

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]

Response to stakeholder organisation comments on the draft remit and draft scope

Please note: Comments received in the course of consultations carried out by NICE are published in the interests of openness and transparency, and to promote understanding of how recommendations are developed. The comments are published as a record of the submissions that NICE has received, and are not endorsed by NICE, its officers or advisory committees.

Comment 1: the draft remit and proposed process

Section	Stakeholder	Comments [sic]	Action
Appropriateness of an evaluation and proposed evaluation route	AstraZeneca	No comments.	No action required.
	British Thoracic Oncology Group	N/a	No action required.
Wording	AstraZeneca	The wording reflects the issues regarding this technology.	Thank you for your comment. No action required.
	British Thoracic Oncology Group	Yes	Thank you for your comment. No action required.
Timing issues	AstraZeneca	Although osimertinib monotherapy is available to patients with untreated advanced epidermal growth factor receptor mutation-positive (EGFRm) non-	Thank you for your comment. NICE has

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		small-cell lung cancer (NSCLC) and represents standard of care, there remains an unmet need for improved clinical outcomes in these patients.	scheduled this topic into its work programme and aims to provide draft guidance to the NHS as soon as possible after marketing authorisation. No action required.
	British Thoracic Oncology Group	Clinically urgent as impacts on treatment options for newly diagnosed lung cancer patients	Thank you for your comment. NICE has scheduled this topic into its work programme and aims to provide draft guidance to the NHS as soon as possible after marketing authorisation. No action required.
Additional comments on the draft remit	AstraZeneca	No comments provided.	No action required.
	British Thoracic Oncology Group	No comments provided.	No action required.

Comment 2: the draft scope

Section	Consultee/ Commentator	Comments [sic]	Action
	AstraZeneca	No comments.	No action required.

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Background information	British Thoracic Oncology Group	No concerns	Thank you for your comment. No action required.
Population	AstraZeneca	The population is defined appropriately.	Thank you for your comment. No action required.
	British Thoracic Oncology Group	Yes	Thank you for your comment. No action required.
Subgroups	AstraZeneca	<p>The FLAURA2 trial demonstrated consistent efficacy across subgroups.¹ Ninety-five percent of the FLAURA2 trial population is metastatic therefore, subgroup analyses by disease stage, as proposed in the draft scope, are not considered appropriate. Additionally, the trial is not powered for tumour histology subgroups.</p> <p><u>References</u></p> <ol style="list-style-type: none"> Jänne PA, Planchard D, Cheng Y, et al. (2023) Osimertinib with/without platinum-based chemotherapy as first-line treatment in patients with EGFRm advanced NSCLC (FLAURA2) [oral presentation]. Poster presented at World Conference on Lung Cancer (WCLC), 9-12 September, 2023, Singapore 	Thank you for your comments. The scope has been updated to remove specific reference to NSCLC stage and tumour histology subgroups. If evidence allows, results for relevant subgroups will be considered by the committee during the appraisal.
	British Thoracic Oncology Group	n/a	No action required.

