**NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE**

**Health Technology Appraisal**

# Lorlatinib for previously treated ALK-positive advanced non-small-cell lung cancer

**Final scope**

## Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of lorlatinib within its marketing authorisation for previously treated ALK-positive advanced non-small-cell lung cancer.

## Background

Lung cancer falls into 2 histological categories: around 88% are classified as non-small cell lung cancer (NSCLC), with the remaining patients classified as small cell lung cancer.[1] NSCLC may be further 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 (almost exclusively) with adenocarcinoma histology (that is, non-squamous histology) which represent 36% of NSCLC patients and is uncommon in tumours with squamous cell carcinoma histology[1,2].

In 2016, there were 38,381 (20,560 males and 17,821 females) cases of lung cancer registered in England[3]. Approximately 3% of people with NSCLC have ALK fusion genes[4].

For the majority of people with NSCLC, the aims of treatment are to prolong survival and improve quality of life. Treatment choices are influenced by the presence of biological markers (such as mutations in EGFR-TK, ALK or PD-L1 status, histology (squamous or non-squamous) and previous treatment experience. People with confirmed ALK-positive NSCLC are likely to be offered initial treatment with ALK-targeted treatment. People with NSCLC of an unknown ALK status may be offered initial treatment with chemotherapy. For adults with previously treated ALK-positive advanced NSCLC, NICE recommends crizotinib as a treatment option (NICE TA422). For adults with ALK-positive advanced NSCLC who have previously had crizotinib, NICE recommends ceritinib as an option (NICE TA395). NICE is also currently appraising brigatinib for treating ALK-positive NSCLC after crizotinib (NICE technology appraisal guidance ID1328). After therapy with ALK-targeted treatment, people who have not previously had chemotherapy may receive pemetrexed with a platinum-based chemotherapy. Atezolizumab is available as an option for adults with locally advanced or metastatic NSCLC who

have previously had chemotherapy and targeted ALK treatment (NICE TA520). Pembrolizumab is available as an option for treating locally advanced or metastatic PD-L1-NSCLC in adults who have had at least one chemotherapy and targeted ALK treatment (NICE TA428).

## The technology

Lorlatinib (Lorviqua, Pfizer) inhibits the ALK and ROS1 receptor tyrosine kinases, acting against a range of ALK resistant mutations. By inhibiting ALK phosphorylation and ROS1 activity, lorlatinib inhibits the downstream signalling, inducing cell death, which results in the inhibition of tumour cell growth. It is taken orally.

Lorlatinib does not currently have a marketing authorisation in the UK for ALK-positive NSCLC. It has been studied in clinical trials in patients with ALK-positive or ROS1-positive advanced NSCLC (in patients with and without central nervous system metastasis).

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| **Intervention(s)** | Lorlatinib |
| **Population(s)** | People with advanced ALK-positive NSCLC that has:<br>• been previously treated with crizotinib and at least one other ALK- tyrosine kinase inhibitor,<br>• or, has been previously treated with at least one ALK- tyrosine kinase inhibitor other than crizotinib. |
| **Comparators** | For people who have not had previous chemotherapy:<br>• Pemetrexed with cisplatin/carboplatin<br>For people who have had previous chemotherapy:<br>• Atezolizumab (for adults with locally advanced or metastatic NSCLC who have previously received chemotherapy and targeted ALK treatment)<br>• Pembrolizumab (for adults with locally advanced or metastatic PD-L1-NSCLC who have head at least one chemotherapy and targeted ALK treatment)<br>• Best supportive care. |

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| **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. |
| **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>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>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>Costs will be considered from an NHS and Personal Social Services perspective.<br>The availability of any commercial arrangements for the intervention, comparator and subsequent treatment technologies will be taken into account.<br>The use of lorlatinib is conditional on ALK status. The economic modelling should include the costs associated with diagnostic testing for ALK status in people with advanced NSCLC 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. |
| **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>Alectinib for untreated ALK-positive advanced non-small-cell lung cancer (2018) Technology Appraisal 536. Review date: August 2021. |

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| | Atezolizumab for treating locally advanced or metastatic non-small-cell lung cancer after chemotherapy (2018) Technology Appraisal 520. Review date: May 2021.<br><br>Ceritinib for previously treated anaplastic lymphoma kinase positive non-small-cell lung cancer (2016) Technology Appraisal 395. Review date: TBC.<br><br>Crizotinib for previously treated anaplastic lymphoma kinase-positive advanced non-small-cell lung cancer (2016) Technology Appraisal 422. Review date: December 2019.<br><br>Pembrolizumab for treating PD-L1-positive non-small-cell lung cancer after chemotherapy (2017) Technology Appraisal 428. Review date: January 2019.<br><br>Pemetrexed for the treatment of non-small-cell lung cancer (2007) Technology Appraisal 124. Review date: TBC.<br><br>Pemetrexed for the first-line treatment of non-small-cell lung cancer (2009) Technology Appraisal 181. Review date: TBC.<br><br>**Appraisals in development (including suspended appraisals):**<br><br>Brigatinib for treating ALK-positive non-small-cell lung cancer after crizotinib. NICE technology appraisal guidance [ID1328]. Publication expected: TBC<br><br>**Related Guidelines:**<br><br>Lung cancer: diagnosis and management (2011) NICE guidelines CG121. Updated expected: February 2019.<br><br>**Related Quality Standards**:<br><br>Quality standard for lung cancer. (2012) NICE Quality Standard 17. Reviewed 2016, next review August 2017.<br><br>**Related NICE Pathways:**<br><br>Lung cancer (2017) NICE |
| **Related National Policy** | **National Service Frameworks:**<br>Cancer<br><br>**Department of Health:**<br><br>Department of Health (2013) NHS Outcomes Framework 2014–2015<br><br>Department of Health (2011) Improving outcomes: a |

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| | 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 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<br><br>**NHS England:**<br><br>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 |

## References


1 Royal college of physicians (2018). National Lung Cancer Audit: Annual report 2017. Accessed September 2018.

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 Office for National Statistics (2018). Cancer registration statistics, England: first release, 2016. Accessed May 2018.

4 The Clinical Lung Cancer Genome Project (CLCGP) and Network Genomic Medicine (NGM) (2013). A Genomics-Based Classification of Human Lung Tumors. Science Translational Medicine 5: 209