National Institute for Health and Care Excellence

Single Technology Appraisal (STA)

Pembrolizumab for adjuvant treatment of melanoma with high risk of recurrence

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

Comment: the draft remit

Section	Consultee/ Commentator	Comments	Action
Wording	MSD UK	We suggest revision in line with the anticipated indication wording: [redacted]	Comment noted. The wording of the remit aligns with the available clinical trial evidence and related NICE technology appraisals. NICE could only make recommendations on the use of pembrolizumab within the explicit terms of its final marketing authorisation.
Timing Issues	MSD UK	Adjuvant treatment of melanoma patients following tumour resection is not widely used in UK clinical practice. We anticipate that the proposed appraisal should be scheduled to enable	Comment noted.

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		NICE to issue final guidance soon after regulatory approval. The information on anticipated regulatory timelines presented in PharmaScan accurately reflects current expectations.	
	Melanoma Focus	Urgent. Adjuvant therapies could improve cure rate of melanoma. A number of dugs currently seeking NICE approval in this situationa and it is important that the guidance for all are published in a timely manner.	Comment noted.

Comment: the draft scope

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Background information	MSD UK	No comments	Comment noted.
The technology/ intervention	MSD UK	We suggest revision of the wording to better reflect the description of the ongoing clinical trial: …'It is being studied in a clinical trial in high risk patients with complete resection of stage III melanoma ~~at high risk of recurrence~~.'...	Comment noted. Wording amended.
Population	MSD UK	We suggest revision of the population in line with the anticipated indication wording: [redacted]	Comment noted. The wording of the population aligns with the available clinical trial evidence and related NICE

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			technology appraisals. NICE could only make recommendations on the use of pembrolizumab within the explicit terms of its final marketing authorisation.
Comparators	MSD UK	In the absence of any treatments considered to be established clinical practice in the NHS for adjuvant therapy following complete resection melanoma, we agree with the proposed comparator of 'routine surveillance'.	Comment noted.
	Melanoma Focus	No current treatment available. Ongoing NICE appraisals for adjuvant BRAF +/- MEK inhibitors are appropriately referenced. Is there a NICE assessment for adjuvant nivolumab that needs to be considered?	Comment noted. The nivolumab appraisal in the same population which is currently being scoped (ID1316) has been added to the list of appraisals.
Outcomes	MSD UK	We suggest revision of the outcome measures to be considered to those captured in the Phase III clinical trial as follows: • Overall survival • Recurrence-free survival (Note: Disease-free survival is not an outcome measure that will be captured in the clinical trial) • Distant metastases free survival	Comment noted. Recurrence-free survival has been included as an outcome. Duration of response has not been

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		• Adverse effects of treatment • Health related quality of life. 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, we therefore suggest the inclusion of 'Duration of Response' as an additional outcome measure.	included, as pembrolizumab is being used in the adjuvant setting. The listed outcomes are not exhaustive, and the committee will consider evidence submitted in support of a long-term survival benefit.
Economic analysis	MSD UK	No additional comments	Comment noted.
Equality and Diversity	MSD UK	No additional comments	Comment noted.
Innovation	MSD UK	MSD considers pembrolizumab to be innovative in its potential to make a significant and substantial positive impact on health-related benefits. Pembrolizumab has the potential to improve outcomes for [redacted] Incorporation of pembrolizumab as adjuvant treatment into routine clinical practice would represent a step-change in the management of these patients.	Comment noted.
Other	MSD UK	No additional comments	Comment noted.

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considerations	Melanoma Focus	In order to be fully assessed for stage patients need access to Sentinal node biopies. This is variable across the country. For example if SNB is only available for patients with 1-4mm thick melanoma then patients with >4mm melanoma will be staged as stage 2b or c and will not be able to access the adjuvant treatment. Equality of access to SNB needs to be considered and rasied within this technology appraisal. Current NICE guidance on SNB within NG14 do not recommened SNB for all as, at the time, adjuvant treatments were not available.	Comment noted. As part of its deliberations the committee will discuss the current standard of care, which will include any variation in clinical practice.
Questions for consultation	MSD UK	**Question:** Are there any adjuvant treatments considered to be established clinical practice in the NHS for adjuvant treatment following complete resection melanoma? **Answer:** It is our understanding that adjuvant treatments are not currently routinely used in the NHS following resection of melanoma. **Question:** Is pembrolizumab intended to be used in people with high risk of recurrence? How is high risk of recurrence defined? **Answer:** Pembrolizumab is currently being studied in a clinical trial [redacted] Participants in the clinical trial include those with stage IIIA (>1mm metastasis), IIIB and IIIC melanoma. Stage III melanoma patients are at high risk of relapse. According to the data of the most recent AJCC staging committee relapse rates at 5 years for Stage IIIA, Stage IIIB and Stage IIIC are about 35%, 75% and 90% respectively. Patients with a metastasis > 1 mm have a highly significant higher risk of relapse and death than patients with a metastasis < 1 mm. **Question:** Are there any subgroups of people in whom pembrolizumab is	Comments noted.

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		expected to be more clinically effective and cost effective or other groups that should be examined separately? **Answer:** We do not currently anticipate there will be subgroups of people in whom pembrolizumab will be more clinically effective or cost effective. **Question:** Where do you consider pembrolizumab will fit into the existing NICE pathway, Melanoma? **Answer:** In line with the proposed indication, we consider that pembrolizumab will fit into the existing NICE Melanoma pathway as an option for adjuvant treatment of patients with stage III melanoma following complete resection, including complete lymphadenectomy. (Melanoma: assessment and management (NG14), July 2015; Managing stage III melanoma.) **Question:** 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? **Answer:** There are some potential benefits of post-resection adjuvant melanoma therapy with pembrolizumab that will not be captured in the QALY calculation, including: avoiding disease recurrences and any health-related quality of life (HRQoL) benefits derived by carers. **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:** We expect that data will be available from the following multicentre, international, randomised phase III trial: 'Study of Pembrolizumab (MK-3475) versus placebo after complete resection of high-risk stage III melanoma (MK-3475-054/KEYNOTE-054)' – NCT02362594	

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		Question: 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. **Answer:** We do not envisage any barriers to adoption of the technology into practice. **Question:** NICE intends to appraise this technology through its Single Technology Appraisal (STA) Process. We welcome comments on the appropriateness of appraising this topic through this process. **Answer:** We agree that the STA process is appropriate for the appraisal of pembrolizumab [redacted].	