Section	Consultee/ Commentator	Comments [sic]	Action
Comparators	AstraZeneca	<p>Osimertinib is a third-generation epidermal growth factor receptor (EGFR) tyrosine kinase inhibitors (TKIs) and is current standard of care for untreated advanced EGFRm NSCLC (TA654).² Osimertinib monotherapy is currently used as frontline treatment in █████ of EGFRm patients.³</p> <p>Alternative treatments recommended by NICE include first- (erlotinib, gefitinib) and second-generation (afatinib, dacomitinib) EGFR TKIs, but since the recommendation of osimertinib monotherapy for untreated locally advanced or metastatic EGFRm patients (TA654), these therapies are rarely used.³⁻⁷ Clinical experts consulted for TA654 stated that osimertinib was better tolerated and offered fewer side effects compared to existing treatments at the time.²</p> <p>Platinum-based doublet chemotherapy (such as pemetrexed with cisplatin) is the only non-EGFR-TKI treatment recommended by NICE for this population but is only used if the patient is unsuitable for an EGFR-TKI and thus, is not a relevant comparator in the decision problem.⁸</p> <p>Given the above, osimertinib monotherapy is the only relevant comparator for osimertinib with pemetrexed and platinum-based chemotherapy.</p> <p><u>References</u></p> <ol style="list-style-type: none"> 2. AstraZeneca. Data on File (Internal Market Share Data). 2023 3. National Institute for Health and Care Excellence (NICE). Osimertinib for untreated EGFR mutation-positive non-small-cell lung cancer [TA654]. Available at: https://www.nice.org.uk/guidance/ta654 (last accessed 10 Nov 2023). 4. National Institute for Health and Care Excellence (NICE) Erlotinib for the first-line treatment of locally advanced or metastatic EGFR-TK mutation-positive non-small-cell lung cancer [TA258]. Available at: https://www.nice.org.uk/guidance/TA258 (last accessed 10 Nov 2023). 	<p>Thank you for your comments. The scope has been updated to remove platinum-based doublet chemotherapy as a comparator.</p> <p>The remaining comparators have been retained in the scope as these reflect established clinical practice for people with untreated EGFR mutation-positive advanced NSCLC and for whom EGFR-TKIs are suitable. The committee can decide the most appropriate comparators based on evidence presented to it.</p>

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		<p>5. National Institute for Health and Care Excellence (NICE). Gefitinib for the first-line treatment of locally advanced or metastatic non-small-cell lung cancer [TA192]. Available at: https://www.nice.org.uk/guidance/ta192 (last accessed 10 Nov 2023).</p> <p>6. National Institute for Health and Care Excellence (NICE). Afatinib for treating epidermal growth factor receptor mutation-positive locally advanced or metastatic non-small-cell lung cancer [TA310]. Available at: https://www.nice.org.uk/guidance/ta310 (last accessed 10 Nov 2023).</p> <p>7. National Institute for Health and Care Excellence (NICE). Dacomitinib for untreated EGFR mutation-positive non-small-cell lung cancer [TA595]. Available at: https://www.nice.org.uk/guidance/ta595 (last accessed 10 Nov 2023).</p> <p>8. National Institute for Health and Care Excellence (NICE). Pemetrexed for the first-line treatment of non-small-cell lung cancer [TA181]. Available at: https://www.nice.org.uk/guidance/ta181/chapter/1-Guidance (last accessed 10 Nov 2023).</p>	
	British Thoracic Oncology Group	I am not certain platinum pemetrexed is a valid comparator. The only scenario in which this would be used would be if the EGFR status was unknown (in which case access to Osimertinib would [n]ot be possible) or if the patient had an absolute contraindication to a TKI (in which case they would not be a candidate for the regime under appraisal)	Thank you for your comments. The scope has been updated to remove platinum-based doublet chemotherapy as a comparator.
Outcomes	AstraZeneca	No comments.	No action required.

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	British Thoracic Oncology Group	Yes and Yes	Thank you for your comment. No action required.
Equality	AstraZeneca	AstraZeneca is not aware of any equality issues.	Thank you for your comment. No action required.
	British Thoracic Oncology Group	n/a	No action required.
Other considerations	AstraZeneca	<p>The draft scope suggests that 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. Testing for EGFR-TK mutations is well-established in clinical practice and is included in the National Genomic Test Directory.^{9,10}</p> <p>The diagnostic guidelines outline that once a contrast-enhanced CT scan suggests lung cancer, a biopsy should be performed which will enable determination of EGFR-TK mutations.¹⁰ This testing is performed prior to the initiation of treatment, and hence before the point at which a decision is made on which treatment to start. Given the current testing landscape, it is not necessary to include the cost of testing in the economic modelling.</p> <p><u>References</u></p>	Thank you for your comments. The scope has been updated to remove wording around costs associated with testing for EGFR mutation.

