NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Proposed Health Technology Appraisal

Erlotinib for the first line treatment of EGFR mutation positive non-small-cell lung cancer

Draft scope (Pre-referral)

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of erlotinib, within its licensed indication, for the first-line treatment of epidermal growth factor receptor (EGFR) mutation positive locally advanced or metastatic non-small-cell lung cancer.

Background

Lung cancer falls into two main histological categories: around 80% are non-small-cell lung cancers (NSCLC) and the remainder are small-cell lung cancers. The main types of NSCLC are squamous cell carcinoma (45%), adenocarcinoma (45%) and large cell carcinoma (10%). Between 5% and 15% of cases of NSCLC are diagnosed on routine chest radiographic examination, but the majority of cases present with symptoms and signs related either to the site of the growth of the primary tumour, or to the effects of thoracic or metastatic spread. Approximately a third of patients with NSCLC present with local potentially resectable disease and about 50% of these will be suitable for surgery. About 30% of patients present with locally and regionally advanced disease (Stage IIIb) and 40% with advanced disease (Stage IV in which there are distant metastases).

In England and Wales 33,825 people were diagnosed with lung cancer in 2007, with 30,254 deaths registered in 2007. The prognosis for patients with NSCLC is poor, with a one-year survival rate of 28% and a five-year survival rate of 8%. Estimates of the number of patients who receive first line chemotherapy for inoperable NSCLC vary between 1,320 and 6,447 per year. Lung cancer incidence and mortality rates are strongly associated with smoking and socio-economic deprivation.

While one-third of patients with NSCLC have disease which is suitable for potentially curative surgical resection, for the majority of NSCLC patients, cure is not possible and the aims of therapy are to prolong survival and improve quality of life. Treatment may include radiotherapy and supportive care with or without chemotherapy. NICE has published a clinical guideline on the diagnosis and treatment of lung cancer (CG24). It recommends that chemotherapy should be offered to patients with stage III or IV NSCLC and a good performance status. This should be a combination of docetaxel, gemcitabine, paclitaxel or vinorelbine plus carboplatin or cisplatin. Patients who are unable to tolerate a platinum combination may be offered single-agent chemotherapy. NICE technology appraisal 181 recommends

pemetrexed in combination with cisplatin as an option for the first-line treatment of locally advanced or metastatic NSCLC if the histology of the tumour has been confirmed as adenocarcinoma or large-cell carcinoma. NICE also recommends gefitinib as an option for the first-line treatment of people with locally advanced or metastatic NSCLC if they test positive for the EGFR-tyrosine kinase (TK) mutation (NICE Technology Appraisal 192). Bevacizumab within its licensed indication for the treatment of unresectable advanced, metastatic or recurrent non-small-cell lung cancer was referred to NICE for appraisal, but no evidence submission was received from the manufacturer. Therefore NICE was unable to recommend the use of bevacizmab to the NHS (NICE Technology Appraisal 148).

The technology

Erlotinib (Tarceva, Roche Products) is an orally administered inhibitor of EGFR which is overexpressed in various solid tumours including NSCLC. Erlotinib does not currently have a UK marketing authorisation for the first-line treatment of EGFR mutation positive NSCLC. It is being studied as monotherapy in clinical trials compared with gefitinib or docetaxel in combination with platinum based chemotherapy (cisplatin or carboplatin) in adults with advanced NSCLC with the EGFR-TK mutation.

Intervention(s)	Erlotinib
Population(s)	Adults with previously untreated EGFR-TK mutation positive locally advanced or metastatic non-small-cell lung cancer
Comparators	• Gefitinib • Platinum based chemotherapy (carboplatin or cisplatin) in combination with gemcitabine, docetaxel, paclitaxel or vinorelbine For people with non-squamous non-small cell lung cancer of adenocarcinoma or large cell carcinoma histology • Pemetrexed in combination with cisplatin
Outcomes	The outcome measures to be considered include: • overall survival • progression-free survival • response rates • adverse effects of treatment • health-related quality of life

Economic analysis	The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year. The reference case stipulates that the time horizon for estimating clinical and cost effectiveness should be sufficiently long to reflect any differences in costs or outcomes between the technologies being compared. Costs will be considered from an NHS and Personal Social Services perspective.
Other considerations	Guidance will only be issued in accordance with the marketing authorisation.
Related NICE recommendations	Related Technology Appraisals: Technology Appraisal No. 192, July 2010, 'Gefitinib for the first-line treatment of locally advanced or metastatic non-small-cell lung cancer. Review date April 2013. Technology Appraisal No. 181, September 2009, 'Pemetrexed for the first-line treatment of non-small-cell lung cancer'. Review date TBC. Technology Appraisal No. 162, November 2008, 'Erlotinib for the treatment of non-small-cell lung cancer'. Review date TBC. Technology Appraisal No.148, June 2008, 'Bevacizumab for the treatment of non-small-cell lung cancer' (terminated appraisal). Technology Appraisal in development, 'Erlotinib monotherapy for the maintenance treatment of non-small-cell lung cancer. Earliest anticipated publication April 2011. Technology Appraisal in development, 'Cetuximab for the treatment of advanced non-small-cell lung cancer' (Suspended). Related Guidelines: Clinical Guideline No.24. February 2005, The diagnosis and treatment of lung cancer. Expected review date May 2011.

Questions for consultation

Should the remit and title specify that this appraisal would only consider the treatment of EGFR-TK mutation positive non-small-cell lung cancer?

Have the most appropriate comparators for erlotinib for the treatment of NSCLC been included in the scope? Are the comparators listed routinely used in clinical practice?

Are there any subgroups of people in whom the technology is expected to be more clinically effective and cost effective or other groups that should be examined separately?

Please consider whether in the remit or the scope there are any issues relevant to equality. Please pay particular attention to whether changes need to be made to the remit or scope in order to promote equality, eliminate unlawful discrimination, or foster good relations between people who share a characteristic protected by the equalities legislation and those who do not share it, or if there is information that could be collected during the assessment process which would enable NICE to take account of equalities issues when developing guidance.

Do you consider erlotinib to be innovative in its potential to make a significant and substantial impact on health-related benefits and how it might improve the way that current need is met (is this a 'step-change' in the management of the condition)?

Do you consider that the use of erlotinib can result in any potential significant and substantial health-related benefits that are unlikely to be included in the QALY calculation?

Please identify the nature of the data which you understand to be available to enable the Appraisal Committee to take account of these benefits

NICE intends to appraise this technology through its Single Technology Appraisal (STA) Process. We welcome comments on the appropriateness of appraising this topic through this process. (Information on the Institute's Technology Appraisal processes is available at http://www.nice.org.uk/aboutnice/howwework/devnicetech/technologyappraisalprocessguides/technology_appraisal_process_guides.jsp)