NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Proposed Health Technology Appraisal

Afatinib for the treatment of epidermal growth factor receptor mutation positive locally advanced or metastatic non-small cell lung cancer

Draft scope

Draft remit/appraisal objective

To appraise the clinical and cost-effectiveness of afatinib within its licensed indication for the treatment of epidermal growth factor receptor mutation positive locally advanced or metastatic non-small cell lung cancer.

Background

Non-small cell lung cancer (NSCLC) accounts for around 90% of all lung cancer cases. The three most common types of NSCLC are squamous cell carcinoma, adenocarcinoma and large cell carcinoma. NSCLC with epidermal growth factor receptor (EGFR) activating mutations is considered to be a genetically distinct form of lung cancer which is most common in people with adenocarcinoma, non-smokers, people of Asian origin and females. Overexpression of EGFR has been detected in 10-15% of NSCLC.

Around 35,000 people are diagnosed with lung cancer in England and Wales each year of which 87% are aged over 60 years. The majority of these diagnoses (approximately 75%) are at a late stage (stage III and stage IV), which means they are unlikely to be treated with curative intent. Lung cancer is the leading cause of cancer death for both men and women in the UK, with more than 30,000 people dying from the condition each year in England and Wales. In England and Wales, lung cancer incidence and mortality rates are strongly associated with socioeconomic deprivation. Incidence rates are more than double in the most deprived groups compared with the least deprived groups (75.2 compared with 29.8 per 100,000 population).

NICE clinical guideline 121 'Lung cancer' recommends that patients with stage III or IV NSCLC and good performance status should be offered chemotherapy to improve survival, disease control and quality of life. Chemotherapy should comprise a platinum drug (carboplatin or cisplatin) in combination with a third-generation drug (docetaxel, gemcitabine, paclitaxel or vinorelbine). Patients who are unable to tolerate a platinum combination may be offered single-agent chemotherapy with a third-generation drug. Gefitinib is recommended as an option for patients who test positive for the epidermal growth factor receptor tyrosine kinase (EGFR-TK) mutation (NICE technology appraisal guidance 192 'Gefitinib for the first-line treatment of locally advanced or metastatic non-small-cell lung cancer'). NICE is currently appraising erlotinib for the first line treatment of EGFR-TK mutation positive non-small-cell lung cancer with publication expected in June 2012. Pemetrexed in combination with cisplatin is recommended as an option if the

tumour is an adenocarcinoma or large-cell carcinoma (NICE technology appraisal guidance 181 'Pemetrexed for the first-line treatment of non-small-cell lung cancer'). Pemetrexed is also recommended as maintenance treatment in non-squamous cell histology following treatment with platinum-based chemotherapy in combination with gemcitabine, paclitaxel or docetaxel (NICE technology appraisal guidance 190 'Pemetrexed for the maintenance treatment of non-small-cell lung cancer'). Erlotinib is not recommended for maintenance treatment in people who have stable disease after platinum-based first-line chemotherapy.

The technology

Afatinib (brand name unknown, Boehringer Ingelheim) is a selective, irreversible inhibitor of the epidermal growth factor receptor and human epidermal growth factor receptor 2 (HER2) tyrosine kinases. The EGFR-tyrosine kinase is an enzyme that regulates intracellular signalling pathways implicated in the proliferation and survival of cancer cells. Afatinib is administered orally. Afatinib does not currently have a UK marketing authorisation. It is currently being studied in clinical trials compared with chemotherapy (gefitinib, cisplatin plus gemcitabine,cisplatin plus pemetrexed, erlotinib) in adults for the treatment of EGFR mutation positive locally advanced or metastatic non-small cell lung cancer.

Intervention(s)	Afatinib
Population(s)	People with locally advanced or metastatic non-small cell lung cancer with positive epidermal growth factor receptor mutation
Comparators	First line: • gefitinib • erlotinib • gemcitabine, docetaxel, paclitaxel or vinorelbine in combination with carboplatin or cisplatin For people with non-small cell lung cancer other than predominantly squamous cell histology: • pemetrexed in combination with cisplatin Second line: • erlotinib • docetaxel

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.
Related NICE recommendations	Related Technology Appraisals: Technology Appraisal No. 192, July 2010, 'Gefitinib for the first-line treatment of locally advanced or metastatic non-small-cell lung cancer'. Review date April 2013. Technology Appraisal No. 190, June 2010, 'Pemetrexed for the maintenance treatment of non-small cell lung cancer.' Review date November 2012. Technology Appraisal No. 181, September 2009, 'Pemetrexed for the first-line treatment of non-small cell lung cancer'. Review date August 2012. Technology Appraisal No. 124, November 2007, 'Pemetrexed for the treatment of non-small-cell lung cancer'. Review date January 2010 Technology Appraisal No. 162, November 2008, 'Erlotinib for the treatment of non-small cell lung cancer'. Review date June 2010 Technology Appraisal in development, 'Erlotinib for the first line treatment of EGFR-TK mutation positive non-small-cell lung cancer'. Earliest anticipated publication June 2012. Technology Appraisal in development, 'Cetuximab for the treatment of advanced non-small cell lung cancer'. Earliest

	anticipated publication TBC. Terminated Technology Appraisal No. 175, 'Gefitinib for the second-line treatment of locally advanced or metastatic non-small cell lung cancer.' Terminated Technology Appraisal No. 148, 'Bevacizumab for the treatment of non-small cell lung cancer.' Suspended Technology Appraisal, 'Afatinib for the treatment of locally advanced or metastatic non-small cell lung cancer after previous platinum containing chemotherapy and gefitinib or erlotinib.' Proposed Technology Appraisal, 'BIBF 1120 for advanced and/or metastatic non-small cell lung cancer', publication TBC. Proposed Technology Appraisal, 'Pemetrexed (Alimata) for non-squamous advanced non-small cell lung cancer', publication TBC. Related Guidelines: Clinical Guideline No.121. April 2011, 'The diagnosis and treatment of lung cancer' (update of Clinical Guideline 24). Review date April 2014. Related Quality Standards: 'Lung cancer' http://www.nice.org.uk/guidance/qualitystandards/qualitystandards.jsp

Questions for consultation

What is the likely place of afatinib in the treatment pathway of EGFR mutation positive locally advanced or metastatic NSCLC?

Have the most appropriate comparators for afatinib for the treatment of EGFR mutation positive locally advanced or metastatic NCSLC been included in the scope? Are the comparators listed routinely used in clinical practice?

Are there any subgroups of people in whom the technology is expected to be more clinically effective and cost effective or other groups that should be examined separately?

NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others. Please let us know if you think that the proposed remit and scope may need changing in order to meet these aims. In particular, please tell us if the proposed remit and scope:

- could exclude from full consideration any people protected by the equality legislation who fall within the patient population for which afatinib will be licensed;

- could lead to recommendations that have a different impact on people protected by the equality legislation than on the wider population, e.g. by making it more difficult in practice for a specific group to access the technology;

- could have any adverse impact on people with a particular disability or disabilities.

Please tell us what evidence should be obtained to enable the Committee to identify and consider such impacts.

Do you consider the technology to be innovative in its potential to make a significant and substantial impact on health-related benefits and how it might improve the way that current need is met (is this a 'step-change' in the management of the condition)?

Do you consider that the use of the technology can result in any potential significant and substantial health-related benefits that are unlikely to be included in the QALY calculation?

Please identify the nature of the data which you understand to be available to enable the Appraisal Committee to take account of these benefits

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)