# NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

## Health Technology Appraisal

## Alectinib for untreated anaplastic lymphoma kinase-positive advanced non-small-cell lung cancer

## Draft scope

### Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of alectinib within its marketing authorisation for untreated, anaplastic lymphoma kinase-positive (ALK-positive) advanced non-small-cell lung cancer.

### Background

Lung cancer falls into two main histological categories: non-small-cell lung cancers (NSCLC), which account for 85–90% of all lung cancers[1], and small-cell lung cancers. NSCLC may be grouped by tumour histology into squamous cell carcinoma, adenocarcinoma and large-cell carcinoma, with the latter 2 being collectively referred to as 'non-squamous' lung cancer.

Anaplastic lymphoma kinase (ALK) fusion genes are chromosomal alterations that occur between the tyrosine kinase portion of the ALK gene and other genes. They are believed to be involved in the growth of tumours. ALK translocation can occur in NSCLC of any histology, although it is thought to be most common in tumours with adenocarcinoma histology (that is, non-squamous histology) and is uncommon in tumours with squamous cell carcinoma histology.[2] People with NSCLC who have an ALK fusion gene are unlikely to have epidermal growth factor receptor (EGFR) mutations. Accordingly, people with the ALK fusion gene do not usually receive drugs that inhibit EGFR tyrosine kinase, such as erlotinib and gefitinib.

Most 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 2015, approximately 31,700 people were diagnosed with NSCLC in England, of whom 74% had stage III or stage IV disease[1]. Approximately 5% of people with stage III or IV NSCLC have ALK fusion genes, equating to around 1170 people in England.[3]

NICE clinical guideline 121 recommends platinum-based chemotherapy (cisplatin or carboplatin with either docetaxel, gemcitabine, paclitaxel, or vinorelbine) as a first-line treatment for people with stage III or IV NSCLC and good performance status. In current clinical practice, these combinations are used to treat squamous-cell NSCLC and not usually offered to people with non-squamous NSCLC. For non-squamous advanced NSCLC, NICE

technology appraisal guidance 181 recommends pemetrexed in combination with cisplatin. For non-squamous NSCLC that has not progressed immediately following initial therapy with a NICE-recommended platinum-based chemotherapy regimen, maintenance treatment with pemetrexed is recommended as an option (NICE technology appraisal guidance 190 and 402). For people with untreated ALK-positive advanced NSCLC, NICE technology appraisal guidance 406 recommends crizotinib as an option.

## The technology

Alectinib (Alecensa, Roche Products) selectively inhibits the ALK receptor tyrosine kinase and triggers tumour cell death. It is administered orally.

Alectinib does not currently have a marketing authorisation in the UK for untreated ALK-positive advanced NSCLC. It has been studied as monotherapy in clinical trials, compared with crizotinib, in adults with ALK-positive advanced, recurrent or metastatic NSCLC who have not had chemotherapy for their advanced disease.

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| **Intervention(s)** | Alectinib |
| **Population(s)** | People with untreated anaplastic lymphoma kinase-positive (ALK-positive) advanced non-small-cell lung cancer (NSCLC) |
| **Comparators** | • Crizotinib<br>• Pemetrexed in combination with a platinum drug (carboplatin or cisplatin) (for people with adenocarcinoma or large cell carcinoma only)<br>  ○ with or without pemetrexed maintenance treatment (following cisplatin-containing regimens only) |
| **Outcomes** | The outcome measures to be considered include:<br>• overall survival<br>• progression-free survival<br>• response rates<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>If the technology is likely to provide similar or greater health benefits at similar or lower cost than technologies recommended in published NICE technology appraisal guidance for the same indication, a cost-comparison may be carried out.<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 will be taken into account. |
| **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>Crizotinib for untreated anaplastic lymphoma kinase-positive advanced non-small-cell lung cancer (2016) NICE Technology Appraisal 406. Review date: September 2019<br><br>Pemetrexed for the first-line treatment of non-small-cell lung cancer (2009) NICE Technology Appraisal 181 Guidance on static list<br><br>Pemetrexed maintenance treatment for non-squamous non-small-cell lung cancer after pemetrexed and cisplatin (2016) NICE Technology Appraisal 402. Review proposal date August 2019<br><br>Pemetrexed for the maintenance treatment of non-small-cell lung cancer (2010) NICE Technology Appraisal 190. On static list<br><br>Terminated appraisals |

