

NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Single Technology Appraisal

Pemetrexed for maintenance treatment following induction therapy with pemetrexed and cisplatin for non-squamous non-small-cell lung cancer**Final scope****Remit/appraisal objective**

To appraise the clinical and cost effectiveness of pemetrexed, within its licensed indication, for maintenance treatment of non-squamous non-small-cell lung cancer for people whose disease has not progressed following induction therapy with pemetrexed and cisplatin.

Background

Lung cancer falls into two main histological categories: non-small-cell lung cancers (NSCLC; 85–90%) and small-cell lung cancers (approximately 10–15%). NSCLCs are further sub-divided into squamous cell carcinomas (45%), adenocarcinomas (45%) and large-cell carcinomas (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. About 30% of patients present with locally and regionally advanced disease (stage IIIB) and 40% with advanced disease (stage IV in which the cancer has spread to other parts of the body or there are other symptoms such as a build up of fluid around the lungs or heart which is known as 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 patients with NSCLC is poor, with a 1-year survival rate of 28% and a 5-year survival rate of 8%. Estimates of the number of patients 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 factors.

While one-third of patients with NSCLC have disease which is suitable for potentially curative surgical resection, for the majority of NSCLC patients, the aims of therapy are to prolong survival and improve quality of life. Approximately 25% of patients with advanced NSCLC receive first-line chemotherapy and around 20–40% of these patients may receive second-line therapy. Treatment options for stage IIIB or IV NSCLC include radiation therapy, chemotherapy with radiotherapy, and chemotherapy alone.

NICE has published a clinical guideline on the diagnosis and treatment of lung cancer (CG121). 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. CG121 goes on to define best/active supportive care in lung cancer as including the use of palliative radiotherapy, non-drug interventions, management of endobronchial obstruction, bone pain and pathological fractures. 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 technology appraisal 190 recommends pemetrexed as an option for the maintenance treatment of people with locally advanced or metastatic NSCLC other than predominantly squamous cell histology if the disease has not progressed immediately following platinum-based chemotherapy in combination with gemcitabine, paclitaxel or docetaxel. This guidance (TA190) does not cover people who have received pemetrexed in combination with cisplatin as first-line chemotherapy; this was not included in the maintenance indication for pemetrexed at the time of the appraisal.

The technology

Pemetrexed (Alimta, Eli Lilly) is an antifolate agent that works by disrupting folate-dependent metabolic processes essential for cancer cell replication and survival. It is administered as an intravenous infusion.

Pemetrexed has received an extension to its existing maintenance indication which now includes pemetrexed maintenance therapy after induction therapy with pemetrexed and cisplatin. The UK marketing authorisation for pemetrexed monotherapy is for the maintenance treatment of locally advanced or metastatic non-small-cell lung cancer other than predominantly squamous cell histology in patients whose disease has not progressed immediately following platinum-based chemotherapy.

Intervention(s)	Pemetrexed
Population(s)	People with advanced or metastatic (stage IIIB and IV) NSCLC, other than predominately squamous histology, whose disease has not progressed following induction treatment with pemetrexed and cisplatin
Comparators	<ul style="list-style-type: none"> • Best supportive care (includes bisphosphonates and palliative radiotherapy)
Outcomes	<p>The outcome measures to be considered include:</p> <ul style="list-style-type: none"> • overall survival • progression-free survival • response rates

	<ul style="list-style-type: none"> • adverse effects of treatment (according to grade) • health-related quality of life.
<p>Economic analysis</p>	<p>The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year.</p> <p>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.</p> <p>Costs will be considered from an NHS and Personal Social Services perspective.</p>
<p>Other considerations</p>	<p>Guidance will only be issued in accordance with the marketing authorisation</p>
<p>Related NICE recommendations</p>	<p>Related Technology Appraisals:</p> <p>Technology Appraisal No. 227, June 2011, 'Erlotinib monotherapy for maintenance treatment of non-small-cell lung cancer'. Review date April 2013.</p> <p>Technology Appraisal No. 190, June 2010, 'Pemetrexed for the maintenance treatment of non-small-cell lung cancer'. Review date November 2012.</p> <p>Technology Appraisal No. 181, September 2009, 'Pemetrexed for the first-line treatment of non-small-cell lung cancer'. Review date TBC.</p> <p>Technology Appraisal No.148, June 2008, 'Bevacizumab for the treatment of non-small-cell lung cancer' (terminated appraisal).</p> <p>Technology Appraisal No. 124, August 2007, 'Pemetrexed for the treatment of non-small-cell lung cancer'. Guidance on static list.</p> <p>Related Guidelines:</p> <p>Clinical Guideline 121, April 2011, The diagnosis and treatment of lung cancer (update of NICE clinical guideline 24). Review date April 2014.</p>