National Institute for Health and Care Excellence

Single Technology Appraisal (STA)

Pembrolizumab with carboplatin and paclitaxel or nab-paclitaxel for untreated metastatic squamous non-small-cell lung cancer [ID1306]

Response to consultee and commentator 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

Section	Consultee/ Commentator	Comments [sic]	Action
Wording	Royal College of Pathologists	*Does the wording of the remit reflect the issue(s) of clinical and cost effectiveness about this technology or technologies that NICE should consider?* YES	Comment noted. No action needed.
	MSD UK	The wording in the remit reflects the population included in the KEYNOTE-407 clinical trial, the pivotal study that provides the main evidence for this appraisal.	Comment noted. No action needed.
	NCRI-ACP-RCP-RCR-BTOG	Wording is appropriate for palliative treatment for advanced squamous cell NSCLC	Comment noted. No action needed.
Timing Issues	Royal College of Pathologists	*What is the relative urgency of this appraisal to the NHS?*	Comment noted. An appraisal of

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		URGENT	pembrolizumab has been scheduled into NICE's technology appraisal work programme. No action needed.
	MSD UK	There is a significant need for new, and effective, therapies for patients with squamous lung cancer. The proposed appraisal timelines should be scheduled to ensure patients have the opportunity to access pembrolizumab treatment as soon as possible after marketing authorisation.	Comment noted. An appraisal of pembrolizumab has been scheduled into NICE's technology appraisal work programme. No action needed.
	NCRI-ACP-RCP-RCR-BTOG	This is not an unmet need as single agent treatment with pembrolizumab (>50% PDL1) or chemotherapy is available for these patients.	Comment noted. No action needed.
Additional comments on the draft remit	MSD UK	No additional comments	Noted.

Comment 2: the draft scope

Section	Consultee/ Commentator	Comments [sic]	Action
Background information	MSD UK	No additional comments	Noted. No action needed.
	NCRI-ACP-RCP-RCR-BTOG	Background is accurate for advanced squamous cell NSCLC	Comment noted. No action needed.
The technology/ intervention	MSD UK	Yes	Noted. No action needed.
	NCRI-ACP-RCP-RCR-BTOG	Pembrolizumab and chemotherapy combination in squamous cell lung cancer	Noted. No action needed.
Population	MSD UK	The population is defined appropriately.	Comment noted. No action needed.
	NCRI-ACP-RCP-RCR-BTOG	Population is correctly defined Groups are not yet able to be defined as better biomarker for the population responding best to this treatment is yet to be determined	Comment noted. No action needed.
Comparators	Royal College of Pathologists	The issue for pathologists in relation to treatment with this kind of drug is the need for an associated diagnostic test that may decide whether the patient is eligible for treatment. In this instance, there is already a funding mechanism and testing network in the NHS to deal with pembrolizumab as currently licensed so, as long as the testing procedures and scoring systems are the same, then RCPath do not need to be involved with this appraisal.	Comments noted. As stated in the scope, the economic modelling should include the costs associated with diagnostic testing, so it will become clear what diagnostic tests are

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		If the test(s) differ or scoring differs, then we may need to be involved, dependent on the variation.	needed during the course of the appraisal. No action needed.
	MSD UK	We agree with the proposed comparators	Comment noted. No action needed.
	NCRI-ACP-RCP-RCR-BTOG	In the UK carboplatin/taxol or abraxane is not SOC for squamous cell NSCLC. Gemcitabine/carboplatin or vinorelbine/carboplatin are usually combinations given in the NHS. Carb/taxol is a common licensed treatment in the USA. This is also not usual in the rest of Europe	Comments noted. The comparators detailed in the scope are in line with NICE guidance and NHS practice. No action needed.
Outcomes	MSD UK	MSD agrees with the proposed outcome measures. In addition, it is known that the response to immunotherapies (immuno-oncology drugs) may be delayed, but once triggered, is likely to be durable, bringing unquantifiable long term survival benefit for a subset of patients. This benefit is not captured by the proposed outcome measures, thus MSD suggests the inclusion of “Duration of Response” as an additional outcome measure.	Comments noted. Duration of response has been added to the list of outcomes in the scope.
	NCRI-ACP-RCP-RCR-BTOG	The combination pembro/chemotherapy approach is rationalised by the very fast progression seen in at least 20% of patients when on single agent pembrolizumab as their first treatment. The theory is that these fast progressors will be rescued by the chemotherapy part of treatment until the PD1 inhibitor has a chance to stimulate the immune system to act on the cancer	Comments noted. No action needed.
	MSD UK	No comments	Noted.

