National Institute for Health and Care Excellence

Single Technology Appraisal (STA)

Pembrolizumab for treating advanced or recurrent PD-L1 positive non-small-cell lung cancer after progression with platinum-based chemotherapy (ID840)

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

Comment 1: the draft remit

Section	Consultee/ Commentator	Comments	Action
Appropriateness	British Thoracic Society	Yes it is appropriate to refer this topic to NICE for appraisal	Comment noted.
	Merck Sharp & Dohme Ltd	MSD agrees that it is appropriate for this topic to be referred to NICE for appraisal.	Comment noted.
	National Lung Cancer Forum for nurses	Appears appropriate	Comment noted.
Wording	Merck Sharp & Dohme Ltd	No additional comments	Comment noted.
	National Lung Cancer Forum for nurses	Appears appropriate	Comment noted.
Timing Issues	Merck Sharp &	We anticipate that the proposed appraisal should be scheduled to enable	Comment noted.

Section	Consultee/ Commentator	Comments	Action
	Dohme Ltd	NICE to issue final guidance soon after regulatory approval.	

Comment 2: the draft scope

Section	Consultee/ Commentator	Comments	Action
Background information	Merck Sharp & Dohme Ltd	No additional comments	Comment noted.
	National Lung Cancer Forum for nurses	Appears appropriate	Comment noted.
The technology/ intervention	Merck Sharp & Dohme Ltd	Yes	Comment noted.
	National Lung Cancer Forum for nurses	Appears appropriate	Comment noted.
Population	Merck Sharp & Dohme Ltd	Yes	Comment noted.
	National Lung Cancer Forum for nurses	Appears appropriate	Comment noted.
Comparators	Merck Sharp &	This appraisal will be focused on the population of patients with advanced	Comment noted.

Section	Consultee/ Commentator	Comments	Action
	Dohme Ltd	non-small-cell lung cancer (NSCLC) whose tumours express PD-L1 and who have progressed following platinum based chemotherapy. For such patients, the only active comparator is docetaxel. Best supportive care (no active treatment) should not be considered an appropriate comparator for patients eligible for pembrolizumab, as these patients would otherwise receive alternative active treatments for NSCLC, which are known to impact survival (e.g. docetaxel).	Clinical experts at the scoping workshop agreed that best supportive care is typically considered for patients who cannot tolerate traditional systemic chemotherapy such as docetaxel. However, clinical experts stated that pembrolizumab, as a monoclonal antibody, would also be expected to have lower toxicity than traditional systemic chemotherapy. Scoping workshop attendees agreed that best supportive care was an appropriate comparator for some patients with lower performance status who may be considered appropriate for pembrolizumab.

Section	Consultee/ Commentator	Comments	Action
Outcomes	Merck Sharp & Dohme Ltd	MSD agrees with the proposed outcome measures. However, 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.	Comment noted. Scoping workshop attendees discussed the outcome measure, duration of response, but it was agreed that there were issues of consistency with how it would be defined making comparisons with different treatments using this outcome measure difficult. The scoping workshop attendees discussed how the outcome measures included in the scopes for previous lung cancer appraisals had not included duration of response, and as a matter of consistency it agreed it was not appropriate to include it in the scope.
Economic analysis	Merck Sharp & Dohme Ltd	No additional comments	Comment noted.

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Equality and Diversity	Merck Sharp & Dohme Ltd	No additional comments	Comment noted.
	National Lung Cancer Forum for nurses	Yes	Comment noted.
Innovation	Merck Sharp & Dohme Ltd	MSD considers pembrolizumab to be innovative in its potential to make a significant and substantial impact on health-related benefits. Pembrolizumab will be the first anti PD-1 pathway targeting agent to be approved with a companion diagnostic to identify patients whose tumours express PD-L1 as determined by a validated test. Pembrolizumab has the potential to improve outcomes for PD-L1 positive patients, being a step-change in the management of advanced NSCLC.	Comment noted.
Other considerations	Merck Sharp & Dohme Ltd	No additional comments	Comment noted.
Questions for consultation	Merck Sharp & Dohme Ltd	**Question**: What is the size of the relevant population in England who are likely to be treated with pembrolizumab? **Answer**: approximately 6 patients in 100,000 population may be eligible for pembrolizumab, based on the following assumptions: o Approximately 59 patients diagnosed with NSCLC (squamous and non-squamous) each year in 100,000 population[1,2] o Approximately 32 patients diagnosed with stage IIIB or IV NSCLC in 100,000 population[3] o Approximately 18, 8 and 3 patients treated in 100,000 across first, second and third lines respectively[4]	

