NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Health Technology Appraisal

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

Draft scope (pre-referral)

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of cetuximab in 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, adenocarcinoma and large cell carcinoma accounting for approximately 35-45%, 15% and 10% of all lung cancer cases respectively in the UK. 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 85% of these patients will have advanced disease which is inoperable. This includes patients with locally and regionally advanced stage IIIb disease and stage IV disease in which there are 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. Within the UK, there is a north/ south differential in lung cancer mortality rates that reflect regional smoking patterns. There is also some variation among ethnic groups with south Asians in the UK known to have lower incidence of lung cancer.

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. Chemotherapy for NSCLC includes combination of a single third-generation drug (gemcitabine, docetaxel, paclitaxel or vinorelbine) with a platinum drug (carboplatin or

cisplatin) or single agent chemotherapy with a third generation drug for patients who cannot tolerate a platinum combination.

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. In ongoing randomised controlled trials, cetuximab has been administered, in combination with other chemotherapies, by intravenous infusion with an initial dose of 400mg/m^2 followed by a weekly dose of 250mg/m^2 for a period of approximately 12 weeks, in combination with current chemotherapy options. The exact proposed license indication is still to be determined and is dependent upon the outcomes of several clinical trials.

Intervention(s)	Cetuximab in combination with other chemotherapy
Population(s)	People who have untreated stage IIIb or stage IV non-small cell lung cancer.
Standard comparators	• Single agent gemcitabine, docetaxel, paclitaxel and vinorelbine • Combinations of platinum-based chemotherapy with or without gemcitabine, docetaxel, paclitaxel or vinorelbine
Outcomes	The outcome measures to be considered include: • Overall survival • Progression-free survival • Tumour or 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 patient populations in whom the technology is clinically effective and cost effective should be considered.
Related NICE recommendations	Related Technology Appraisals in progress: Erlotinib for the treatment of non-small cell lung cancer. Expected, March 2007 Pemetrexed for the treatment of non-small cell lung cancer. Expected, March 2007 Related Guidelines: Lung cancer: the diagnosis and treatment of lung cancer, February 2005.

Questions for consultation

- Would best supportive care, radiotherapy and radiotherapy plus chemotherapy be appropriate comparators or would they be used in different patient populations to that in which cetuximab is likely to be used?

- The Institute would welcome comments as to whether this technology is suitable for the Single Technology Appraisal process.