**NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE**

**Health Technology Appraisal**

# Amivantamab for treating EGFR Exon 20 insertion-positive non-small-cell lung cancer after platinum-based chemotherapy

**Draft scope**

## Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of amivantamab within its marketing authorisation for treating EGFR Exon 20 insertion-positive non-small-cell lung cancer.

## Background

Lung cancer is the third most common cancer and the most common cause of cancer death in the UK, accounting for 13% of all new cancer cases and 21% of all cancer deaths in 2017.[1] There are around 48,000 new lung cancer cases and 35,000 deaths from lung cancer in the UK every year. Around 85% of lung cancers are non-small-cell lung cancers (NSCLC).[2]

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), and usually cannot be surgically removed. In 2017, 39,205 people were diagnosed with NSCLC in England & Wales, and around 65% had stage IIIB or stage IV disease[3]. For the majority of people with NSCLC, the aims of therapy are to prolong survival and improve quality of life. Treatment choices are influenced by the presence of biological markers (such as mutations in epidermal growth factor receptor-tyrosine kinase (EGFR-TK), anaplastic-lymphoma-kinase (ALK) or PD-L1 status), histology (squamous or non-squamous) and previous treatment experience.

An estimated 10% to 35% of people with NSCLC have mutations to the protein epidermal growth factor receptor (EGFR).[4] Exon 20 is part of the EGFR gene that can be mutated by an addition to the DNA sequence.

For people whose locally advanced or metastatic disease tests positive for the activating EGFR-TK mutation and who have not previously had treatment, NICE guidance recommends the tyrosine kinase inhibitors (TKIs) osimertinib, dacomitinib, afatinib, erlotinib, and gefitinib as treatment options (NICE technology appraisal guidance 654, 595, 310, 258, and 192 respectively).

Following disease progression with a TKI, osimertinib is available for EGFR T790M mutation-positive disease (NICE technology appraisal 653). Otherwise, atezolizumab in combination and pemetrexed with carboplatin or other platinum doublet chemotherapy are treatment options (NICE technology appraisal 584 and NICE guideline 121).

If disease continues to worsen after chemotherapy, atezolizumab, nintedanib with docetaxel or docetaxel monotherapy are treatment options (NICE technology appraisals 520, 347 and NICE guideline 121 respectively). Pembrolizumab and nivolumab (nivolumab is only available on the cancer drugs fund) are available for PD-L1 positive tumors (NICE technology appraisals 428, 484).

There are currently no available therapies that specifically target EGFR Exon 20 insertion mutations.

**The technology**

Amivantamab (brand name unknown, Janssen-Cilag) is a human bispecific antibody that targets both EGFR and hepatocyte growth factor receptor. Amivantamab is administered as an intravenous infusion.

Amivantamab does not have a marketing authorisation in the UK for the treatment of EGFR mutation-positive NSCLC. It is being studied in a phase 1 & 2 study to treat metastatic or unresectable EGFR mutation-positive NSCLC. The first part of this study is dose-finding. The second part of this study aims to examine amivantamab as a monotherapy and combined with lazertinib. The study included people with several EGFR mutations including the Exon20 insertion mutation.

