National Institute for Health and Care Excellence

Single Technology Appraisal (STA)

Dacomitinib for untreated EGFR-positive non-small-cell lung cancer [ID1346]

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	Pfizer	The proposed wording is adequate.	Thank you for your comment.
	Boehringer Ingelheim	Draft remit - not available for review	Thank you for your comment. The draft remit was available to review at the top of scoping document.
Timing Issues	Boehringer Ingelheim	Draft remit - not available for review	Thank you for your comment. The draft remit was available to review at the top the draft scope.

Section	Consultee/ Commentator	Comments [sic]	Action
Additional comments on the draft remit	Boehringer Ingelheim	Draft remit - not available for review	Thank you for your comment. The draft remit was available to review at the top of the draft scope.

Comment 2: the draft scope

Section	Consultee/ Commentator	Comments [sic]	Action
Background information	Pfizer	The background information is accurate and comprehensive.	Thank you for your comment.
	Boehringer Ingelheim	Agree	Thank you for your comment.
The technology/ intervention	Pfizer	The brand name of dacomitinib will be Vizimpro.	Thank you for your comment. The brand name will be included in the scope.
	AstraZeneca	Spelling mistake in final sentence – “systematic” should be changed to “systemic”	Thank you for your comment. This error has been corrected.
	Boehringer Ingelheim	Like afatinib, dacomitinib is a second generation TKI – with the same mechanism of action (as opposed to the first generation TKIs, erlotinib and gefitinib).	Comment noted.

Section	Consultee/ Commentator	Comments [sic]	Action
		LUX-LUNG7 was the first head to head trial of TKIs, with afatinib shown to be clinically superior to gefitinib (Park, *et al.* 2016 https://www.ncbi.nlm.nih.gov/pubmed/27083334)	
Population	Pfizer	The population is defined appropriately.	Thank you for your comment.
	AstraZeneca	It should be made clear that the pivotal study of dacomitinib in this indication (ARCHER1050), excluded patients with brain metastases.	Thank you for your comment. The description of the technology in the scope has been updated to better reflect the ARCHER1050 trial population.
	Boehringer Ingelheim	Pivotal trial (ARCHER 1050): Only patients with specific EGFR mutations were included Relevant Inclusion Criteria: • Evidence of histo or cytopathology confirmed, advanced NSCLC (with known histology) with the presence of EGFR activating mutation (exon 19 deletion or the L858R mutation in exon 21). • It is acceptable for subjects with the presence of the exon 20 T790M mutation together with either EGFR activating mutation (exon 19 deletion or the L858R mutation in exon 21) to be included in this study Relevant Exclusion Criteria: • Any other mutation other than exon 19 deletion or L858R in exon 21, with or without the presence of the exon 20 T790M mutation.	Thank you for your comment. The description of the technology in the scope has been updated to better reflect the ARCHER1050 trial population.

Section	Consultee/ Commentator	Comments [sic]	Action
		The pivotal trial also excluded patients with “any history of brain metastases or leptomeningeal metastases”. We therefore expect the population of interest to be only this population	
Comparators	Pfizer	The comparators are defined appropriately.	Thank you for your comment.
	AstraZeneca	No comment	Noted.
	Boehringer Ingelheim	Agree Additionally, ID1302 (Publication expected December 2018) ‘Osimertinib for untreated EGFR-positive non-small-cell lung cancer’ is listed under “Appraisals in development”. For this TA, ID1346, this will be relevant	Thank you for your comment. Although osimertinib [ID1302] is under appraisal for a similar indication to dacomitinib, it is unlikely to be in routine use at the time this scope is issued.
Outcomes	Pfizer	The outcomes are defined appropriately.	Thank you for your comment.
	AstraZeneca	Given the results of the pivotal study of dacomitinib in this indication (ARCHER1050), we would recommend that additional outcomes are considered: • Dose reductions • AE’s leading to discontinuation	Thank you for your comment. Dose reductions and adverse events leading to discontinuation should be captured through the ‘adverse effects of treatment’ outcome

Section	Consultee/ Commentator	Comments [sic]	Action
			included in the final scope.
	Boehringer Ingelheim	Agree	Thank you for your comment.
Economic analysis	Pfizer	Pfizer does not believe it to be necessary to include the costs associated with diagnostic testing for EGFR mutation. All the stated comparators also require EGFR positivity before treatment and so the inclusion of these costs will not make any difference to cost-effectiveness results. Discussion with clinicians suggests that such testing is generally widely available in the UK.	Thank you for your comment. According to the NICE methods guide (section 5.9), costs of companion diagnostic tests should be incorporated into the assessments of clinical and cost effectiveness where appropriate. The scope states that the economic modelling should include the costs associated with diagnostic testing only in people who would not otherwise have been tested. If appropriate, a sensitivity analysis can be provided without the cost of the diagnostic test.
	AstraZeneca	No comments	Noted.

