# NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

## Single Technology Appraisal

## Osimertinib for untreated epidermal growth factor receptor (EGFR) mutation-positive non-small-cell lung cancer

## Final scope

### Remit/appraisal objective

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

### Background

Lung cancer falls into two main histological categories: around 85–90% are non-small-cell lung cancers (NSCLC) and the remainder are small-cell lung cancers. NSCLC can be further classified into 3 histological sub-types of large-cell undifferentiated carcinoma, squamous cell carcinoma and adenocarcinoma. The majority of 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 2015, around 33,000 people were estimated to be diagnosed with NSCLC in England.[1,2] Around 12% have stage IIIA, 9% had stage IIIB and 53% had stage IV disease[1]. The prognosis for people with non-small-cell lung cancer is generally poor. Between 2011 and 2015 around 39% of people with lung cancer survived for 1 year or longer and only 15% survived for 5 years or longer.[2]

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] and mutations in epidermal growth factor receptor-tyrosine kinase [EGFR-TK] or anaplastic-lymphoma-kinase [ALK], or), histology (squamous or non-squamous) and previous treatment experience.

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

## The technology

Osimertinib (Tagrisso, AstraZeneca) is a small molecule inhibitor that targets the sensitising and T790M mutant forms of the EGFR-TK. It is administered orally.

Osimertinib 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 or erlotinib in patients with locally advanced or metastatic EGFR mutation-positive (Ex19del or L858R) NSCLC who have not received prior treatment.

Osimertinib has a marketing authorisation in the UK for treating locally advanced or metastatic, EGFR T790M mutation positive NSCLC. NICE technology appraisal guidance 416 recommends osimertinib as an option for use within the Cancer Drugs Fund for locally advanced or metastatic, EGFR T790M mutation positive NSCLC whose disease has progressed only after first-line treatment with an EGFR tyrosine kinase inhibitor and if the conditions in the managed access agreement for osimertinib are followed.

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| **Intervention** | Osimertinib |
| **Population** | People with previously untreated locally advanced or metastatic, EGFR mutation-positive non-small-cell lung cancer |
| **Comparators** | • Afatinib<br>• Erlotinib<br>• Gefitinib |
| **Outcomes** | The outcome measures to be considered include:<br>• overall survival<br>• progression-free survival<br>• response rate<br>• response duration<br>• adverse effects of treatment<br>• health-related quality of life. |

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| **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><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><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><br>Costs will be considered from an NHS and Personal Social Services perspective.<br><br>The availability of any patient access schemes for the intervention or comparator technologies will be taken into account.<br><br>The use of osimertinib 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. 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><br>'Afatinib for treating epidermal growth factor receptor mutation-positive locally advanced or metastatic non-small-cell lung cancer' (2014) NICE Technology Appraisal 310. Review proposal in progress.<br><br>'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. Review proposal in progress.<br><br>'Gefitinib for the first-line treatment of locally advanced or metastatic non-small-cell lung cancer' (2010) NICE |

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| | Technology Appraisal 192. Guidance on static list. Review proposal in progress.<br><br>'Osimertinib for treating locally advanced or metastatic EGFR T790M mutation-positive non-small-cell lung cancer' (2016) NICE Technology Appraisal 416. Review date March 2019.<br><br>**Terminated appraisals:**<br><br>'Bevacizumab for treating EGFR mutation-positive non-small-cell lung cancer' (terminated appraisal) (2017) NICE technology appraisal guidance 436<br><br>**Related Guidelines:**<br><br>Lung Cancer: The diagnosis and treatment of lung cancer (2011). NICE guideline 121. Review ongoing.<br><br>**Guidelines in development**<br><br>'Lung cancer: diagnosis and management (update)'. Publication expected January 2019.<br><br>**Related Quality Standards:**<br><br>Quality standard for lung cancer. (2012). NICE Quality Standard No. 17<br><br>http://www.nice.org.uk/guidance/qualitystandards/qualitystandards.jsp<br><br>**Related NICE Pathways:**<br><br>NICE Pathway: Lung cancer. Pathway created: March 2012. http://pathways.nice.org.uk/pathways/lung-cancer |
| **Related National Policy** | NHS England, Manual for prescribed specialised services, service 105: specialist cancer services (adults), Jan 2014. http://www.england.nhs.uk/wp-content/uploads/2014/01/pss-manual.pdf<br><br>Department of Health, NHS Outcomes Framework 2015-2016, Dec 2014. Domains 1, 2, 4 and 5. https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/385749/NHS_Outcomes_Framework.pdf<br><br>Independent Cancer Taskforce (2015) Achieving world-class cancer outcomes: a strategy for England 2015-2020<br><br>Department of Health (2014) Improving outcomes: a strategy for cancer, 4th annual report<br><br>Department of Health (2011) Improving outcomes: a |

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| | strategy for cancer<br>Department of Health (2011) Cancer commissioning services |

## References

1 National lung cancer audit 2016 (2017). Royal college of Physicians. Accessed October 2017.

2 Cancer survival in England: adult, stage at diagnosis and childhood-patients followed up to 2016 (2017) Office for National Statistics. Accessed October 2017