ERLOTINIB

An option for treating locally advanced or metastatic NSCLC after non-targeted chemotherapy because of delayed confirmation that the tumour is EGFR +ve
An option for locally advanced or metastatic NSCLC that has progressed after non-targeted chemotherapy in patients with unknown EGFR status, only if the diagnostic test is unobtainable due to inadequate tissue sample or poor quality DNA **and** the clinician considers that it is very likely to be EGFR +ve
NICE approved Dec 2015

N.B. No funding for patients who are known to be EGFR mutation negative

Drug/Dosage: **Erlotinib** initiate at 150mg po once daily as continuous therapy

Administration: Erlotinib available as 25mg, 100mg and 150mg tablets, which are not scored or divisible. The daily dose should be taken once daily at least one hour before, or two hours after, any food.

Frequency: continuous therapy until progression, or unacceptable toxicity
Clinical review every 4 weeks, plus toxicity review 2 weeks after starting

Main Toxicities: rash; diarrhoea

Anti- emetics: none usually needed, but some patients may have nausea

Regular:	FBC	monthly
Investigations:	LFTs	monthly
	U&Es	monthly
	CT scan	every 3 months

Comments: Encourage routine use of a moisturiser at the start of erlotinib treatment to prevent and minimise problems with skin dryness.
Aveeno colloidal oatmeal lotion is our recommended moisturiser. This is a moisturiser with anti-inflammatory properties that is available from retail chemists and has been shown in small studies to have good efficacy and no toxicity[1,2]. However, if the patient prefers, they may use a moisturiser of their choice.

Elimination of erlotinib is mainly through hepatic metabolism. Concomitant use of enzyme inducers, phenytoin, rifampicin, carbamazepine, barbiturates or St John's Wort with erlotinib should be avoided, as this may increase the risk of therapeutic failure.

Co-administration of erlotinib with the enzyme inhibitors itraconazole, erythromycin or clarithromycin should also be avoided. If this is not possible, the dose of erlotinib may need to be reduced according to tolerability.

Grapefruit and grapefruit juice should also be avoided while on erlotinib, as this may increase erlotinib toxicity[3].

Drugs that reduce gastric acidity reduce the solubility of erlotinib (which has a decreased solubility above pH 5), thereby reducing its absorption. Therefore, the manufacturers of erlotinib advise against the concurrent use of proton pump inhibitors or H_2-receptor antagonists. If the use of ranitidine is essential, administration should be separated, with the

erlotinib taken 2 hours before, or 10 hours after, the ranitidine. Although antacids are also predicted to interact, antacid interactions can usually be minimised by separation of administration. The manufacturer recommends that, if treatment with antacids is essential, they should be taken at least 4 hours before, or 2 hours after, erlotinib.

If the patient is taking warfarin, monitor the INR closely when initiating erlotinib.

Dose Modifications

Haematological Toxicity:	Erlotinib is not myelosuppressive. Patients may continue erlotinib during periods of mild myelosuppression. Discuss with doctor if concerned.
Primary Rash:	Ensure moisturiser is being used regularly. The recommended frequency of application for Aveeno colloidal oatmeal lotion is three times daily. Consider using topical hydrocortisone 1% early in patients with mild rash, but use cautiously, especially for severe rash, as efficacy may be limited by inability to penetrate skin. Analgesia may be of benefit. Topical acne medications are **not** recommended. Severe rash may require an interruption in treatment until resolved, then an erlotinib dose reduction, initially to 100mg once daily. Further dose reductions may be considered if excessive toxicity returns; doses as low as 25mg daily in patients with known EGFR mutations have been used with impressive response rates.[4] If in doubt, discuss with Consultant.
Infected Rash:	If a pustular component, consider a short course of oral doxycycline or flucloxacillin. Use of topical antibiotics is not encouraged, and needs to be discussed with Microbiology first.
Diarrhoea:	Moderate or severe diarrhoea should be treated with loperamide. In the event of severe diarrhoea, or diarrhoea associated with dehydration, erlotinib therapy should be interrupted until resolved. A subsequent dose reduction, initially down to 100mg daily, may be necessary. Further dose reductions may be considered if excessive toxicity returns; doses as low as 25mg daily in patients with known EGFR mutations have been used with impressive response rates.[4] If in doubt, discuss with Consultant.
Hepatic Impairment:	Erlotinib is eliminated by hepatic metabolism, so use with caution in patients with hepatic impairment. It is not recommended in severe hepatic impairment. The FDA advise that erlotinib should be used with extra caution if bilirubin > 3 x ULN, and its safety or efficacy has not been studied in patients with AST / ALT > 5 x ULN. So that patients do not have unnecessary delays waiting for their prescription, LFT results from the previous visit may be used if they are within normal limits and stable.
Renal Impairment:	Erlotinib and its metabolites are not significantly excreted by the kidney. No clinically significant relationship was observed between erlotinib clearance and CrCl, but there are no data available for patients with CrCl <15 ml/min.

References:
Shepherd, FA et al; NEJM 2005; 353:123 – 132
Rash advice adapted from HER1/EGFR Inhibitor Rash Management Forum, 2005
[1]Alexandrescu, D et al; Clinical and Experimental Dermatology 2006; 32: 71 – 74
[2]Talsania, T et al; Clinical and Experimental Dermatology 2008; 33 (1): 108
[3]Roche Medicines Information recommendation, although not in the PIL for Tarceva
[4]Yeo, WL et al; J Thorac Oncol 2010; 5 (7): 1048 - 1053