National Institute for Health and Care Excellence

Single Technology Appraisal (STA)

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

Response to consultee and commentator comments on the draft remit and draft scope (pre-referral)

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

Section	Consultee/ Commentator	Comments [sic]	Action
Wording	Boehringer Ingelheim Limited	We support the current draft remit wording. However, it needs to be noted alongside the remit that the current marketing authorisation is for EGFR mutation positive patients harbouring a T790M mutation only as a second-line treatment option.	Thank you, the current marketing authorisation for osimertinib is included in the technology section.
	BTOG-NCRI-ACP-RCP-RCR	To appraise the clinical and cost effectiveness of osimertinib within its marketing authorisation for treating previously untreated epidermal growth factor receptor (EGFR) mutation-positive non-small-cell lung cancer.	Thank you for your comment. The remit has been amended to specify the untreated population.
Timing Issues	Boehringer Ingelheim Limited	Given the availability of three other effective treatment options in the first-line and osimertinib itself via the CDF in the second line, we do not consider this appraisal to be urgent.	Thank you, your comment has been noted. No changes to the scope are needed.

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	BTOG-NCRI-ACP-RCP-RCR	Relatively important – although it should be noted that osimertinib is already available to NSCLC patients that have both progressed during treatment with a first-line EGFR tyrosine kinase inhibitor and have NSCLC with a T790M mutation.	Thank you, your comment has been noted. No changes to the scope are needed.
Additional comments on the draft remit	Boehringer Ingelheim Limited	No additional comments to those covered below.	Thank you.
	BTOG-NCRI-ACP-RCP-RCR	N/A	Noted.

Comment 2: the draft scope

Section	Consultee/ Commentator	Comments [sic]	Action
Background information	Boehringer Ingelheim Limited	No comments	Thank you.
	BTOG-NCRI-ACP-RCP-RCR	Worth including that in Western populations, EGFR mutations are identified in approximately 10 – 15% of NSCLC patients.	Thank you, your comment has been noted. This section intends to provide a brief background summary. No changes to the scope are needed.

Section	Consultee/ Commentator	Comments [sic]	Action
The technology/ intervention	Boehringer Ingelheim Limited	No comments	Thank you.
	BTOG-NCRI-ACP-RCP-RCR	Should clarify that NICE guidance (TA416) specifically recommends osimertinib as an option for treating locally advanced or metastatic epidermal growth factor receptor (EGFR) T790M mutation-positive non-small-cell lung cancer in adults whose disease has progressed after first-line treatment with an EGFR tyrosine kinase inhibitor.	Thank you for your comment. The scope has been amended to clarify that TA416 recommends osimertinib within the CDF only for disease progression after first-line EGFR TKI.
Population	Boehringer Ingelheim Limited	1. Osimertinib data is largely in patients with the most common EGFR mutations (Ex19del or L858R). 2. Current population wording does not specify TKI-naïve vs TKI-pretreated. Given existing access for osimeritinib via CDF, this would be important to clarify going forwards.	Thank you for your comments. The wording is in line with the population in the clinical trials. This section has been amended to refer to a previously untreated population.
	BTOG-NCRI-ACP-RCP-RCR	People with locally advanced or metastatic EGFR mutation-positive non-squamous non-small-cell lung cancer	Thank you for your comments. The wording is in line with the population in the clinical trial which does not specify non-squamous

