NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Proposed Health Technology Appraisal

BIBW 2992 for the treatment of non-small cell lung cancer

Draft scope (Pre-referral)

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of BIBW 2992 within its licensed indication for the treatment of non-small cell lung cancer after previous platinum containing chemotherapy and gefitinib or erlotinib.

Background

Lung cancer is a common cause of death in the UK. In England and Wales there were 33,450 new cases diagnosed in 2006, and 29,574 deaths registered in 2007. In England and Wales, 25% of people with lung cancer are alive after one year and 7% are alive after five years. Non-small cell lung cancer (NSCLC) accounts for approximately 80% of all lung cancers.

Staging describes how far the cancer has spread. In stage IIIB, the tumour may be any size and has spread to lymph nodes above the collar bone or the opposite side of the chest from the tumour; and/or to any of the organs in the thoracic cavity. Stage IV non-small cell lung cancer may have spread to lymph nodes and has spread to another lobe of the lungs or to other parts of the body, such as the brain, liver, adrenal glands, kidneys, or bone. Approximately 75% of newly diagnosed patients already have advanced (stage III or IV) disease (equating to around 24,536 patients in England and Wales), with a five-year survival rate of less than 1%.

Approximately 25% of patients with advanced NSCLC receive first-line chemotherapy and around 30-40% 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. Chemotherapy may be recommended for patients with non-resectable stage III or IV disease if they are able to tolerate it. A NICE Clinical Guideline on lung cancer (CG24) recommends that first-line chemotherapy should include a combination of a platinum drug (cisplatin or carboplatin) and a drug such as docetaxel, gemcitabine, paclitaxel or vinorelbine. Pemetrexed in combination with cisplatin is also recommended by NICE 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 (TA181). Erlotinib is recommended by NICE as an option for second-line treatment (TA162). Alternative licensed second-line therapy options include docetaxel and gefitinib. Best supportive care may be considered for some people.

The technology

BIBW 2992 (Tovok, Boehringer Ingelheim Pharmaceuticals) is a dual kinase inhibitor of the epidermal growth factor receptor and the human epidermal growth factor receptor 2. BIBW 2992 is administered orally once daily.

BIBW 2992 does not currently have a UK marketing authorisation. It is being studied in comparison to placebo in people with NSCLC who have progressive disease that has been treated with at least one but not more than two lines of platinum-containing chemotherapy and at least 12 weeks of prior treatment with erlotinib or gefitinib.

Intervention(s)	BIBW 2992
Population(s)	People with stage IIIB and IV NSCLC whose disease has progressed following treatment with platinum-based chemotherapy and either erlotinib or gefitinib.
Comparators	• docetaxel • erlotinib • best supportive care Additionally for NSCLC with activating mutations of EGFR-TK: • gefitinib
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 the evidence allows, subgroups such as those defined by: performance status, histology (squamous/ non squamous), EGFR and HER2 mutational status, and response to prior treatment will be considered. The costs in the economic model should take into account the patient access scheme for erlotinib. If this topic is referred, details of the effective cost of these drugs as a result of the scheme should be sought and made available to manufacturers submitting evidence. Guidance will only be issued in accordance with the marketing authorisation.
Related NICE recommendations	Related Technology Appraisals: Technology Appraisal 124, August 2007, Pemetrexed for the treatment of non small cell lung cancer. Expected review date: January 2010. Technology Appraisal 148 (terminated), June 2008, Bevacizumab for the treatment of non-small cell lung cancer. Technology Appraisal 175 (terminated), July 2009, Gefitinib for the second-line treatment of non-small cell lung cancer. Technology Appraisal 162, November 2008, Erlotinib for the treatment of non-small cell lung cancer. Expected review date: June 2010. Technology Appraisal 181, September 2009, Pemetrexed for the first-line treatment of advanced or metastatic non-small cell lung cancer. Expected review date: July 2010. Technology Appraisal in preparation, Gefitinib for the first-line treatment of non-small cell lung cancer. Expected date of publication: June 2010. Technology Appraisal in preparation, Erlotinib (in combination with bevacizumab) for the maintenance treatment of advanced or metastatic non-small-cell lung cancer. Expected date of publication: June 2011. Technology Appraisal in preparation, Pemetrexed for maintenance treatment following first line chemotherapy for non-small-cell lung cancer. Expected date of publication: May 2010. Related Guidelines:

	Clinical Guideline 24, February 2005, The diagnosis and treatment of lung cancer (currently under review, expected date of publication December 2010). Related Interventional Procedures: Interventional Procedure 185, July 2006, Percutaneous radiofrequency ablation for primary and secondary lung cancers.

Questions for consultation

Is erlotinib an appropriate comparator?

Is gefitinib an appropriate comparator?

What consideration needs to be given to people with EGFR mutations (for example, the usual pathway of care, possible comparators etc)?

How should best supportive care be defined?

Are the subgroups suggested in 'other considerations' appropriate? Are there any other subgroups of patients in whom the technology is expected to be more clinically and cost effective or other groups who should be examined separately?

Are there any issues that require special attention in light of the duty to have due regard to the need to eliminate unlawful discrimination and promote equality?

NICE intends to appraise this technology through its Single Technology Appraisal (STA) Process. We welcome comments on the appropriateness of appraising this topic through this process. (Information on the Institute's Technology Appraisal processes is available at http://www.nice.org.uk/aboutnice/howwework/devnicetech/technologyappraisalprocessguides/technology_appraisal_process_guides.jsp)