NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Single Technology Appraisal

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

Final scope

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) tyrosine kinase (TK) mutation positive locally advanced or metastatic non-small-cell lung cancer.

Background

Lung cancer falls into two main histological categories: around 85-90% 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 people with NSCLC are diagnosed on routine chest radiographic examination, but the majority 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 people with NSCLC present with local potentially resectable disease and about 50% of these will be suitable for surgery. About 30% of people present with locally and regionally advanced disease (Stage IIIb) and 40% with advanced disease (Stage IV in which there are distant metastases or a pleural or pericardial effusion).

In England and Wales 34,949 people were diagnosed with lung cancer in 2008, with 30,254 deaths registered in 2008. The prognosis for people 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 people who receive first line chemotherapy for inoperable NSCLC vary between 1320 and 6447 per year. Lung cancer incidence and mortality rates are strongly associated with smoking and socio-economic deprivation.

While one-third of people with NSCLC have disease which is suitable for potentially curative surgical resection, for the majority of people with NSCLC, 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 (CG121). It recommends that chemotherapy should be offered to people 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. People 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-TK mutation (NICE technology appraisal 192). Erlotinib monotherapy is not recommended as a maintenance treatment for people with locally advanced or metastatic NSCLC who have stable disease after platinum-based first-line chemotherapy in NICE technology appraisal 227. Bevacizumab was referred to NICE for appraisal for the treatment of unresectable advanced, metastatic or recurrent non-small-cell lung cancer, but no evidence submission was received from the manufacturer. Therefore NICE was unable to recommend the use of bevacizmab for this indication 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-TK mutation positive NSCLC. It is being studied as monotherapy in clinical trials compared with gemcitabine or docetaxel in combination with platinum based chemotherapy (cisplatin or carboplatin) as a first-line treatment for adults with advanced NSCLC whose tumours have an activating 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 For people with non-squamous non-small cell lung cancer of adenocarcinoma or large cell carcinoma histology • Pemetrexed in combination with cisplatin or carboplatin
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. Costs of any additional mutational testing required for this treatment should be considered in the economic analysis.
Other considerations	Guidance will only be issued in accordance with the marketing authorisation.
Related NICE recommendations	Related Technology Appraisals: Technology Appraisal No. 227, June 2011, 'Erlotinib monotherapy for the maintenance treatment of non-small-cell lung cancer'. Review date: April 2013. 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 mid 2011. Technology Appraisal No.148, June 2008, 'Bevacizumab for the treatment of non-small-cell lung cancer' (terminated appraisal). Related Guidelines: Clinical Guideline No. 121. April 2011, 'The diagnosis and treatment of lung cancer (update of NICE clinical guideline 24)'. Clinical Guideline No. 24. February 2005, 'The diagnosis and treatment of lung cancer'. Replaced by CG121.