NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Proposed Health Technology Appraisal

Alectinib for previously treated anaplastic lymphoma kinase-positive non-small-cell lung cancer

Draft scope (pre-referral)

Draft remit/appraisal objective

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

Background

Lung cancer falls into two main histological categories: around 85–90% are non-small-cell lung cancers and the remainder are 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 two 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]

People with non-small-cell lung cancer who have an ALK fusion gene mutation are unlikely to have epidermal growth factor receptor (EGFR) mutations. ALK fusion genes are strongly associated with resistance to EGFR tyrosine kinase inhibitors such as erlotinib and gefitinib.

In England, there were 36,828 people newly diagnosed with lung cancer in 2013.[2] Approximately 20% 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 50% with metastatic disease (stage IV; the cancer has spread to another part of the body).[3] It is estimated that approximately 5% of people with stage III or IV non-small-cell lung cancer have ALK fusion genes, equating to around 925 patients in England.[4,5]

For most people with non-small-cell lung cancer, the aim of treatment is to improve survival, 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. In addition, NICE technology appraisal guidance 181 and 190 recommend pemetrexed as an option for the first-line treatment and

maintenance treatment of locally advanced or metastatic non-squamous non-small-cell lung cancer. If second-line treatment is appropriate for people with locally advanced or metastatic non-small-cell lung cancer in whom relapse has occurred after previous chemotherapy, docetaxel monotherapy should be considered (NICE clinical guideline 121). Crizotinib is not recommended in NICE technology appraisal guidance 296 for adults with previously treated AKL-positive advanced non-small-cell lung cancer but is available through the Cancer Drugs Fund for the second- or subsequent-line treatment of ALK-positive advanced or metastatic non-small-cell lung cancer after first-line treatment with combination chemotherapy. No treatment options are currently recommended by NICE after disease progression on second-line treatment.

The technology

Alectinib (Alecensa, Roche Products) selectively inhibits the ALK receptor tyrosine kinase. This has been found to induce the death of cancer cells harbouring ALK fusion genes. It is administered orally.

Alectinib does not currently have a marketing authorisation in the UK for previously treated anaplastic lymphoma kinase-positive (ALK-positive) advanced non-small-cell lung cancer. It is currently being studied in single arm clinical trials as monotherapy in people with ALK-positive metastatic or locally advanced non-small-cell lung cancer which has progressed after treatment with crizotinib. It is also being studied as monotherapy in people with ALK-positive metastatic or locally advanced non-small-cell lung cancer which has progressed after treatment with crizotinib compared with erlotinib in combination with alectinib for people with EGFR mutation.

Intervention(s)	Alectinib
Population(s)	People with anaplastic lymphoma kinase-positive (ALK-positive) advanced non-small-cell lung cancer previously treated with crizotinib
Comparators	Best supportive care
Outcomes	The outcome measures to be considered include: • overall survival • progression-free survival • response rate • adverse effects of treatment • health-related quality of life.

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. 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. Costs will be considered from an NHS and Personal Social Services perspective.
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: '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 'Nintedanib for previously treated locally advanced or metastatic non-small cell lung cancer' (2015) NICE Technology Appraisal 347 'Pemetrexed for the first-line treatment of non-small-cell lung cancer**'** (2009) NICE Technology appraisals guidance 181 Guidance on static list. Technology Appraisal in preparation: 'Ceritinib for previously treated anaplastic-lymphoma-kinase-positive non-small-cell lung cancer' ID729. Anticipated date of publication January 2016 Related Guidelines: Lung cancer: diagnosis and management. (2011) NICE guideline 121 Review date March 2016. Related Quality Standards: 'Lung cancer for adults' (2012) NICE quality standard 17 Related NICE Pathways: Lung Cancer (2012) NICE pathway
Related National Policy	**National Service Frameworks**

	Cancer **Department of Health** Department of Health (2013) NHS Outcomes Framework 2014–2015 Department of Health (2011) Improving outcomes: a strategy for cancer Department of Health (2009) Cancer commissioning guidance Department of Health (2007) Cancer reform strategy NHS England (2014) Manual for Prescribed Specialised Services 2013/14. Chapter 105: Specialist cancer services (adults) http://www.england.nhs.uk/wp-content/uploads/2014/01/pss-manual.pdf Department of Health, NHS Outcomes Framework 2014-2015, Nov 2013. Domains 1,2, 4 and 5. https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/256456/NHS_outcomes.pdf

Questions for consultation

Have all relevant comparators for alectinib been included in the scope? Which treatments are considered to be established clinical practice in the NHS for anaplastic lymphoma kinase-positive non-small-cell lung cancer previously treated with crizotinib?

How should best supportive care be defined?

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, 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.

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 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 National Cancer Intelligence Network (2015) Cancer breakdown by stage 2013. Accessed November 2015

3 Cancer Research UK (2015) Lung cancer statistics. Accessed October 2015

4 National Institute for Health and Clinical Excellence (2015) Ceritinib for previously treated anaplastic lymphoma kinase-positive non-small-cell lung cancer. Final scope. Accessed March 2015

5 Cancer Research UK (2014) Biological therapy for lung cancer. Accessed October 2015