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Economic analysis	NCRI-ACP-RCP-RCR-BTOG	Rapid increase in options for lung cancer patients.	Noted. No action needed.
Equality and Diversity	MSD UK	No comments	Noted.
	NCRI-ACP-RCP-RCR-BTOG	None.	Noted. No action needed.
Other considerations	MSD UK	No comments	Noted.
Innovation	MSD UK	MSD considers pembrolizumab to be innovative in its potential to make a significant and substantial impact on health-related benefits. Pembrolizumab was the first anti PD-1 pathway targeting agent to be approved as monotherapy for the first line treatment of patients with squamous NSCLC whose tumours have high levels of PD-L1 expression. Data from KEYNOTE-407 are expected to lead to pembrolizumab being the first approved PD-1 targeting treatment for first line use in squamous NSCLC, regardless of PD-L1 expression levels.	Comments noted. The potential innovative nature of the technology will be considered by the appraisal committee. No action needed.
	NCRI-ACP-RCP-RCR-BTOG	All treatments will be combined and given upfront. This is likely to IMPROVE capacity as compared to sequential treatment as this would entail more chemotherapy chair time and more visits over time. The toxicity does not appear to be compounded when treatment given together and for <50% PDL1 expressors, efficacy is greater when pembro/chemo combined.	Comments noted. The potential innovative nature of the technology will be considered by the appraisal

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			committee. No action needed.
Questions for consultation	MSD UK	*Q: Are there any subgroups of people in whom pembrolizumab with carboplatin and paclitaxel or nab-paclitaxel is expected to be more clinically effective and cost effective or other groups that should be examined separately?* Re: The ongoing clinical trial will assess efficacy in subgroups of participants with different levels of PD-L1 tumour expression. *Q: Where do you consider pembrolizumab will fit into the existing NICE pathway, Lung cancer?* Re: Pembrolizumab is expected to displace the use of chemotherapy as first-line treatment in patients with metastatic squamous NSCLC. *Q: Do you consider pembrolizumab with carboplatin and paclitaxel or nab-paclitaxel to be a step-change in the management of the condition?* Re: We believe pembrolizumab with carboplatin and paclitaxel or nab-paclitaxel offers significant additional clinical efficacy with an acceptable tolerability profile which will lead to improved outcomes for squamous NSCLC patients, a patient population which has typically not responded as well to treatment as those with non-squamous disease. As such, we believe pembrolizumab with carboplatin and paclitaxel or nab-paclitaxel does represent a step-change in the management of patients with this condition. *Q: Do you consider that the use of pembrolizumab can result in any potential significant and substantial health-related benefits that are unlikely to be included in the QALY calculation?*	Comments noted. No action needed.

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		Re: The benefits for carers/family will not be captured, nor any of the societal benefits from selected individuals returning to work or remaining in work for longer. *Q: Please identify the nature of the data which you understand to be available to enable the Appraisal Committee to take account of these benefits.* Re: MSD estimates that data will be available from the following multicentre, international, randomised, phase III trial: 'A Study of Carboplatin-Paclitaxel/Nab-Paclitaxel Chemotherapy With or Without Pembrolizumab (MK-3475) in Adults With First Line Metastatic Squamous Non-small Cell Lung Cancer (MK-3475-407/KEYNOTE-407)' - NCT02775435 *Q: To help NICE prioritise topics for additional adoption support, do you consider that there will be any barriers to adoption of this technology into practice? If yes, please describe briefly.* Re: MSD does not consider that there will be any barriers to adoption of this technology since pembrolizumab is already recommended by NICE in additional NSCLC indications. *Q: Is it appropriate to appraise the technology through the NICE Single Technology Appraisal (STA) process?* Re: Yes, we believe the STA process is appropriate. *Q: Would it be appropriate to use the cost comparison methodology for this topic?* Re: We do not consider the cost comparison methodology is appropriate for this topic.	

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		Q: Is the new technology likely to be similar in its clinical efficacy and resource use to any of the comparators? Re: We anticipate that pembrolizumab will offer significant additional clinical efficacy over current comparators, at incremental cost. *Q: Is the primary outcome that was measured in the trial or used to drive the model for the comparator(s) still clinically relevant?* Re: Yes, the primary outcome measure of overall survival used in the pivotal KEYNOTE-407 trial remains the most clinically relevant endpoint for a cancer study. *Q: Is there any substantial new evidence for the comparator technologies that has not been considered? Are there any important ongoing trials reporting in the next year?* Re: MSD is not aware of any substantial new evidence for the comparator technologies considered.	
	NCRI-ACP-RCP-RCR-BTOG	Any additional biomarkers such as TMB (tumour mutational burden) identified to more clearly define the population that definitely benefit?	Comment noted. The identification of biomarkers which may show differential benefit in a subgroup analysis will depend on the clinical evidence identified by the company. No action needed.

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Additional comments on the draft scope	MSD UK	No additional comments	Noted.

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