NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Proposed Health Technology Appraisal

LDK378 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 LDK378 within its licensed indication for previously treated anaplastic lymphoma kinase-positive 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. 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). The prognosis for people with non-small-cell lung cancer is generally poor, with a 5-year survival rate of 9%.

Approximately 5% of people with stage III or IV non-small-cell lung cancer have chromosomal alterations described as anaplastic lymphoma kinase (ALK) fusion genes, which gives a total of 925 patients in England. ALK fusion genes occur between the tyrosine kinase portion of the ALK gene and other genes and are believed to be involved in the growth of tumours. 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.

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 advanced and 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 treatments are currently recommended by NICE after disease progression on a second-line therapy.

The technology

LDK378 (brand name unknown, Novartis) selectively inhibits the ALK receptor tyrosine kinase. This has been found to induce the death of the cancer cells harbouring ALK fusion genes. LDK378 is administered orally.

LDK378 does not currently have a UK marketing authorisation for previously treated ALK-positive non-small-cell lung cancer. It has been studied in single-arm clinical trials in adults with ALK-positive non-small-cell lung cancer previously treated with chemotherapy, and separately in adults previously treated with chemotherapy and crizotinib. It has also been studied compared with docetaxel and pemetrexed (both as monotherapy) in adults with ALK-positive advanced non-small-cell lung cancer previously treated with chemotherapy and crizotinib.

Intervention(s)	LDK378
Population(s)	People with previously treated anaplastic lymphoma kinase-positive (ALK-positive) non-small-cell lung cancer.
Comparators	For people with ALK-positive non-small-cell lung cancer who have received chemotherapy: • Docetaxel • Crizotinib • Best supportive care For people with ALK-positive non-small-cell lung cancer who have received chemotherapy and crizotinib: • Best supportive care
Outcomes	The outcome measures to be considered include: • overall survival • progression-free survival • overall 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. The implications of additional testing requirements should be considered.
Related NICE recommendations and NICE Pathways	Related Technology Appraisals: Technology Appraisal No. 296, September 2013, 'Crizotinib for previously treated non-small-cell lung cancer associated with an anaplastic lymphoma kinase fusion gene' Review Proposal Date May 2016. Technology Appraisal No. 124, August 2007, 'Pemetrexed for the treatment of non-small-cell lung' Guidance on static list. Technology Appraisal in Preparation, 'Nintedanib for previously treated locally advanced or metastatic non-small cell lung cancer' Earliest Anticipated Date of Publication April 2015. Related Guidelines: Clinical Guideline No. 121, April 2011, 'Lung cancer: The diagnosis and treatment of lung cancer' Review Proposal Date TBC. Related Quality Standards Quality Standard No. 17, March 2012, 'Lung cancer for adults' Review Proposal Date March 2017. Related NICE Pathways NICE Pathway: Lung Cancer, Pathway created: March 2012.
Related National Policy	**Manual for Prescribed Specialised Services** **National Service Frameworks**: Cancer **Department of Health documents**: Department of Health (2012) NHS Outcomes

	Framework 2013-2014 Department of Health (2011) Improving outcomes: a strategy for cancer Department of Health (2009) Cancer commissioning guidance Department of Health (2007) Cancer reform strategy

Questions for consultation

Have all relevant comparators for LDK378 been included in the scope? Which treatments are considered to be established clinical practice in the NHS for previously treated ALK-positive non-small-cell lung cancer?

How should best supportive care be defined?

Are there any subgroups of people in whom LDK378 is expected to be more clinically effective and cost effective or other groups that should be examined separately?

Where do you consider LDK378 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 LDK378 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 LDK378;
- 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 LDK378 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 LDK378 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 LDK378 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/aboutnice/howwework/devnicetech/technologyappraisalprocessguides/technology_appraisal_process_guides.jsp)