NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Aumolertinib for untreated EGFR mutation-positive non-small-cell lung cancer

Draft scope

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of aumolertinib within its marketing authorisation for treating epidermal growth factor receptor (EGFR) mutation-positive metastatic non-small-cell lung cancer that has not previously been treated.

Background

Lung cancer falls into two main histological categories: around 88% 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 85% 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 3) or to other parts of the body (metastatic disease; stage 4).

In 2018, 21,878 people were diagnosed with NSCLC in England, and around 68% had stage 3 or 4 disease.[3] Around a third of people with lung cancer survive for more than 1 year after diagnosis, however this is reduced to around a fifth of people diagnosed at stage 4.[4]

For the majority of people with NSCLC, the aims of therapy are to prolong survival and improve quality of life. Treatment choices may be influenced by the presence of biological markers such as the checkpoint inhibitor programmed death-ligand 1 (PD-L1), mutations in EGFR or anaplastic-lymphoma-kinase (ALK), histology (squamous or non-squamous) and previous treatment experience.

For people whose locally advanced or metastatic disease tests positive for the EGFR mutation and who have not previously had treatment, NICE guidance recommends the tyrosine kinase inhibitors afatinib, dacomitinib, erlotinib, gefitinib, and osimertinib as treatment options (NICE technology appraisal guidance 310, 595, 258, 192, and 654 respectively).

The technology

Aumolertinib (brand name unknown, EQRx) is a small molecule inhibitor that targets mutant forms of EGFR. It prevents overactivation of the tyrosine kinase activity of the receptor and aids tumour cell death. It is administered orally.

Aumolertinib does not currently have a marketing authorisation in the UK for untreated advanced EGFR mutation-positive NSCLC. It has been studied in a clinical trial compared with gefitinib in people with locally advanced or metastatic EGFR mutation-positive NSCLC.

Intervention(s)	Aumolertinib
Population(s)	People with untreated locally advanced or metastatic NSCLC with EGFR activating mutation(s)
Comparators	• Afatinib • Dacomitinib • Erlotinib • Gefitinib • Osimertinib
Outcomes	The outcome measures to be considered include: • overall survival • progression-free survival • response rate • response duration • 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 or subsequent treatment technologies will be taken into account. The use of aumolertinib is conditional on the presence of EGFR mutation status. The economic modelling should include the costs associated with diagnostic testing for EGFR mutation in people with NSCLC who would not otherwise have been tested. If appropriate, 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** Gefitinib for the first-line treatment of locally advanced or metastatic non-small-cell lung cancer (2010) NICE Technology Appraisal 192. Guidance on static list. Erlotinib for the first-line treatment of locally advanced or metastatic EGFR-TK mutation-positive non-small-cell lung cancer (2012) NICE Technology Appraisal 258. Guidance on static list. Afatinib for treating epidermal growth factor receptor mutation-positive locally advanced or metastatic non-small-cell lung cancer (2014) NICE Technology Appraisal 310. Guidance on static list. Dacomitinib for untreated EGFR mutation-positive non-small-cell lung cancer (2019) NICE Technology Appraisal 595. Review date: 2022 Osimertinib for untreated EGFR mutation-positive non-small-cell lung cancer (2020). NICE Technology Appraisal 654. Review date: 2023 **Terminated appraisals** Bevacizumab for the treatment of non-small-cell lung cancer (terminated appraisal) (2008). NICE Technology Appraisal 148. Bevacizumab for treating EGFR mutation-positive non-small-cell lung cancer (terminated appraisal) (2017). NICE Technology Appraisal 436. Ramucirumab with erlotinib for untreated EGFR-positive metastatic non-small-cell lung cancer (terminated appraisal) (2020). NICE Technology Appraisal 635. **Appraisals in development (including suspended appraisals**) Sugemalimab with chemotherapy for untreated advanced non-small-cell lung cancer. Proposed NICE technology appraisal [ID4001]. Publication date to be confirmed. Osimertinib for adjuvant treatment of EGFR mutation-positive non-small-cell lung cancer after complete tumour resection. Proposed NICE technology appraisal [ID3835]. Publication date to be confirmed. Atezolizumab for adjuvant treatment of resected non-small-cell lung cancer. Proposed NICE technology appraisal

	[ID3852]. Publication expected July 2022. Atezolizumab with chemotherapy for neoadjuvant and adjuvant treatment of resectable non-small-cell lung cancer. Proposed NICE technology appraisal [ID3894]. Publication date to be confirmed. **Related Guidelines** Lung cancer: diagnosis and management (2019). NICE guideline 122. Review date to be confirmed. **Related Quality Standards** Lung cancer in adults (2019). NICE quality standard 17 **Related NICE Pathways** Treating non-small-cell lung cancer (2020) NICE pathway
Related National Policy	The NHS Long Term Plan, 2019. NHS Long Term Plan Independent Cancer Taskforce (2015) Achieving world-class cancer outcomes: a strategy for England 2015-2020 Department of Health (2014). Improving outcomes: a strategy for cancer, 4th annual report Department of Health and Social Care, NHS Outcomes Framework 2016-2017: Domains 1 and 4. https://www.gov.uk/government/publications/nhs-outcomes-framework-2016-to-2017

Questions for consultation

Have all relevant comparators for aumolertinib been included in the scope? Which treatments are considered to be established clinical practice in the NHS for EGFR-positive NSCLC?

Are the outcomes listed appropriate?

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

Is it common practice to test for EGFR mutation status in people with NSCLC, or would the adoption of aumolertinib require additional diagnostic tests to be undertaken?

Where do you consider aumolertinib 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 aumolertinib 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 aumolertinib 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 aumolertinib 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 Fast Track Appraisal (FTA) Process. We welcome comments on the appropriateness of appraising this topic through this process.

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 that has not been considered? Are there any important ongoing trials reporting in the next year?

References

1 National Lung Cancer Audit (2020). Royal College of Physicians. Accessed September 2021.

2 Non-small cell lung cancer treatment. National Cancer Institute. Accessed September 2021.

3 National Lung Cancer Audit: 2019 information sheet (for the audit period 2018) (2020). Royal College of Physicians. Accessed September 2021.

4 Lung cancer survival statistics (2010-11). Cancer Research UK. Accessed September 2021.