NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Single Technology Appraisal

Crizotinib for the treatment of previously treated non-small-cell lung cancer associated with an anaplastic lymphoma kinase fusion gene

Final scope

Remit/appraisal objective

To appraise the clinical and cost effectiveness of crizotinib within its licensed indication for the treatment of previously treated non-small-cell lung cancer associated with an anaplastic lymphoma kinase fusion gene.

Background

In England and Wales 34,949 people were diagnosed with lung cancer in 2008, with 30,254 deaths registered in 2008. 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. Approximately 30% 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 the cancer has spread to other parts of the body). The prognosis for people with NSCLC is poor, with a one-year survival rate of 28% and a five-year survival rate of 8%.

It is estimated that approximately 3% to 5% of people with NSCLC have chromosomal alterations described as anaplastic lymphoma kinase (ALK) fusion genes. These are fusions between the tyrosine kinase portion of the ALK gene and other genes and are believed to be involved in tumour cell growth and survival. It is thought that people with NSCLC with an ALK fusion gene mutation do not harbour epidermal growth factor receptor (EGFR) mutations. ALK fusion genes may be associated with resistance to EGFR tyrosine kinase inhibitors such as erlotinib and gefitinib.

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. NICE clinical guideline 121 (CG121) recommends a combination of docetaxel, gemcitabine, paclitaxel or vinorelbine plus carboplatin or cisplatin as first line treatment options for patients with stage III or IV NSCLC and a good performance status. People who are unable to tolerate a platinum combination may be offered single-agent chemotherapy. NICE technology appraisal guidance 192 and 258 recommend gefitinib (TA192) and erlotinib (TA258) as options for the first-line treatment of people with locally advanced or metastatic NSCLC if they test positive for the EGFR-tyrosine kinase mutation. NICE technology appraisal guidance 181 and 190 recommend pemetrexed as an option for the first-line treatment (TA181) and

maintenance treatment (TA190) of advanced and metastatic non-squamous NSCLC. Recommended second line treatment options include erlotinib (TA162), and docetaxel monotherapy (CG121). Pemetrexed is not recommended for treatment of locally advanced or metastatic NSCLC after prior chemotherapy (TA124).

The technology

Crizotinib (Xalkori, Pfizer) is an orally administered inhibitor of ALK fusion protein. Crizotinib does not currently have a UK marketing authorisation for the treatment of NSCLC. It is being studied as monotherapy in clinical trials compared with pemetrexed or docetaxel in adults with previously treated advanced or metastatic NSCLC that is positive for ALK fusion genes.

Intervention(s)	Crizotinib
Population(s)	People with previously treated locally advanced or metastatic non-small-cell lung cancer that is positive for anaplastic lymphoma kinase fusion (ALK) genes.
Comparators	• Docetaxel • Erlotinib • Best supportive care
Outcomes	The outcome measures to be considered include: • overall survival • progression-free survival • response rate • 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	Guidance will only be issued in accordance with the marketing authorisation. This appraisal should consider the implications of

	additional testing.
Related NICE recommendations	Related Technology Appraisals: Technology Appraisal No. 175, July 2009, 'Gefitinib for the second-line treatment of locally advanced or metastatic non-small-cell lung cancer (terminated appraisal)'. Currently being reviewed. Technology Appraisal No. 162, November 2008, 'Erlotinib for the treatment of non-small-cell lung cancer'. Review date: Currently being reviewed. Technology Appraisal No. 124, August 2007, 'Pemetrexed for the treatment of non-small-cell lung cancer'. Guidance on static list. Technology appraisal in preparation, 'Erlotinib and gefitinib for the second-line treatment of non-small-cell lung cancer (review of TA162 and TA175). Earliest anticipated date of publication: June 2014. Related Guidelines: Clinical Guideline No.121. April 2011, 'The diagnosis and treatment of lung cancer' (update of Clinical Guideline 24). Review date TBC.