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			non-small-cell lung cancer.
Comparators	Boehringer Ingelheim Limited	We agree with the comparators chosen, for the TKI naïve population only. If the, TKI pre-treated population is also covered, additional appropriate comparstors will need to be included. Regardless of including the TKI pretreated population in this assessment, we suggest, an additional evaluation of osimertinib's effect on the survival outcomes of TKI naïve patients across both first and second line therapies. With this in mind, we'd suggest adding in second line therapy options as comparators.	Thank you for your comment. The appraisal is currently covering the untreated population only therefore the comparators do not cover second line therapy. The appraisal committee will discuss the most relevant comparators during the development of this appraisal.
	BTOG-NCRI-ACP-RCP-RCR	Broadly yes. The current standard of care for these patients is gefitinib/erlotinib/afatinib, followed by osimertinib in patients progressing on first line therapy due to the presence of the T790M mutation, or chemotherapy in patients where the T790M mutation is not detected. The T790M is found in approximately 50% of the EGFR mutant NSCLC population on progression. The FLAURA trial permitted crossover to osimertinib following a protocol amendment. Results from the crossover were not included in the primary publication, and would in any case be exploratory, but could provide useful supporting data.	Thank you, your comment has been noted. No changes to the scope are needed.
Outcomes	Boehringer Ingelheim Limited	No comments	Thank you.

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	BTOG-NCRI-ACP-RCP-RCR	Yes. Should also include response duration.	Thank you for your comment. Response duration has been added as an outcome.
Economic analysis	Boehringer Ingelheim Limited	As in our comments above regarding the population and comparators, we'd emphasise that the best value assessment of osimertinib for patients and the NHS would be by looking at survival outcomes with and without osimertinib used in TKI naïve and pre-treated patients followed through to at least second-line treatment. Appropriate sequencing of therapy, now that newer therapies are available, will be crucial for optimal outcomes for patients.	Thank you for your comment. The appraisal is currently covering the untreated population only.
	BTOG-NCRI-ACP-RCP-RCR	No additional EGFR testing of the patient population would be required. Indeed, adoption of first line osimertinib would remove the current need to test for the presence of the T790M mutation on disease progression.	Thank you, your comment has been noted. No changes to the scope are needed.
Equality and Diversity	Boehringer Ingelheim Limited	Patients currently have the option of one of the three currently reimbursed therapies when they are TKI naïve - followed by osimertinib for the appropriate patients when they progress. (T790M mutation is seen in only about 8% patients in the TKI naïve population, but is seen in around 50-60% patients after progressing). If osimertinib were to be reimbursed in the TKI naïve population without T790M mutation, progressing patients may have limited subsequent treatment options.	Thank you for your comment. This is not considered to be an equality issue that could be addressed by the appraisal committee. Treatment options for the untreated population should not be restricted based on treatment options after disease progression. Please see the

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			equalities impact assessment form.
	BTOG-NCRI-ACP-RCP-RCR	No specific issues.	Thank you.
Other considerations	Boehringer Ingelheim Limited	No comments	Thank you.
	BTOG-NCRI-ACP-RCP-RCR	Our experts believe that there is value in considering the results of AURA3 (osimertinib for T790M-positive advanced non–small-cell lung cancer in patients that have progressed after first line EGFR tyrosine kinase inhibitors) in the evidence submission.	Thank you, your comment has been noted. Results of the AURA 3 trial will be considered separately in the CDF review of TA416. No changes to the scope are needed.
Innovation	Boehringer Ingelheim Limited	No comments	Thank you.
	BTOG-NCRI-ACP-RCP-RCR	Yes, innovative. Available data that should be considered include results from FLAURA and AURA3 (phase 3 trials of osimertinib first and second line respectively), and NICE guidance TA416.	Thank you, your comment has been noted. Results of the AURA 3 trial will be considered separately in the CDF review of

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			TA416. No changes to the scope are needed.
Questions for consultation	Boehringer Ingelheim Limited	No comments	Thank you.
	BTOG-NCRI-ACP-RCP-RCR	Is osimertinib expected to be used in non-small-cell lung cancers with activating mutations of EGFR other than Ex19del and L858R? Yes, but other (non-Ex19del and L858R) EGFR mutations account for only 10% of EGFR mutations.	Thank you, your comment has been noted. No changes to the scope are needed.
Additional comments on the draft scope	Boehringer Ingelheim Limited	No additional comments.	Thank you.
	BTOG-NCRI-ACP-RCP-RCR	N/A	Noted

The following consultees/commentators indicated that they had no comments on the draft remit and/or the draft scope

AstraZeneca UK, Roche