# NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

## Proposed Health Technology Appraisal

## Bevacizumab for treating EGFR mutation-positive non-small-cell lung cancer [ID958]

## Draft scope (pre-referral)

### Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of bevacizumab within its marketing authorisation for treating advanced, metastatic or recurrent EGFR mutation positive non-small cell lung cancer.

### Background

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. NSCLC can be further classified into 3 histological sub-types of large-cell undifferentiated carcinoma, squamous cell carcinoma and adenocarcinoma. The majority of lung cancers are diagnosed at an advanced stage, when the cancer has spread to lymph nodes and other organs in the chest (locally advanced disease; stage III) or to other parts of the body (metastatic disease; stage IV).

In 2013, approximately 26,800 people were diagnosed with NSCLC in England, of whom 21% had stage III and 48% had stage IV disease. Approximately 15% of NSCLC is evaluated as EGFR positive, 36% of patients with metastatic NSCLC are suitable for first line therapy and of these, 11% of tumours will be EGFR positive[1]. The prognosis for people with non-small-cell lung cancer is generally poor. The median survival with lung cancer (all stages) is approximately 6 months; 35% of people with lung cancer, and 14% of people with stage IV disease, survive for more than 1 year.[2]

For the majority of people with NSCLC, the aims of therapy are to prolong survival and improve quality of life. Treatment choices may be influenced by the presence of biological markers (such as the checkpoint inhibitor programmed death-ligand 1 [PD-L1] and mutations in epidermal growth factor receptor-tyrosine kinase [EGFR-TK] or anaplastic-lymphoma-kinase [ALK], or), histology (squamous or non-squamous) and previous treatment experience. 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. For

[1] NIHR Horizon Scanning Centre briefing note
[2] Cancer Research UK (2014) Lung cancer statistics. Accessed February 2016

people whose disease tests positive for the EGFR-TK mutation and who have not previously received treatment, NICE guidance recommends the Tyrosine Kinase Inhibitors (TKI) afatinib, erlotinib and gefitinib as treatment options (NICE technology appraisal guidance 310, 258 and 192 respectively).

**The technology**

Bevacizumab (Roche Products) is a humanised immunoglobin (IgG10) monoclonal antibody that binds to vascular endothelial growth factor (VEGF) preventing tumour growth. It is administered via intravenous (IV) infusion.

Bevacizumab does not currently have a marketing authorisation in the UK for treating advanced, metastatic or recurrent EGFR-TK mutation positive non-small cell lung cancer. Bevacizumab is currently being studied in clinical trials in combination with erlotinib compared with erlotinib alone in people with stage IIIB/IV or recurrent non-squamous EGFR-TK mutation positive NSCLC.

Bevacizumab, in addition to platinum based chemotherapy is currently licensed for the first line treatment of adults with advanced, metastatic or recurrent NSCLC with other than predominantly squamous cell histology.

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| **Intervention(s)** | Bevacizumab in combination with erlotinib |
| **Population(s)** | People with advanced, metastatic or recurrent EGFR-TK positive non-small cell lung cancer |
| **Comparators** | • Afatinib<br>• Erlotinib<br>• Gefitinib |
| **Outcomes** | The outcome measures to be considered include:<br>• overall survival<br>• progression-free survival<br>• response rate<br>• adverse effects of treatment<br>• health-related quality of life. |

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| **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.<br><br>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.<br><br>Costs will be considered from an NHS and Personal Social Services perspective.<br><br>The availability of any patient access schemes for the intervention or comparator technologies should be taken into account. |
| **Other considerations** | Guidance will only be issued in accordance with the marketing authorisation. |
| **Related NICE recommendations and NICE Pathways** | Related Technology Appraisals:<br><br>'Afatinib for treating epidermal growth factor receptor mutation-positive locally advanced or metastatic non-small-cell lung cancer' (2014) NICE Technology Appraisal 310. Review date April 2017<br><br>'Erlotinib for the first-line treatment of locally advanced or metastatic EGFR-TK mutation-positive non-small-cell lung cancer' (2012) NICE Technology Appraisal 258. Guidance on static list<br><br>'Gefitinib for the first-line treatment of locally advanced or metastatic non-small-cell lung cancer' (2010) NICE Technology Appraisal 192. Guidance on static list<br><br>Terminated appraisals:<br><br>'Bevacizumab in addition to platinum-based chemotherapy for the first-line treatment of patients with unresectable advanced, metastatic or recurrent non-small-cell lung cancer (other than predominantly squamous cell histology)' (terminated appraisal) (2008). NICE Technology Appraisal 148.<br><br>Related Guidelines:<br><br>Lung Cancer: The diagnosis and treatment of lung cancer (2011). NICE guideline 121. Review date March 2016.<br><br>Related Quality Standards:<br><br>Quality standard for lung cancer. (2012). NICE Quality Standard No. 17<br><br>http://www.nice.org.uk/guidance/qualitystandards/quality |

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| | standards.jsp<br>Related NICE Pathways:<br>NICE Pathway: Lung cancer. Pathway created: March 2012. http://pathways.nice.org.uk/pathways/lung-cancer |
| **Related National Policy** | NHS England, Manual for prescribed specialised services, service 105: specialist cancer services (adults), Jan 2014. http://www.england.nhs.uk/wp-content/uploads/2014/01/pss-manual.pdf<br>Department of Health, NHS Outcomes Framework 2015-2016, Dec 2014. Domains 1, 2, 4 and 5. https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/385749/NHS_Outcomes_Framework.pdf<br>Independent Cancer Taskforce (2015) Achieving world-class cancer outcomes: a strategy for England 2015-2020<br>Department of Health (2014) Improving outcomes: a strategy for cancer, 4th annual report<br>Department of Health (2011) Improving outcomes: a strategy for cancer<br>Department of Health (2011) Cancer commissioning services |

**Questions for consultation**

Have all relevant comparators for bevacizumab been included in the scope?

Which treatments are considered to be established clinical practice in the NHS for first-line treatment of patients with advanced, metastatic or recurrent non-squamous non-small cell lung cancer with EGFR activating mutations?

Are the outcomes listed appropriate?

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

Where do you consider bevacizumab will fit into the existing NICE pathway, NICE Pathway: Lung cancer. Pathway created: March 2012.

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 bevacizumab 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 bevacizumab 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 bevacizumab 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/article/pmg19/chapter/1-Introduction)