NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

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

Draft scope

Draft 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.

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.

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Osimertinib</th>
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<tbody>
<tr>
<td>Population</td>
<td>People with locally advanced or metastatic, EGFR mutation-positive non-small-cell lung cancer</td>
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<tr>
<td>Comparators</td>
<td>• Afatinib</td>
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<td></td>
<td>• Erlotinib</td>
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<td></td>
<td>• Gefitinib</td>
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<td>Outcomes</td>
<td>The outcome measures to be considered include:</td>
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<td>• overall survival</td>
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<td>• progression-free survival</td>
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<td>• response rate</td>
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<td>• adverse effects of treatment</td>
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<td>• health-related quality of life.</td>
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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.

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 patient access schemes for the intervention or comparator technologies will be taken into account.

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:**


Appendix B

Review proposal in progress.

**Terminated appraisals:**

NICE technology appraisal guidance 436

**Related Guidelines:**


**Guidelines in development**


**Related Quality Standards:**


[http://www.nice.org.uk/guidance/qualitystandards/qualitystandards.jsp](http://www.nice.org.uk/guidance/qualitystandards/qualitystandards.jsp)

**Related NICE Pathways:**


**Related National Policy**


Questions for consultation

Which treatments are considered to be established clinical practice in the NHS for untreated advanced, metastatic or recurrent non-squamous non-small cell lung cancer with EGFR activating mutations?

Is osimertinib expected to be used in non-small-cell lung cancers with activating mutations of EGFR other than Ex19del and L858R?

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

Are the outcomes listed appropriate?

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

Where do you consider osimertinib 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 osimertinib 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 osimertinib 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 osimertinib 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 technologies that has not been considered? Are there any important ongoing trials reporting in the next year?

References