NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

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

Final scope

Remit/appraisal objective

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

Background

Lung cancer falls into 2 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. Around 85% of NSCLC cases 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). People with NSCLC can have either EGFR-positive or EGFR-negative lung cancer. NSCLC with EGFR activating mutations is considered to be a genetically distinct form of lung cancer which is most common in people with adenocarcinoma, non-smokers, people of Asian origin and females. Overexpression of EGFR has been detected in 10-15% of NSCLC.

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 most 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, anaplastic-lymphoma-kinase (ALK), receptor tyrosine kinase (ROS1) or KRAS, 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 gefitinib, erlotinib, afatinib, dacomitinib and osimertinib as treatment options (NICE technology appraisal guidance 192, 258, 310, 595 and 654 respectively).

The technology

Aumolertinib (brand name unknown, EQRx) is a small molecule inhibitor that selectively targets the sensitising (exon 19 deletions and exon 21 L858R point mutations) and T790M mutant forms of EGFR. It is administered orally.

Aumolertinib does not currently have a marketing authorisation in the UK for untreated EGFR mutation-positive NSCLC. It has been studied in a clinical trial compared with gefitinib in people with locally advanced or metastatic NSCLC with an exon 19 deletion or L858R EGFR mutation.

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.
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 to be confirmed. Osimertinib for untreated EGFR mutation-positive non-small-cell lung cancer (2020). NICE Technology Appraisal 654. Review date to be confirmed. **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**) 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. Pembrolizumab with platinum chemotherapy, pemetrexed

	and lenvatinib for untreated advanced non-squamous non-small-cell lung cancer. Proposed NICE technology appraisal [ID3985]. 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 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

References

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

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

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

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