

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Single Technology Appraisal

Crizotinib 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 crizotinib within its marketing authorisation for previously untreated, anaplastic lymphoma kinase-positive (ALK-positive) advanced non-small cell lung cancer.

Background

Lung cancer falls into 2 histological categories: non-small-cell lung cancers, which account for 85–90% of all lung cancers, and small-cell lung cancers. Non-small-cell lung cancer 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. Some non-small-cell lung cancers are associated with chromosomal alterations described as anaplastic lymphoma kinase (ALK) fusion genes. ALK fusion genes 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 non-small cell lung cancer of any histology, although it is thought to be most common in tumours with adenocarcinoma histology and is uncommon in tumours with squamous cell carcinoma histology.¹

In England, there were 34,889 people newly diagnosed with lung cancer in 2011. Approximately 30% of people present with locally advanced disease (stage III; the cancer may have grown into the surrounding tissues and there may be cancer cells in the lymph nodes) and 40% with metastatic disease (stage IV; the cancer has spread to another part of the body).² It is estimated that approximately 3% of people with stage III or IV non-small-cell lung cancer have ALK fusion genes, equating to around 735 patients in England.³

For most people with non-small-cell lung cancer, the aim of treatment is to extend survival, and improve disease control and quality of life. NICE clinical guideline 121 recommends platinum-based chemotherapy as a first-line treatment for people with stage III or IV non-small-cell lung cancer and good performance status. For people with non-small-cell lung cancer of non-squamous tumour histology, NICE technology appraisal guidance 181 recommends pemetrexed in combination with cisplatin as an option for the first-line treatment of locally advanced or metastatic disease.

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The technology

Crizotinib (Xalkori, Pfizer) is a selective small-molecule inhibitor of the anaplastic lymphoma kinase receptor tyrosine kinase and its oncogenic variants (that is, ALK fusion events and selected ALK mutations). Crizotinib is administered orally.

The Committee for Medicinal Products for Human Use has recommended that a marketing authorisation should be granted for crizotinib for treating adults with previously untreated, ALK-positive, advanced non-small cell lung cancer.

Crizotinib has a marketing authorisation in the UK for the treatment of adults with previously treated, ALK-positive, advanced non-small cell lung cancer.

Intervention(s)	Crizotinib
Population(s)	People with untreated, anaplastic lymphoma kinase-positive (ALK-positive) advanced non-small cell lung cancer.
Comparators	<p>For people with non-squamous tumour histology:</p> <ul style="list-style-type: none">• Pemetrexed in combination with platinum chemotherapy (cisplatin or carboplatin) <p>For people with squamous tumour histology:</p> <ul style="list-style-type: none">• A third-generation drug (for example, gemcitabine or vinorelbine) in combination with platinum chemotherapy (cisplatin or carboplatin) <p>For people with non-squamous or squamous tumour histology for whom treatment with a platinum drug is not appropriate:</p> <ul style="list-style-type: none">• Single-agent chemotherapy with a third-generation drug (for example, gemcitabine or vinorelbine)
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.

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<p>Economic analysis</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>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 use of crizotinib is conditional on the presence of ALK mutation. The economic modelling should include the costs associated with diagnostic testing for ALK mutation in people with advanced non-small-cell lung cancer 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.</p>
<p>Other considerations</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>Related NICE recommendations and NICE Pathways</p>	<p>Related Technology Appraisals:</p> <p>‘Crizotinib for previously treated non-small-cell lung cancer associated with an anaplastic lymphoma kinase fusion gene’ (2013) NICE Technology Appraisal 296 Review date May 2016</p> <p>‘Pemetrexed for the first-line treatment of non-small-cell lung cancer’ (2009) NICE Technology Appraisal 181 Guidance on static list</p> <p>Appraisals in development:</p> <p>‘Ceritinib for previously treated anaplastic lymphoma kinase-positive non-small-cell lung cancer’ NICE technology appraisals guidance [ID729]. Publication expected January 2016</p> <p>Related Guidelines:</p> <p>‘Lung cancer: The diagnosis and treatment of lung cancer’ (2011) NICE guideline 121 Review date December 2015</p> <p>Related Quality Standards:</p>

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	<p>'Lung cancer for adults' (2012) NICE quality standard 17</p> <p>Related NICE Pathways:</p> <p>Lung Cancer (2012) NICE pathway</p>
Related National Policy	<p>National Service Frameworks</p> <p>Cancer</p> <p>Department of Health</p> <p>Department of Health (2011) Improving outcomes: a strategy for cancer</p> <p>Department of Health (2009) Cancer commissioning guidance</p> <p>Department of Health (2007) Cancer reform strategy</p> <p>NHS England (2014) Manual for Prescribed Specialised Services 2013/14. Chapter 105: Specialist cancer services (adults)</p> <p>http://www.england.nhs.uk/wp-content/uploads/2014/01/pss-manual.pdf</p> <p>Department of Health, NHS Outcomes Framework 2014-2015, Nov 2013. Domains 1,2, 4 and 5.</p> <p>https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/256456/NHS_outcomes.pdf</p>

References

- 1 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.
- 2 Cancer Research UK (2011) [Lung cancer statistics](#). Accessed March 2015.
- 3 Thomas A, Büttner R, Wolf J et al. (2013) Genomics-based classification of human lung tumors. *Science Translational Medicine* 5(209): 209ra153.