National Institute for Health and Care Excellence

Health Technology Evaluation

Selpercatinib for previously treated RET fusion-positive advanced non-small-cell lung cancer (MA review of TA760) [ID6293]

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	Eli Lilly (company)	Lilly consider an evaluation and the proposed evaluation route appropriate.	Thank you for your comment. No action required.
	British Thoracic Oncology Group	Appropriate. This is an important component of personalised treatment for lung cancer	Thank you for your comment. No action required.
Wording	Eli Lilly (company)	Yes	Thank you for your comment. No action required.

Section	Stakeholder	Comments [sic]	Action
Additional comments on the draft remit		No comments	

Comment 2: the draft scope

Section	Consultee/ Commentator	Comments [sic]	Action
Background information	Eli Lilly (company)	The draft scope states that testing for rearranged during transfection (*RET*) fusion status is not routinely carried out as standard of care (SOC) in the United Kingdom (UK). However, *RET* fusion testing is specified to be routinely conducted by the national genomic test directory commissioned by the National Health Service (NHS). As such, Lilly request that the wording of the draft scope be changed to reflect that testing for *RET* fusion status is routinely carried out as SOC in the UK	Thank you for your comment. The background section has been updated to reference the indication for genetic testing in NSCLC.
Population	Eli Lilly (company)	The population is defined appropriately.	Thank you for your comment. No action required.
Subgroups	Eli Lilly (company)	The subgroups listed in the draft scope are clinically appropriate to consider and are defined appropriately.	Thank you for your comment. No action required.
	British Thoracic Oncology Group	Acces to NHS genomics testing is at last extending to a larger proportion of incident NSCLC cases, so access to targeted therapies for driver mutations identified is become more and more important. The proportion of incident cases which have a RET rearrangement remains small of course	Thank you for your comment. No action required.

Section	Consultee/ Commentator	Comments [sic]	Action
Comparators	Eli Lilly (company)	No comments at this stage. The refined comparator set will be confirmed nearer the date of submission based on expert clinical validation of current clinical practice.	Thank you for your comment. No action required.
	British Thoracic Oncology Group	Randomised data is now available showing that selpercatinib is superior to 1st line chemotherapy in terms of PFS, and this is reflected in NICE TA911.	Thank you for your comment. No action required.
Outcomes	Eli Lilly (company)	Outcomes are appropriate.	Thank you for your comment. No action required.
Equality	Eli Lilly (company)	No concerns.	Thank you for your comment. No action required.
	British Thoracic Oncology Group	Despite access in the 1st line setting (see above), it is important to retain access for previously-treated patients: - at present there are many who started first line chemotherapy before TA911 was in place - some patients start first line treatment before RET rearrangement status is known, because of delays or failures in access to NGS	Thank you for your comment. NICE will appraise selpercatinib within its marketing authorisation for treating people with RET fusion-positive advanced non-small-cell lung cancer that is previously untreated with a RET inhibitor.

Section	Consultee/ Commentator	Comments [sic]	Action
Other considerations		No comments	
Questions for consultation	Eli Lilly (company)	**Under what circumstances would RET gene fusion be tested for?** As detailed above, testing of RET fusion status is routine in clinical practice in the UK, as genetic drivers of non-small-cell lung cancer (NSCLC), including RET fusion status, are tested for according to the national genomic test directory commissioned by the NHS. As a result, the cost of RET fusion testing is anticipated to be absorbed by the NHS. This means that the cost-effectiveness of selpercatinib may be underestimated in a model which includes the costs associated with the detection of RET fusion-positive patients. Despite this, it is anticipated that the model base case of this submission will include a cost incurred by RET fusion testing, is in line with the preferences of the NICE Committee in both TA760 and TA911. The exclusion of the incurred cost of RET fusion testing will be explored in a scenario analysis. **Is the proportion of people with RET gene fusion in the background accurate for NHS clinical practice?** Established data in clinical research is aligned with RET fusion mutations being detected in 1–2% of NSCLC patients. This is in line with the population estimate used in prior NICE appraisals of selpercatinib (TA760, TA911). **Where do you consider selpercatinib will fit into the existing care pathway for RET positive NSCLC?** Aside from availability of selpercatinib for previously-treated RET fusion-positive advanced NSCLC via the Cancer Drugs Fund (CDF) (TA760), selpercatinib is also reimbursed in the first-line setting for RET fusion-positive	Thank you for your comments. The background section has been updated to reference the indication for genetic testing in NSCLC. The characteristics of the condition, clinical pathway and extent of unmet need in the population will be considered during the appraisal.

Section	Consultee/ Commentator	Comments [sic]	Action
		advanced NSCLC via the CDF (TA911). Consequently, all eligible patients could in theory receive selpercatinib in the first-line setting. However, in practice, a proportion of eligible, untreated patients begin SOC chemotherapy prior to receiving the results of RET fusion testing in clinical practice, since the advanced stage of their disease and resulting disease burden makes waiting for these results prior to treatment commencement clinically inappropriate. These bridging therapies are essential for extending patient survival but mean that patients who start SOC chemotherapy and are then subsequently diagnosed with RET fusion-positive NSCLC are pre-treated by the time eligibility for selpercatinib has been established. Should selpercatinib be recommended for use in this second-line setting, it would be the only targeted treatment available for these patients. In the absence of selpercatinib, RET fusion-positive patients who received SOC chemotherapy in the first-line setting would not be able to access targeted RET inhibitor therapy as a second-line treatment, representing a significant unmet need for this patient population. Moreover, this would place this patient population in stark contrast with RET fusion-positive patients who receive results of RET fusion testing in sufficient time to enable them to receive selpercatinib in the first-line setting. **Do you consider that the use of selpercatinib can result in any potential substantial health-related benefits that are unlikely to be included in QALY calculation?** It is clinically important that patients diagnosed with RET fusion-positive NSCLC after starting SOC chemotherapy are given access to selpercatinib, as its recommendation would make it the only effective, targeted treatment available in the second-line setting. If availability of selpercatinib to treat RET fusion-positive advanced NSCLC in the second-line setting were not maintained, SOC chemotherapy would represent the sole treatment option in	

Section	Consultee/ Commentator	Comments [sic]	Action
		this population, leaving patients without any hope of transitioning to a targeted therapy. This impact on hope for a highly effective and well-tolerated treatment option in the second-line setting on patient well-being is not captured within the cost per QALY framework.	
Additional comments on the draft scope		No comments	

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

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