

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Evaluation

Osimertinib with pemetrexed and platinum-based chemotherapy for untreated EGFR mutation-positive advanced non-small-cell lung cancer ID6328

Draft scope

Draft remit/evaluation objective

To appraise the clinical and cost effectiveness of osimertinib with pemetrexed and platinum-based chemotherapy within its marketing authorisation for treating untreated EGFR mutation-positive advanced non-small-cell lung cancer.

Background

Lung cancer falls into 2 main histological categories: around 80 to 85% are non-small-cell lung cancers (NSCLC) and the remainder are small-cell lung cancers.¹ The 3 main subtypes of NSCLC are adenocarcinoma, large-cell (undifferentiated) carcinoma and squamous cell carcinoma.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), and usually cannot be surgically removed.³ Epidermal growth factor receptor (EGFR) is a protein found on the surface of cells that is involved in the regulation of cell proliferation. EGFR includes a tyrosine kinase domain which when activated initiates signalling pathways for cell growth and division.⁴ Some NSCLC tumours are caused by mutations in the tyrosine kinase domain of the EGFR gene.

In 2018, around 34,627 cases of NSCLC were diagnosed in England and 57% were diagnosed with advanced disease.⁵ Around 15% of advanced NSCLC tumours have EGFR mutations.⁶

Treatment depends on the location and stage of the cancer. The treatment pathway for NSCLC can be divided into interconnected decision points based on the number staging system and line of therapy. Treatment choices are influenced by the presence of biological markers (including mutations in EGFR-tyrosine kinase), oncogenic driver genetic alterations, histology (squamous or non-squamous) and previous treatment. [NICE's Technology Appraisal Pathway Pilot scope for treatments for non-small-cell lung cancer](#) outlines in more detail the full NSCLC treatment pathway.

For previously untreated advanced NSCLC which tests positive for the activating EGFR-tyrosine kinase mutation, [NICE guideline 122 Lung cancer: diagnosis and management](#) recommends platinum-based doublet chemotherapy or treatment with a tyrosine kinase inhibitor. NICE technology appraisal (TA) guidance recommends the tyrosine kinase inhibitors osimertinib ([TA654](#)), dacomitinib ([TA595](#)), afatinib ([TA310](#)), erlotinib ([TA258](#)) and gefitinib ([TA192](#)) as treatment options for untreated advanced EGFR mutation-positive NSCLC. Acquired resistance to tyrosine kinase inhibitors may develop in EGFR mutation-positive NSCLC and can limit the efficacy of treatment.⁷

The technology

Osimertinib (Tagrisso, AstraZeneca) with pemetrexed and platinum-based chemotherapy does not have a marketing authorisation in the UK for untreated EGFR mutation-positive NSCLC. It has been studied in a clinical trial compared with osimertinib alone in adults with untreated locally advanced or metastatic EGFR mutation-positive NSCLC. Osimertinib as monotherapy is currently licensed in the UK for the following related indications:

- stage 1B to 3A NSCLC tumours with EGFR exon 19 deletions or exon 21 substitution mutations (after complete tumour resection)
- untreated locally advanced or metastatic NSCLC with activating EGFR mutations
- locally advanced or metastatic EGFR T790M mutation-positive NSCLC.

Intervention	Osimertinib with pemetrexed and platinum-based chemotherapy
Population	Adults with untreated advanced EGFR mutation-positive NSCLC
Subgroups	If the evidence allows the following subgroups will be considered: <ul style="list-style-type: none"> • NSCLC stage and • tumour histology (non-squamous or mixed histology)
Comparators	Established clinical management without osimertinib with pemetrexed and platinum-based chemotherapy including: <ul style="list-style-type: none"> • Platinum-based doublet chemotherapy (such as pemetrexed with cisplatin) • Osimertinib • Dacomitinib • Afatinib • Erlotinib • Gefitinib
Outcomes	The outcome measures to be considered include: <ul style="list-style-type: none"> • overall survival • progression-free survival • response rates • duration of response • time to treatment discontinuation • adverse effects of treatment • health-related quality of life.

