

**NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE****Single Technology Appraisal****Alectinib for untreated anaplastic lymphoma kinase-positive advanced non-small-cell lung cancer****Final scope****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<sup>1</sup>, 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.<sup>2</sup> 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<sup>1</sup>. Approximately 5% of people with stage III or IV NSCLC have ALK fusion genes, equating to around 1170 people in England.<sup>3</sup>

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.

<b>Intervention(s)</b>	Alectinib
<b>Population(s)</b>	Adults with untreated anaplastic lymphoma kinase-positive (ALK-positive) advanced non-small-cell lung cancer (NSCLC)
<b>Comparators</b>	Crizotinib
<b>Outcomes</b>	The outcome measures to be considered include: <ul style="list-style-type: none"> <li>• overall survival</li> <li>• progression-free survival</li> <li>• response rates</li> <li>• adverse effects of treatment</li> <li>• health-related quality of life.</li> </ul>

<p><b>Economic analysis</b></p>	<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>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.</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 will be taken into account.</p>
<p><b>Other considerations</b></p>	<p>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.</p>
<p><b>Related NICE recommendations and NICE Pathways</b></p>	<p><b>Related Technology Appraisals:</b></p> <p><a href="#">Crizotinib for untreated anaplastic lymphoma kinase-positive advanced non-small-cell lung cancer</a> (2016) NICE Technology Appraisal 406. Review date: September 2019</p> <p><a href="#">Pemetrexed for the first-line treatment of non-small-cell lung cancer</a> (2009) NICE Technology Appraisal 181 Guidance on static list</p> <p><a href="#">Pemetrexed maintenance treatment for non-squamous non-small-cell lung cancer after pemetrexed and cisplatin</a> (2016) NICE Technology Appraisal 402. Review proposal date August 2019</p> <p><a href="#">Pemetrexed for the maintenance treatment of non-small-cell lung cancer</a> (2010) NICE Technology Appraisal 190. On static list</p> <p>Terminated appraisals</p> <p><a href="#">Alectinib for previously treated anaplastic lymphoma kinase-positive advanced non-small-cell lung cancer (terminated appraisal)</a> (2017) NICE Technology</p>

	<p>Appraisal 438.</p> <p>Appraisals in development</p> <p><a href="#">Ceritinib for untreated anaplastic lymphoma kinase positive non-small-cell lung cancer NICE technology appraisals guidance [ID1117]</a>. Publication expected April 2018.</p> <p><a href="#">Pembrolizumab with pemetrexed and platinum-based chemotherapy for untreated non-small-cell lung cancer [ID1173]</a>. Publication date to be confirmed.</p> <p><b>Related Guidelines:</b></p> <p><a href="#">Lung cancer: diagnosis and management</a>. (2011) NICE guideline 121. Review date TBC.</p> <p><b>Related Quality Standards:</b></p> <p><a href="#">Lung cancer in adults</a> (2012) NICE quality standard 17</p> <p><b>Related NICE Pathways:</b></p> <p><a href="#">Lung Cancer</a> (2012) NICE pathway</p>
<p><b>Related National Policy</b></p>	<p><b>National Service Frameworks</b></p> <p><a href="#">Cancer</a></p> <p><b>Department of Health</b></p> <p>Department of Health (2011) <a href="#">Improving outcomes: a strategy for cancer</a></p> <p>Department of Health (2009) <a href="#">Cancer commissioning guidance</a></p> <p>Department of Health (2007) <a href="#">Cancer reform strategy</a></p> <p>Department of Health, NHS Outcomes Framework 2016-2017 (published 2016): Domains 1, 2 4 and 5. <a href="https://www.gov.uk/government/publications/nhs-outcomes-framework-2016-to-2017">https://www.gov.uk/government/publications/nhs-outcomes-framework-2016-to-2017</a></p> <p><b>NHS England</b></p> <p>NHS England (2016) Manual for Prescribed Specialised Services 2016/17. Chapter 105: Specialist cancer services (adults)</p> <p><a href="https://www.england.nhs.uk/commissioning/wp-content/uploads/sites/12/2016/06/pss-manual-may16.pdf">https://www.england.nhs.uk/commissioning/wp-content/uploads/sites/12/2016/06/pss-manual-may16.pdf</a></p>

**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