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| | Alectinib for previously treated anaplastic lymphoma kinase-positive advanced non-small-cell lung cancer (terminated appraisal) (2017) NICE Technology Appraisal 438.<br><br>Appraisals in development<br><br>Ceritinib for untreated anaplastic lymphoma kinase positive non-small-cell lung cancer NICE technology appraisals guidance [ID1117]. Publication expected April 2018.<br><br>Pembrolizumab with pemetrexed and platinum-based chemotherapy for untreated non-small-cell lung cancer [ID1173]. Publication date to be confirmed.<br><br>**Related Guidelines:**<br><br>Lung cancer: diagnosis and management. (2011) NICE guideline 121. Review date TBC.<br><br>**Related Quality Standards:**<br><br>Lung cancer in adults (2012) NICE quality standard 17<br><br>**Related NICE Pathways:**<br><br>Lung Cancer (2012) NICE pathway |
| **Related National Policy** | **National Service Frameworks**<br>Cancer<br><br>**Department of Health**<br><br>Department of Health (2011) Improving outcomes: a strategy for cancer<br><br>Department of Health (2009) Cancer commissioning guidance<br><br>Department of Health (2007) Cancer reform strategy<br><br>Department of Health, NHS Outcomes Framework 2016-2017 (published 2016): Domains 1, 2 4 and 5. https://www.gov.uk/government/publications/nhs-outcomes-framework-2016-to-2017<br><br>**NHS England**<br><br>NHS England (2016) Manual for Prescribed Specialised Services 2016/17. Chapter 105: Specialist cancer services (adults)<br><br>https://www.england.nhs.uk/commissioning/wp-content/uploads/sites/12/2016/06/pss-manual- |

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**Questions for consultation**

Are non-squamous tumours routinely tested for the ALK mutation in current NHS practice? Is the same test used throughout the NHS? Would a different test be used depending on the treatment being considered (that is, do alectinib and crizotinib have specific companion diagnostics)?

Would alectinib be used in people with ALK-positive **squamous** NSCLC?

Would alectinib be suitable for people who are unable to tolerate a platinum combination (for whom the NICE clinical guideline recommends single-agent chemotherapy with a third-generation chemotherapy drug)?

The NICE clinical guideline recommends platinum plus a third-generation drug (docetaxel, gemcitabine, paclitaxel, or vinorelbine) as first line treatment for advanced NSCLC. Are these combinations still used in clinical practice for untreated ALK-positive NSCLC? Are they used for squamous **and** non-squamous NSCLC?

Have all relevant comparators for alectinib been included in the scope? Which treatments are considered to be established clinical practice in the NHS for untreated ALK-positive non-small-cell lung cancer?

Are the outcomes listed appropriate?

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

Where do you consider alectinib will fit into the existing NICE pathway for 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 alectinib 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 alectinib 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 alectinib 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).

NICE has published an addendum to its guide to the methods of technology appraisal (available at https://www.nice.org.uk/Media/Default/About/what-we-do/NICE-guidance/NICE-technology-appraisals/methods-guide-addendum-cost-comparison.pdf), which states the methods to be used where a cost comparison case is made. We welcome comments on the appropriateness and suitability of the cost comparison methodology to this topic.

- Is the new technology likely to be similar in its clinical efficacy and resource use to any of the comparators?

- Is the primary outcome that was measured in the trial or used to drive the model for the comparator(s) still clinically relevant?

- Is there any substantial new evidence for the comparator technology/ies that has not been considered? Are there any important ongoing trials reporting in the next year?

## References

1 Royal College of Physicians (2017) National Lung Cancer Audit annual report 2016 (for the audit period 2015). Accessed July 2017

2 Scagliotti G, Stahel RA, Rosell R et al. (2012) ALK translocation and crizotinib in non-small cell lung cancer: An evolving paradigm in oncology drug development. European Journal of Cancer 48: 961-973

3 Cancer Research UK (2014) Biological therapy for lung cancer. Accessed July 2017