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		○ Approximately 4 patients in 100,000 population whose disease has progressed on or following platinum-based chemotherapy and who express PD-L1 across second line therapy, may be considered eligible for pembrolizumab[4,5] ○ Approximately 2 patients in 100,000 population whose disease has progressed on or following platinum-based chemotherapy and who express PD-L1 across third line therapy, may be considered eligible for pembrolizumab[4,5] ○ Approximately 6 patients in 100,000 population may be considered eligible for pembrolizumab across second and third lines of therapy (4 and 2 patients per 100,000 respectively) Reference 1: Cancer Research UK. Lung cancer incidence statistics. Available at: http://www.cancerresearchuk.org/cancer-info/cancerstats/types/lung/incidence/ (accessed June 2015) Reference 2: Office of National Statistics. Available at http://www.ons.gov.uk/ons/rel/pop-estimate/population-estimates-for-uk--england-and-wales--scotland-and-northern-ireland/2013/info-population-estimates.html (Accessed June 2015) Reference 3: Lung cancer: distribution of AJCC 6th Edition stage by year (2004-2010) and comparison with AJCC 7th (2010 only) Reference 4: Data on file. MSD Market Research Reference 5: Rizvi N et al. Safety and Clinical Activity of Pembrolizumab (MK-3475) as Initial Therapy in Patients With Advanced Non-Small Cell Lung Cancer (NSCLC). ASCO 2014 **Question**: How is PD-L1 status tested? Are validated tests readily available? Is it tested routinely in current clinical practice? **Answer**: PD-L1 status is tested by immunohistochemistry (IHC) assay. PD-	

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		L1 status is not currently tested in routine clinical practice, but validated tests will be readily available at time of regulatory approval. **Question**: Which treatments are considered to be established clinical practice in the NHS for advanced or recurrent PD-L1 positive non-small-cell lung cancer after progression with platinum-based chemotherapy? **Answer**: None. Pembrolizumab is the first targeted drug for patients with PD-L1 positive NSCLC. **Question**: How should best supportive care be defined? **Answer**: MSD suggests that best supportive care should be defined as no active treatment, i.e. any care given when patients are not eligible to receive any further active treatment (palliative care only). **Question**: Is docetaxel a relevant comparator? **Answer**: Yes. **Question**: Are the subgroups suggested in 'other considerations' appropriate? **Answer**: Yes. **Question**: Where do you consider pembrolizumab will fit into the existing NICE pathway, Lung cancer? **Answer:** MSD considers pembrolizumab to be the treatment option for patients with advanced NSCLC, whose tumours express PD-L1 and who have progressed following platinum based chemotherapy [proposed STA ID 840]. For such patients, we envisage pembrolizumab being used as second or third line treatment option as per the following sequences: • Platinum-based chemotherapy; pembrolizumab	

Section	Consultee/ Commentator	Comments	Action
		• Tyrosine kinase inhibitor; platinum-based chemotherapy; pembrolizumab **Question**: Please identify the nature of the data which you understand to be available to enable the Appraisal Committee to take account of these benefits. **Answer**: MSD estimates that data will be available from the following multi-center, international, randomised, adaptive design phase II/III trial: *"Study of Two Doses of MK-3475 (Pembrolizumab) Versus Docetaxel in Previously-Treated Participants* With *Non-Small Cell Lung Cancer (MK-3475-010/KEYNOTE-010)"*	

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

Department of Health

The British Thoracic Oncology Group

Royal College of Nursing

Response to consultee and commentator comments on the provisional matrix of consultees and commentators (pre-referral)

Version of matrix of consultees and commentators reviewed: Provisional matrix of consultees and commentators sent for consultation					
Summary of comments, action taken, and justification of action:					
	Proposal:	Proposal made by:		Action taken: Removed/Added/Not included/Noted	Justification:
1.	Remove Afiya Trust	NICE Secretariat		Removed	This organisation is no longer actively engaging with NICE. The Afiya Trust has therefore been removed from the matrix of consultees and commentators.
2.	Remove Equalities National Council	NICE Secretariat		Removed	This organisation has confirmed that they do not wish to participate in appraisals of this indication. Equalities National Council has therefore been removed from the matrix of consultees and commentators.

3.	Add British Association for Lung Research	NICE Secretariat		Added	This organisation has an area of interest closely related to this appraisal topic and meets the selection criteria to participate in this appraisal. British Association for Lung Research has been added to the matrix of consultees and commentators under 'relevant research groups'.
4.	Add Cochrane Airways Group	NICE Secretariat		Added	This organisation has an area of interest closely related to this appraisal topic and meets the selection criteria to participate in this appraisal. Cochrane Airways Group has been added to the matrix of consultees and commentators under 'relevant research groups'.