NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Lorlatinib for untreated ALK-positive advanced non-small-cell lung cancer

Draft scope

Draft remit/appraisal objective

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

Background

Lung cancer falls into two main groups: around 80 to 85% are non-small-cell lung cancers (NSCLC) and the remainder are small cell lung cancers[1]. NSCLC can be further classified into squamous cell carcinoma and non-squamous cell carcinoma. Approximately 70% of NSCLC are of non-squamous histology and can be either large-cell undifferentiated carcinoma or adenocarcinoma[2]. 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 2018, 39,754 people were diagnosed with NSCLC in England & Wales. Of these people, 49% had stage IV disease and 12% had stage IIB/C[3].

Lung cancer caused over 35,000 deaths in the UK between 2016-2018[4]. Forty-five percent of people with lung cancer survive for more than 1 year after diagnosis[5].

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 (almost exclusively) in tumours with adenocarcinoma histology. Approximately 3–7% of all lung tumours contain ALK mutations[6].

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. NICE recommends crizotinib (TA406), ceritinib (TA500), alectinib (TA536) and brigatinib (TA670) as treatment options for adults with untreated ALK-positive advanced NSCLC. People with NSCLC of an unknown ALK status may be offered initial treatment with platinum-doublet chemotherapy.

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 untreated ALK-positive NSCLC. It has been studied in a clinical trial in adults with untreated ALK-positive NSCLC compared with crizotinib. Lorlatinib as monotherapy has marketing authorisation for the treatment of adults with ALK-positive advanced NSCLC that has been previously treated by other ALK-positive advanced tyrosine kinase inhibitors, including alectinib, ceritinib and crizotinib.

Intervention(s)	Lorlatinib
Population(s)	Adults with untreated ALK-positive advanced NSCLC
Comparators	• Alectinib • Brigatinib • Ceritinib • Crizotinib
Outcomes	The outcome measures to be considered include: • overall survival • progression-free survival • response rates • 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. 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. 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. The availability of any commercial arrangements for the intervention, comparator and subsequent treatment technologies will be taken into account. The availability of any managed access arrangement for the intervention will be taken into account.

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:** Brigatinib for ALK-positive advanced non-small-cell lung cancer that has not been previously treated with an ALK inhibitor (2021). NICE Technology Appraisal 607. Review date: 2024. Alectinib for untreated ALK-positive advanced non-small-cell lung cancer (2018). NICE Technology Appraisal 536. Review date: August 2021. Ceritinib for untreated ALK-positive non-small-cell-lung cancer (2018). NICE Technology Appraisal 500. Review date: January 2021. Crizotinib for untreated anaplastic lymphoma kinase- positive advanced non-small-cell lung cancer (2016). NICE Technology Appraisal 406. Review date: September 2019. **Terminated appraisals** None **Appraisals in development (including suspended appraisals)** None **Proposed appraisals** None **Related Guidelines:** Lung cancer: diagnosis and management (2019). NICE guideline 122. **Related Quality Standards:** Lung cancer in adults (2019). NICE Quality Standard 17. **Related NICE Pathways:** Lung cancer. Updated 2021. NICE pathway.
Related National Policy	The NHS Long Term Plan, 2019. NHS Long Term Plan NHS England (2018/2019) NHS manual for prescribed specialist services (2018/2019). Chapters 18 and 105. Department of Health and Social Care, NHS Outcomes Framework 2016-2017: Domains 1, 2 and 4. https://www.gov.uk/government/publications/nhs-outcomes-framework-2016-to-2017

Questions for consultation

Have all relevant comparators for lorlatinib been included in the scope?

Which treatments are considered to be established clinical practice in the NHS for untreated ALK-positive metastatic NSCLC?
Are the outcomes listed appropriate?

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

Where do you consider lorlatinib 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 lorlatinib 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 lorlatinib 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 lorlatinib 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.

To help NICE prioritise topics for additional adoption support, do you consider that there will be any barriers to adoption of this technology into practice? If yes, please describe briefly.

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).

NICE has published an addendum to its guide to the methods of technology appraisal (available at https://www.nice.org.uk/Media/Default/About/what-we-do/NICE-guidance/NICE-technology-appraisals/methods-guide-addendum-cost-comparison.pdf), which states the methods to be used where a cost comparison case is made.

- Would it be appropriate to use the cost comparison methodology for this topic?
- Is the new technology likely to be similar in its clinical efficacy and resource use to any of the comparators?
- Is the primary outcome that was measured in the trial or used to drive the model for the comparator(s) still clinically relevant?
- Is there any substantial new evidence for the comparator technology/ies that has not been considered? Are there any important ongoing trials reporting in the next year?

References

1 Types of lung cancer. Cancer Research UK. Accessed February 2021.

2 Howlader N, Noone AM, Krapcho M, Miller D, Brest A, Yu M, Ruhl J, Tatalovich Z, Mariotto A, Lewis DR, Chen HS, Feuer EJ, Cronin KA (eds). SEER Cancer Statistics Review, 1975-2016, National Cancer Institute. [Available from: https://seer.cancer.gov/csr/1975_2016/]. Accessed February 2021.

3 National Lung Cancer Audit annual report (for the audit period 2018) (2020). Royal College of Physicians. Accessed February 2021.

4 Lung cancer mortality statistics (2018). Cancer Research UK. Accessed February 2021.

5 Lung cancer survival statistics (2013 - 2017). Cancer Research UK. Accessed February 2021.

6 Zappa C, Mousa S (2016). Non-small cell lung cancer: current treatment and future advances. Translational Lung Cancer Research. Accessed February 2021.