Section	Consultee/ Commentator	Comments [sic]	Action
	Boehringer Ingelheim	Agree	Thank you for your comment.
Equality and Diversity	Pfizer	No comment.	Noted.
	AstraZeneca	No comment	Noted.
	Boehringer Ingelheim	Not identified	Thank you for your comment.
Other considerations	Pfizer	None.	Noted.
	Boehringer Ingelheim	None	Noted.
Innovation	Pfizer	Dacomitinib is the first and only EGFR TKI to show overall survival benefit in a phase 3 randomised trial (ARCHER 1050). The median OS was 34.1 months with dacomitinib versus 26.8 months with gefitinib (HR 0.76) (1). Of the current approved treatments for EGFR+ NSCLC, dacomitinib has the numerically longest PFS data. Median progression free survival according to independent review was 14.7 months in the dacomitinib arm and 9.2 months in the gefitinib arm (HR 0.59) (2). Investigator assessed median progression free survival was 16.6 months in the dacomitinib arm and 11 months in the gefitinib arm (HR 0.62). Sources: 1) Tony S. Mok, Ying Cheng, Xiandong Zhou, et al. Improvement in Overall Survival in a Randomized Study Comparing Dacomitinib With Gefitinib in	Thank you for your comment. The company will have an opportunity to provide evidence on the innovative nature of its product in its submission. The appraisal committee will consider whether there are any benefits of the technology associated with innovation.

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		Patients With Advanced Non-Small Cell Lung Cancer Harboring EGFR-Activating Mutations. ASCO, 2018 (presentation). 2) Wu YL, Cheng Y, Zhou X et al. Dacomitinib versus gefitinib as first-line treatment for patients with EGFR-mutation-positive non-small-cell lung cancer (ARCHER 1050): a randomised, open-label, phase 3 trial. Lancet Oncol. 2017 Nov;18(11):1454-1466	
	AstraZeneca	Dacomitinib is the second of the so-called “2nd generation TKIs” (after afatanib) and should not be considered particularly innovative.	Thank you for your comment. The company will have an opportunity to provide evidence on the innovative nature of its product in its submission. The appraisal committee will consider whether there are any benefits of the technology associated with innovation.
	Boehringer Ingelheim	Like afatinib (reimbursed in 2014), dacomitinib is a second generation TKI – with the same mechanism of action (as opposed to the first generation TKIs erlotinib and gefitinib).	Thank you for your comment. The company will have an opportunity to provide evidence on the innovative nature of its product in its submission. The appraisal committee will consider whether there are any benefits of the

Section	Consultee/ Commentator	Comments [sic]	Action
			technology associated with innovation.
Questions for consultation	AstraZeneca	The exclusion of patients with brain metastases in ARCHER1050, means that the available evidence-base for dacomitinib in this indication will limited relevance for patients diagnosed in the UK with locally advanced or metastatic NSCLC with EGFRm tumours. The observation that approximately two-thirds of patients in ARCHER1050 had to reduce the dose of dacomitinib because of tolerability concerns, suggests that there is likely to be the potential for an impact on health-related quality of life which may or may not be captured adequately in the QALY calculation.	Thank you for your comments. The description of the technology in the scope has been updated to better reflect the ARCHER1050 trial population.
	Boehringer Ingelheim	*Are there any subgroups of people in whom dacomitinib is expected to be more clinically effective and cost effective or other groups that should be examined separately?* Please see our response under the section 'population' above. Additionally, the published results from the pivotal trial, (Wu *et al.*, 2017), shows (Figure 3) that the PFS results were significant only in the Asian population, and not in the non-Asian population. Wu et al., Lancet Oncol 2017; 18: 1454–66 https://doi.org/10.1016/S1470-2045(17)30608-3	Thank you for your comments. The description of the technology in the scope has been updated to better reflect the ARCHER1050 trial population.
Additional comments on the draft scope	Pfizer	None.	Noted.
	Boehringer Ingelheim	None	Noted.

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

Department of Health and Social Care