<p>Economic analysis</p>	<p>The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year.</p> <p>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.</p> <p>Costs will be considered from an NHS and Personal Social Services perspective.</p> <p>The availability of any commercial arrangements for the intervention, comparator and subsequent treatment technologies will be taken into account.</p> <p>The availability and cost of biosimilar and generic products should be taken into account.</p> <p>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 advanced NSCLC who would not otherwise have been tested. A sensitivity analysis should be provided without the cost of the diagnostic test. See section 4.8 of the guidance development manual (available here: https://www.nice.org.uk/process/pmg36/chapter/introduction-to-health-technology-evaluation).</p>
<p>Other considerations</p>	<p>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.</p>
<p>Related NICE recommendations</p>	<p>Related technology appraisals:</p> <p>Osimertinib for untreated EGFR mutation-positive non-small-cell lung cancer (2020) NICE technology appraisal guidance 654</p> <p>Dacomitinib for untreated EGFR mutation-positive non-small-cell lung cancer (2019) NICE technology appraisal guidance 595</p> <p>Afatinib for treating epidermal growth factor receptor mutation-positive locally advanced or metastatic non-small-cell lung cancer (2014) NICE technology appraisal guidance 310</p> <p>Erlotinib for the first-line treatment of locally advanced or metastatic EGFR-TK mutation-positive non-small-cell lung cancer (2012) NICE technology appraisal guidance 258</p>

	<p>Gefitinib for the first-line treatment of locally advanced or metastatic non-small-cell lung cancer (2010) NICE technology appraisal guidance 192</p> <p>Related NICE guidelines:</p> <p>Lung cancer: diagnosis and management (2019; updated 2023) NICE guideline 122</p> <p>Related interventional procedures:</p> <p>Photodynamic therapy for advanced bronchial carcinoma (2004) NICE interventional procedures guidance 87</p> <p>Related quality standards:</p> <p>Lung cancer in adults (2012; updated 2019) NICE quality standard 17</p>
Related National Policy	<p>NHS Digital (2022) NHS Outcomes Framework Indicators</p> <p>The NHS Long Term Plan (2019) NHS Long Term Plan</p> <p>NHS England (2023) NHS manual for prescribed specialist services. Chapter 105: Specialist cancer services (adults)</p>

Questions for consultation

Where do you consider osimertinib with pemetrexed and platinum-based chemotherapy will fit into the existing care pathway for advanced EGFR mutation-positive NSCLC?

Is platinum-based doublet chemotherapy used in NHS clinical practice for untreated advanced EGFR mutation-positive NSCLC? If so, does this usually consist of pemetrexed with cisplatin or are other chemotherapy combinations used?

Within the population under consideration, should people with newly diagnosed versus recurrent disease be considered separately?

Would the population who would be eligible for osimertinib with pemetrexed and platinum-based chemotherapy in NHS clinical practice be those with only non-squamous NSCLC?

Would osimertinib with pemetrexed and platinum-based chemotherapy be a candidate for managed access?

Do you consider that the use of osimertinib with pemetrexed and platinum-based chemotherapy can result in any potential 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 committee to take account of these benefits.

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 with pemetrexed and platinum-based chemotherapy 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.

NICE intends to evaluate this technology through its Single Technology Appraisal process. (Information on NICE's health technology evaluation processes is available at <https://www.nice.org.uk/about/what-we-do/our-programmes/nice-guidance/nice-technology-appraisal-guidance/changes-to-health-technology-evaluation>).

References

1. Cancer Research UK. [Types of lung cancer](#). Accessed September 2023.
2. ESMO. [Non-Small-Cell Lung Cancer: A Guide for Patients](#). Accessed September 2023.
3. NHS Digital. [Cancer Registration Statistics, England 2020 - Cancer incidence by stage](#). Accessed September 2023.
4. Ayati A, Moghimi S et al (2020). [A review on progression of epidermal growth factor receptor \(EGFR\) inhibitors as an efficient approach in cancer targeted therapy](#). Accessed September 2023.
5. NHS Digital. [NICE Technology Appraisals in the NHS in England \(Innovation Scorecard\) to December 2021 – Estimates Report](#). Accessed September 2023.
6. Van Sanden S, Murton M et al (2022). [Prevalence of Epidermal Growth Factor Receptor Exon 20 Insertion Mutations in Non-small-Cell Lung Cancer in Europe: A Pragmatic Literature Review and Meta-analysis](#). Accessed September 2023
7. Laurila N, Koivunen, J.P (2015). [EGFR inhibitor and chemotherapy combinations for acquired TKI resistance in EGFR-mutant NSCLC models](#). Accessed September 2023.