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| **Intervention(s)** | Amivantamab alone or in combination with chemotherapy |
| **Population(s)** | Adults with EGFR Exon 20 insertion-positive non-small-cell lung cancer after previous platinum-based chemotherapy |
| **Comparators** | Established clinical management without amivantamab including but not limited to:<br>• atezolizumab<br>• nivolumab (subject to an ongoing NICE appraisal)<br>• pembrolizumab (for disease with PD-L1>1%)<br>• chemotherapy such as docetaxel alone or with nintedanib, pemetrexed and carboplatin |
| **Outcomes** | The outcome measures to be considered include:<br>• overall survival<br>• disease-free survival<br>• time to treatment discontinuation<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 commercial arrangements for the intervention, comparator and subsequent treatment technologies will be taken into account.<br><br>The use of amivantamab is conditional on the presence of an EGFR mutation. The economic modelling should include the costs associated with diagnostic testing for EGFR in people with NSCLC who would not otherwise have been tested. A sensitivity analysis should be provided without the cost of the diagnostic test. See section 5.9 of the Guide to the Methods of Technology Appraisals. |
| **Other considerations** | Guidance will only be issued in accordance with the marketing authorisation. Where the wording of the therapeutic indication does not include specific treatment combinations, guidance will be issued only in the context of the evidence that has underpinned the marketing authorisation granted by the regulator. |
| **Related NICE recommendations and NICE Pathways** | **Related Technology Appraisals:**<br><br>Atezolizumab for treating locally advanced or metastatic non-small-cell lung cancer after chemotherapy (2018) NICE technology appraisal guidance 520. Review date June 2021.<br><br>Nivolumab for previously treated non-squamous non-small-cell lung cancer. (2017) Technology appraisal guidance 484. Review in progress.<br><br>Pembrolizumab for treating PD-L1-positive non-small-cell lung cancer after chemotherapy. (2017) Technology appraisal guidance 428. Review date September 2020.<br><br>Nintedanib for previously treated locally advanced, metastatic, or locally recurrent non-small-cell lung cancer. (2015) NICE technology appraisal guidance 347.<br><br>**Appraisals in development (including suspended appraisals)**<br><br>Cimavax for treating wild-type EGFR-positive non-small-cell lung cancer NICE technology appraisals guidance [ID1259]. Publication date to be confirmed<br><br>**Related Guidelines:**<br><br>Lung cancer: diagnosis and management (2019) NICE |

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| | guideline 122<br>**Related Quality Standards:**<br>Lung cancer in adults (2012; updated 2019) Quality standard 17<br>**Related NICE Pathways:**<br>Treating non-small-cell lung cancer (2020) NICE pathway |
| **Related National Policy** | **National Service Frameworks:**<br>Cancer<br>**Department of Health:**<br>Department of Health, NHS Outcomes Framework 2016-2017<br>Department of Health (2014) The national cancer strategy: 4th annual report<br>Department of Health (2011) Improving outcomes: a strategy for cancer<br>Department of Health (2009) Cancer commissioning guidance<br>Department of Health (2007) Cancer reform strategy<br>The NHS Long Term Plan, 2019. NHS Long Term Plan<br>NHS England (2018/2019) NHS manual for prescribed specialist services (2018/2019) Chapter 105: Specialist cancer services (adults)<br>Department of Health and Social Care, NHS Outcomes Framework 2016-2017 (published 2016): Domains 1, 2, 4, 5.<br>https://www.gov.uk/government/publications/nhs-outcomes-framework-2016-to-2017<br>**Other policies**<br>Independent Cancer Taskforce (2015) Achieving world-class cancer outcomes: a strategy for England 2015-2020 |

**Questions for consultation**

Is the current treatment pathway for EGFR mutation-positive disease also used for EGFR Exon 20 insertion-positive NSCLC?

What current treatment is used for people with EGFR Exon 20 insertion-positive NSCLC after chemotherapy?

- Are atezolizumab or pembrolizumab used?
- Have all relevant comparators for amivantamab been included in the scope?

In clinical practice, is amivantamab likely to be used after previous platinum-based chemotherapy?

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

Where do you consider amivantamab will fit into the existing NICE pathway, Treating non-small-cell lung cancer?

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 amivantamab 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 amivantamab 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 amivantamab 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.

To help NICE prioritise topics for additional adoption support, do you consider that there will be any barriers to adoption of this technology into practice? If yes, please describe briefly.

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).

**References**

1. Lung cancer incidence. Cancer Research UK. Accessed November 2020.

2. Types of lung cancer. Cancer Research UK. Accessed November 2020.

3. NLCA annual report 2018. Accessed November 2020.

4. Osimertinib for EGFR-positive non-small cell lung cancer – adjuvant. NIHR Innovation Observatory Health Technology Briefing. November 2020.