National Institute for Health and Care Excellence

Single Technology Appraisal

Ceritinib for untreated anaplastic lymphoma kinase-positive advanced 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	**Novartis Oncology**	Yes	Comment noted.
Timing Issues	**Novartis Oncology**	Ceritinib is an ALK inhibitor with proven efficacy that is expected to be granted a licence by the EMA in [redacted] for previously untreated advanced ALK positive NSCLC. CHMP opinion is expected on the [redacted].	Comment noted.

Comment 2: the draft scope

Section	Consultee/ Commentator	Comments [sic]	Action
Background information	**Novartis Oncology**	Yes.	Comment noted.

Section	Consultee/ Commentator	Comments [sic]	Action
The technology/ intervention	**Novartis Oncology**	Yes	Comment noted.
Population	**Novartis Oncology**	Yes.	Comment noted.
Comparators	**Novartis Oncology**	Since the approval of first-line crizotinib for the treatment of ALK positive advanced NSCLC patients in 2016,[1] we understand all ALK positive NSCLC patients with advanced disease will receive it as their first-line treatment. A clinical expert statement made in the appraisal of crizotinib, included the following, "*When crizotinib is approved and available it **will replace** first line combination chemotherapy for patients with ALK-driven disease*".[1] Novartis has contacted clinical experts to establish what their current practice is in this defined group of patients and the above assertion was confirmed as being realised. The clinical experts contacted by Novartis stated that they would treat >90% of ALK positive advanced NSCLC patients with crizotinib.[2] In light of this, Novartis recommends that crizotinib should be the only comparator used in this appraisal. On the rare occasion that crizotinib cannot be used, then Pemetrexed maintenance would be used (See TAG 402).[3] However, both Novartis, and clinicians consulted believe that these two chemotherapeutic treatment options have been superseded by crizotinib and therefore are no longer appropriate comparators. Further, the recently updated ESMO guidelines state that,"*first-line treatment with crizotinib is the preferred treatment of patients with ALK-rearranged NSCLC.*"[5]	Comment noted. The comparators section of the scope is intended to include all treatments that could be used in clinical practice. Any differences from the scope for the appraisal must be justified in the company submission.
Outcomes	**Novartis Oncology**	Yes.	Comment noted.

Section	Consultee/ Commentator	Comments [sic]	Action
Economic analysis	**Novartis Oncology**	As per reference case. The time horizons used in previous appraisals in advanced NSCLC patients have ranged from 10-20 years.	Comment noted.
Equality and Diversity	**Novartis Oncology**	No comments.	Comment noted.
Innovation	**Novartis Oncology**	Ceritinib is a second-generation ALK inhibitor and its clinical effectiveness has been demonstrated in a large multi-centre (134 centres), international (28 countries), randomized, phase III study. The study assessed the efficacy, safety and HRQOL of ceritinib which will inform the forthcoming submission.	Comment noted.
Questions for consultation	**Novartis Oncology**	• Would ceritinib be used in people with ALK-positive squamous non-small cell lung cancer? No. • Have all relevant comparators for ceritinib been included in the scope? Please see 'comparator' section. • Which treatments are considered to be established clinical practice in the NHS for untreated ALK-positive advanced non-small cell lung cancer? Please see comparator section. Crizotinib is now the standard of care for this group of patients. Are the outcomes listed appropriate?	Comment noted.

Section	Consultee/ Commentator	Comments [sic]	Action
		Yes Are there any subgroups of people in whom ceritinib is expected to be more clinically effective and cost effective or other groups that should be examined separately? In the ASCEND-4 study the PFS benefit in favour of ceritinib was observed across most predefined subgroups, except in subgroups where there was large variability due to a small sample size (prior neo-adjuvant chemotherapy, patients of South American origin).[4] • Where do you consider ceritinib will fit into the existing NICE pathway, Lung Cancer? As first-line therapy for adult patients with previously untreated ALK-positive advanced NSCLC patients.	
Additional comments on the draft scope	**Novartis Oncology**	None.	Comment noted.

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

British Thoracic Society, Department of Health.