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		<p>9. NHSE England. National genomic test directory. Available at: https://www.england.nhs.uk/publication/national-genomic-test-directories/ (last accessed 10 Nov 2023).</p> <p>10. National Institute for Health and Care Excellence (NICE). EGFR-TK mutation testing in adults with locally advanced or metastatic non-small-cell lung cancer [DG9]. Available at: https://www.nice.org.uk/guidance/dg9/chapter/3-clinical-need-and-practice (last accessed 10 Nov 2023).</p>	
	British Thoracic Oncology Group	n/a	No action required.
Questions for consultation	AstraZeneca	<p>Where do you consider osimertinib with pemetrexed and platinum-based chemotherapy will fit into the existing care pathway for advanced EGFR mutation-positive NSCLC?</p> <p>Osimertinib with pemetrexed and platinum-based chemotherapy will offer a combination therapy option for untreated advanced EGFRm NSCLC patients. It is expected to be positioned alongside osimertinib monotherapy as an option for a more comprehensive treatment approach. The FLAURA2 trial appropriately offers a head-to-head comparison of these two treatment approaches.</p> <p>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?</p> <p>Platinum-based doublet chemotherapy is currently only used in EGFRm NSCLC where EGFR-TKIs are unsuitable. Osimertinib monotherapy is standard of care for EGFRm patients.³ Where platinum-based doublet</p>	Thank you for your comments. No action required.

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		<p>chemotherapy is used for EGFRm NSCLC, pemetrexed can be used with cisplatin or carboplatin.¹¹ The FLAURA2 trial allows for pemetrexed to be used with cisplatin or carboplatin, reflective of UK clinical practice.¹</p> <p>Within the population under consideration, should people with newly diagnosed versus recurrent disease be considered separately?</p> <p>The population under consideration should be untreated patients with both newly diagnosed and recurrent NSCLC. The FLAURA2 population is defined as untreated metastatic patients. Patients could be newly diagnosed or have recurrent NSCLC.</p> <p>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?</p> <p>There are no current restrictions for the use of osimertinib monotherapy relating to squamous or non-squamous NSCLC.¹¹ The FLAURA2 trial permitted mixed pathology.</p> <p>Would osimertinib with pemetrexed and platinum-based chemotherapy be a candidate for managed access?</p> <p>This is a topic to be discussed during the appraisal process.</p> <p>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?</p> <p>Please identify the nature of the data which you understand to be available to enable the committee to take account of these benefits.</p>	

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		<p>The QALY calculation likely captures the health-related benefits of osimertinib with pemetrexed and platinum-based chemotherapy sufficiently.</p> <p>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:</p> <ul style="list-style-type: none"> • 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. <p>Please tell us what evidence should be obtained to enable the committee to identify and consider such impacts.</p> <p>AstraZeneca is not aware of any equality issues.</p> <p><u>References</u></p>	

Section	Consultee/ Commentator	Comments [sic]	Action
		11. National Institute for Health and Care Excellence (NICE). Lung cancer: diagnosis and management [NG122]. Available at: https://www.nice.org.uk/guidance/ng122 (last accessed 10 Nov 2023).	
	British Thoracic Oncology Group	<p>Where do you consider osimertinib with pemetrexed and platinum-based chemotherapy will fit into the existing care pathway for advanced EGFR mutation-positive NSCLC?</p> <p>Based on the date from FLAURA2 I expect this regime to be incorporated as a first line treatment option for patients with advanced EGFR mutated NSCLC who are fit enough to receive it</p> <p>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?</p> <p>See comment above</p> <p>Within the population under consideration, should people with newly diagnosed versus recurrent disease be considered separately?</p> <p>No – as long as they have not been exposed to adjuvant Osimertinib</p> <p>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?</p> <p>Yes</p>	Thank you for your comments. No action required.

Section	Consultee/ Commentator	Comments [sic]	Action
Additional comments on the draft scope	AstraZeneca	No additional comments.	Thank you for your comment. No action required.
	British Thoracic Oncology Group	n/a	No action required.