

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Single Technology Appraisal

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

Final scope

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.

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 and erlotinib are recommended as first line treatment options for people 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' and 258 'Erlotinib for the first line treatment of locally advanced or metastatic EGFR-TK mutation positive non-small-cell lung cancer'). Pemetrexed in combination with cisplatin is recommended as a first line 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'). NICE is currently appraising erlotinib and gefitinib for the treatment of non-small-cell lung cancer following prior chemotherapy' (review of TA 162 and TA 175). There are no specific NICE appraisals of second line treatments for EGFR-TK mutation positive NSCLC.

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, 3 and 4 (HER2, HER3 and HER4) 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 (cisplatin plus gemcitabine, cisplatin plus pemetrexed), targeted therapies (gefitinib, erlotinib) and best supportive care for the treatment of EGFR mutation positive locally advanced or metastatic non-small cell lung cancer for treatment naïve patients and for people who have received at least one prior systemic treatment.

Intervention(s)	Afatinib
Population(s)	People with locally advanced or metastatic non-small cell lung cancer with positive epidermal growth factor receptor tyrosine kinase mutation
Comparators	<p>First line:</p> <ul style="list-style-type: none"> • gefitinib • erlotinib <p>Second line:</p> <ul style="list-style-type: none"> • gemcitabine, docetaxel, paclitaxel or vinorelbine in combination with carboplatin or cisplatin <p>For people with non-small cell lung cancer other than predominantly squamous cell histology:</p> <ul style="list-style-type: none"> • pemetrexed in combination with cisplatin <p>For people who are unable to tolerate a platinum combination:</p> <ul style="list-style-type: none"> • single-agent gemcitabine, docetaxel, paclitaxel or vinorelbine <p>Third/ fourth line:</p> <ul style="list-style-type: none"> • docetaxel monotherapy

	<ul style="list-style-type: none"> • best supportive care
Outcomes	<p>The outcome measures to be considered include:</p> <ul style="list-style-type: none"> • overall survival • progression-free survival • response rate • adverse effects of treatment • health-related quality of life.
Economic analysis	<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>The availability of any patient access schemes for the intervention or comparator technologies should be taken into account.</p>
Other considerations	<p>Guidance will only be issued in accordance with the marketing authorisation.</p>
Related NICE recommendations	<p>Related Technology Appraisals:</p> <p>Technology Appraisal No. 258, June 2012, 'Erlotinib for the first-line treatment of locally advanced or metastatic EGFR-TK mutation positive non-small-cell lung cancer'. Currently under review</p> <p>Technology Appraisal No. 192, July 2010, 'Gefitinib for the first-line treatment of locally advanced or metastatic non-small-cell lung cancer'. Currently under review</p> <p>Technology Appraisal No. 190, June 2010, 'Pemetrexed for the maintenance treatment of non-small cell lung cancer.' Currently under review.</p> <p>Technology Appraisal No. 181, September 2009, 'Pemetrexed for the first-line treatment of non-small cell lung cancer'. Currently under review.</p> <p>Technology Appraisal No. 124, November 2007, 'Pemetrexed for the treatment of non-small-cell lung</p>

	<p>cancer'. Review date TBC.</p> <p>Technology Appraisal No. 162, November 2008, 'Erlotinib for the treatment of non-small cell lung cancer'. Currently under review</p> <p>Technology Appraisal in development, 'Pemetrexed for the maintenance treatment following induction therapy with pemetrexed and cisplatin for non-squamous non-small-cell lung cancer'. Expected date of publication June 2013.</p> <p>Technology Appraisal in development, 'Erlotinib and gefitinib for the treatment of non-small-cell lung cancer following prior chemotherapy' (review of TA 162 and TA 175). Expected date of publication June 2014</p> <p>Terminated Technology Appraisal No. 175, 'Gefitinib for the second-line treatment of locally advanced or metastatic non-small cell lung cancer.'</p> <p>Terminated Technology Appraisal No. 148, 'Bevacizumab for the treatment of non-small cell lung cancer.'</p> <p>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.'</p> <p>Suspended Technology Appraisal, 'Cetuximab for the treatment of advanced non-small cell lung cancer'.</p> <p>Related Guidelines:</p> <p>Clinical Guideline No.121. April 2011, 'The diagnosis and treatment of lung cancer' (update of Clinical Guideline 24). Review date April 2014.</p> <p>Related Quality Standards:</p> <p>'Lung cancer'</p> <p>http://www.nice.org.uk/guidance/qualitystandards/qualitystandards.jsp</p> <p>Related NICE Pathways:</p> <p>NICE Pathway: Lung cancer, pathway created: Mar 2012</p> <p>http://pathways.nice.org.uk/pathways/lung-cancer</p>
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