti-Cancer 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	Initial draft	Dr Maccon Keane
2	25/03/2016	Update of indications based on change to SmPC. Inclusion of standard wording re treatment	Dr Maccon Keane
3	01/03/2017	Clarification of dosing with antacids and H2 antagonists in Drug Interactions	Prof Maccon Keane
4	01/02/2019	Updated to new NCCP template Updated emetogenic potential and dosing recommendations for hepatic impairment	Prof Maccon keane
5	10/03/2021	Reviewed. Amended emetogenic potential.	Prof Maccon Keane

Comments and feedback welcome at oncologydrugs@cancercontrol.ie.