NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Health Technology Appraisal

Cetuximab for the treatment of advanced non-small cell lung cancer

Final scope

Remit/appraisal objective

To appraise the clinical and cost effectiveness of cetuximab within its licensed indication for the treatment of advanced 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 respectable 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 is distant metastases.

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. There were 31,900 new diagnoses of lung cancer in England and Wales in 2003 (an incidence of around 60 cases per 100,000 population) and 28,632 deaths in 2005 (a rate of around 54 deaths per 100,000 population).

The prognosis for patients with non-small cell lung cancer (NSCLC) is poor, with an overall median survival of 6 months from diagnosis and 1 year survival of only around 20%. For those with advanced disease, the survival benefits conferred by current treatments are modest, making improvements in quality of life of particular importance.

About one-third of patients with NSCLC have disease which is suitable for potentially curative surgical resection. However, 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. Chemotherapy for advanced

NSCLC should include a combination of a single third-generation drug (gemcitabine, docetaxel, paclitaxel, vinorelbine) with a platinum drug (carboplatin or cisplatin). Bevacizumab in addition to platinum-based chemotherapy for the first-line treatment of patients with unresectable advanced, metastatic or recurrent non-small-cell lung cancer (other than predominantly squamous cell histology) was referred to NICE for appraisal. However no evidence submission was received from the manufacturer or sponsor of the technology. Therefore NICE was unable to recommend the use of this technology to the NHS.

The technology

Cetuximab (Erbitux, Merck) is an anti-epidermal growth factor receptor (EGFR) monoclonal antibody. Cetuximab prevents the proliferation of cells by binding to EGFR and preventing autophosphorylation of the intracellular region. This stops cells from dividing. Cetuximab may also make the cancer cells more sensitive to chemotherapy.

Cetuximab does not currently hold a UK marketing authorisation for NSCLC. Cetuximab has been studied in clinical trials in people with EGFR positive advanced NSCLC in combination with cisplatin and vinorelbine versus cisplatin and vinorelbine alone, and also in combination with docetaxel or pemetrexed versus docetaxel or pemetrexed alone.

Intervention(s)	Cetuximab in combination with other chemotherapy
Population(s)	People with chemotherapy naïve EGFR positive stage IIIb or stage IV NSCLC.
Standard comparators	Platinum based chemotherapy (carboplatin or cisplatin) in combination with gemcitabine, docetaxel, paclitaxel or vinorelbine.
Outcomes	The outcome measures to be considered include: • overall survival • progression-free survival • tumour response • symptom response • health-related quality of life • adverse effects of treatment

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 time horizon for the economic evaluation should reflect the period over which costs and benefits can reasonably be expected given the prognosis of NSCLC. 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. If evidence allows, subgroups of patients defined by performance status, tumour markers, histology or other relevant factors, will be considered.
Related NICE recommendations	Related Technology Appraisals in progress: Technology Appraisal in preparation, 'Erlotinib for the treatment of non-small cell lung cancer'. Earliest anticipated date of publication November 2008. Technology Appraisal in preparation, 'Pemetrexed for the treatment of non-small cell lung cancer'. Earliest anticipated date of publication August 2009. Technology Appraisal in preparation, 'Gefitinib for the treatment of locally advanced or metastatic non-small cell lung cancer'. Earliest anticipated date of publication November 2009. Related Guidelines: Clinical Guideline No. 26, February 2005. 'Lung cancer: diagnosis and treatment'.