# NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE
## Health Technology Evaluation

## Zongertinib for treating HER2-mutated unresectable or metastatic non-small-cell lung cancer ID6573

## Draft scope

### Draft remit/evaluation objective

To appraise the clinical and cost effectiveness of zongertinib within its marketing authorisation for treating HER2-mutated unresectable advanced or metastatic non-small-cell lung cancer.

### Background

In 2023, lung cancer was the third most common diagnosed cancer in England and it was the most common cause of cancer death for men and women in England.[1] There were around 42,082 new lung cancer cases diagnosed and 26,052 deaths from lung cancer in England in 2023.[1] In 2023, 92% of people diagnosed with lung cancer had non-small-cell lung cancer (NSCLC).[1] NSCLC is divided into squamous and non-squamous cell carcinoma.

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 2023, 8.4% had stage 3B or 3C and 43% had stage 4 lung cancer.[2] Around 15% of people with stage 3 lung cancer will survive for 5 years or more after they are diagnosed and for stage 4 lung cancer this is around 5%.[3] It is estimated that approximately 2-4% of people with NSCLC will have HER2-positive tumours and these alterations are associated with a worse prognosis.[4]

As a result of the targeted NHS Lung Health Check programme, which is being rolled out in the UK, it is expected that lung cancer will increasingly be diagnosed at an earlier stage, when treatment may be more successful.

Current clinical management for unresectable advanced or metastatic (stage 3 or 4) NSCLC aims to control the cancer for as long as possible and help with symptoms. Treatment choices are based on cancer stage and line of treatment. They also depend on the presence of biological markers (including PD-L1 status), oncogenic driver genetic alterations, histology (squamous or non-squamous) and ECOG performance status.

There are currently no licensed targeted treatments for people with HER2-positive NSCLC. NICE's Lung cancer: diagnosis and management guideline recommends several options for people with unresectable advanced or metastatic non-small-cell lung cancer. These include but are not limited to pembrolizumab with pemetrexed and platinum-based chemotherapy for adults whose tumours do not harbour EGFR-positive or ALK-positive mutations (TA683) and platinum doublet chemotherapy, pemetrexed and carboplatin or pemetrexed with cisplatin (TA181) only if the the tumour is adenocarcinoma or large-cell carcinoma. In some cases, patients may instead receive best supportive care.

## The technology

Zongertinib (brand name unknown, Boehringer Ingelheim) does not currently have a marketing authorisation in the UK for HER2-mutated unresectable or metastatic non-small-cell-lung cancer. It is being studied in a phase 3 clinical trial compared to pembrolizumab in combination with pemetrexed and platinum based chemotherapy in adults with HER2-mutated untreated unresectable or metastatic non-squmous non-small-cell-lung cancer.

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| **Intervention(s)** | Zongertinib |
| **Population(s)** | Adults with HER2-mutated unresectable or metastatic non-small-cell lung cancer |
| **Subgroups** | If the evidence allows, the following subgroups will be considered:<br>• disease stage<br>• previous treatments had at any stage<br>• type of HER2 mutation (for example, inside or outside the tyrosine kinase domain)<br>• histology (non-squamous or squamous) |
| **Comparators** | • pembrolizumab with pemetrexed and platinum based chemotherapy<br>• pemetrexed in combination with platinum based chemotherapy (carboplatin or cisplatin) (for people with adenocarcinoma or large-cell carcinoma only)<br>• pembrolizumab monotherapy<br>• atezolizumab monotherapy<br>• atezolizumab plus bevacizumab, carboplatin and paclitaxel<br>• Trastuzumab deruxtecan (subject-to-NICE evaluation)<br>• Sevabertinib (subject-to-NICE-evaluation)<br>• best supportive care |
| **Outcomes** | The outcome measures to be considered include:<br>• overall survival<br>• progression-free survival<br>• response rates<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>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 commercial arrangements for the intervention, comparator and subsequent treatment technologies will be taken into account.<br><br>The availability and cost of biosimilar and generic products should be taken into account.<br><br>The use of zongertinib is conditional on the presence of a HER2 mutation. The economic modelling should include the costs associated with diagnostic testing for HER2 in people with non-squamous unresectable or metastatic non-small-cell lung cancer 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) |
| **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** | **Related technology appraisals:**<br><br>Pembrolizumab with pemetrexed and platinum chemotherapy for untreated, metastatic, non-squamous non-small-cell lung cancer (2021) NICE technology appraisal guidance 683.<br><br>Atezolizumab in combination for treating metastatic non-squamous non-small-cell lung cancer (2019) NICE technology appraisal guidance 584.<br><br>Pemetrexed for the first-line treatment of non-small-cell lung cancer (2009) NICE technology appraisal guidance 181.<br><br>**Related NICE guidelines:**<br><br>Lung cancer: diagnosis and management (2019, updated 2024) NICE guideline NG122.<br><br>**Related quality standards:** |

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| | Lung cancer in adults (2012, updated 2019) NICE quality standard 17. |

**Questions for consultation**

Which ICD-10 codes most accurately define the scope population?

Are NSCLC cases in the NHS currently tested for HER2 mutations?

If not, would implementing HER2 mutation testing require a new unit of testing activity. That is, are there people not currently having a genomic test in NHS practice who would need one were zongertinib recommended, or could the HER2 test be added to a panel that is already being carried out?

Where do you consider zongertinib will fit into the existing care pathway for unresectable advanced or metastatic non-squamous NSCLC?

Are the comparators listed appropriate, should any be added, or removed? A comparator is anything that might be displaced by zongertinib if it is recommended.

Could you estimate the proportions of the population which HER2 mutation positive NSCLC that are having each of the comparators?

Would there be any people who currently have best-supportive care but who might have zongertinib were it recommended?

Are the subgroups listed appropriate, should any be added, or removed?

Would zongertinib be a candidate for managed access?

Please outline the clinical trial evidence that could inform this appraisal

(Please specify primary codes and any secondary codes commonly used in NHS practice for this cancer type.)

Are there any concerns about the generalisability of the pivotal trial and/or comparator evidence to the NHS population or NHS treatment pathways?

Would real-world evidence (RWE) or SACT data add value to the evaluation of this technology, if so, how?

Do you consider that the use of zongertinib 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 zongertinib 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. NHS Digital Cancer registration statistics in England 2023 [Accessed April 2026]

2. National Lung Cancer Audit State of the Nation 2025 report [Accessed April 2026]

3. Cancer Research UK Survival for lung cancer [Accessed April 2026]

4. Nutzinger, J, lee, J, B, Low, J, L, Chai, P, L, Wijaya, S, T, Cho, B, C, Lim, S, M, Soo, R, A (2023) Management of HER2 alterations in non-call-cell lung cancer: The past, present, and future. Lung cancer 186