NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Single Technology Appraisal

Pemetrexed for the first-line treatment of locally advanced or metastatic non-small-cell lung cancer

Final scope (Pre-referral)

Remit/appraisal objective

To appraise the clinical and cost effectiveness of pemetrexed, within its licensed indications, for the first-line treatment of 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).

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 NSCLC is poor, with an overall median survival of 6 months from diagnosis and 1 year survival of only around 20%.

Surgical resection and radical dose radiation with or without chemotherapy can be curative for NSCLC. However, approximately 85% (13,800) of patients will present with advanced non-squamous NSCLC not suitable for curative surgical resection. For these patients treatment 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 or vinorelbine) with a platinum drug (carboplatin or cisplatin).

The technology

Pemetrexed (Alimta, Eli Lilly) is a pyrrolo[2,3-d]pyrimidine-based folic acid analogue. It is administered as an intravenous infusion.

Pemetrexed, in combination with cisplatin, has a marketing authorisation for the first-line treatment of patients with locally advanced or metastatic NSCLC other than predominantly squamous cell histology. Its marketing authorisation includes other indications, including the treatment of patients with locally advanced or metastatic NSCLC after prior chemotherapy.

Intervention(s)	Pemetrexed in combination with cisplatin
Population(s)	Patients with chemotherapy-naïve locally advanced or metastatic NSCLC other than predominantly squamous cell histology who are unsuitable for surgery
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 • 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	If evidence allows subgroups of patient populations in whom the technology is clinically effective and cost effective should be considered. These may be related to histology.

Related NICE recommendations	Related Technology Appraisals: Technology Appraisal No.124. August 2007, 'Pemetrexed for the treatment of non small cell lung cancer'. Technology Appraisal No.148. June 2008, 'Bevacizumab for the treatment of non-small-cell lung cancer' (terminated appraisal). 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, 'Cetuximab for the treatment of advanced non-small cell lung cancer'. Earliest anticipated date of publication July 2009. Technology Appraisal in Preparation, 'Gefitinib for the treatment of advanced non-small cell lung cancer'. Earliest anticipated date of publication November 2009. Related Guidelines: Clinical Guideline No.24. February 2005, The diagnosis and treatment of lung cancer.