National Institute for Health and Care Excellence

Single Technology Appraisal (STA)
Pembrolizumab with platinum-based chemotherapy for untreated advanced oesophageal or gastroesophageal cancer
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	Roche	If the study did not allow investigators to choose different chemotherapy regimens, please only include cisplatin plus fluorouracil as chemotherapy option.	Thank you for your comment. The intervention included in the remit has not been changed. This is to allow a broad remit to be evaluated in line with how the intervention is likely to be used in clinical practice. The recommendations made by the committee will be based on the available evidence and its understanding of how this reflects clinical practice.

Section	Consultee/ Commentator	Comments [sic]	Action
	Merck Sharp & Dohme	The anticipated marketing authorisation wording is [redacted]. Please update the draft remit wording to reflect the anticipated marketing authorization.	Thank you for your comment. The remit has been amended.
Timing Issues	Roche	No Comment	Thank you.
	Merck Sharp & Dohme	The provisional scheduling for this topic is appropriate.	Thank you for your comment. This topic has been scheduled into the work programme.
Additional comments on the draft remit	Merck Sharp & Dohme	None	Thank you.

Comment 2: the draft scope

Section	Consultee/ Commentator	Comments [sic]	Action
Background information	Roche	Consider adding information related to the efficacy of immunotherapy in squamous cell carcinoma vs adenocarcinoma. It is well known and reported that the two histological types respond differently to immunotherapy treatments.	Thank you for your comment. The background section provides a broad overview of the disease area and currently available treatments. It

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			is not fully exhaustive. No update required.
	Merck Sharp & Dohme	Background information is accurate and complete.	Thank you for your comment.
The technology/ intervention	Roche	Indicate the use of cisplatin plus fluorouracil instead of chemotherapy if the trial did not include other chemotherapy types.	Thank you for your comment. The intervention has not been updated. This is to allow a broad intervention to be evaluated in line with how the intervention is likely to be used in clinical practice.
	Merck Sharp & Dohme	The description of the technology is accurate.	Thank you for your comment.
Population	Roche	PD-L1 status and tumour histology can be predictive or prognostic of treatment response.	Thank you for your comment. People with PD-L1 positive oesophageal cancer have been added to the scope as a subgroup of interest.
	Merck Sharp & Dohme	Please update the population to reflect the marketing authorisation wording above.	Thank you for your comment. The

Section	Consultee/ Commentator	Comments [sic]	Action
			population has been amended.
Comparators	Roche	No comment	Thank you.
	Merck Sharp & Dohme	We agree with the proposed comparators.	Thank you for your comment.
Outcomes	Roche	Yes.	Thank you for your comment.
	Merck Sharp & Dohme	MSD considers that the outcome measures listed are appropriate. However, it is known that the response to immunotherapies (immuno-oncology drugs) may have a later onset 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 outcome measures listed, thus MSD suggests the inclusion of “Duration of Response” as an additional outcome measure.	Thank you for your comment. The list of outcomes is not exhaustive, but we note that no change to the scope is required as this additional outcome would be covered by the outcome ‘response rates’, which is already stated in the scope.
Economic analysis	Roche	No comment	Thank you.
	Merck Sharp & Dohme	No additional comments.	Thank you.

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Equality and Diversity	Roche	No comment	Thank you.
	Merck Sharp & Dohme	No additional comments.	Thank you.
Other considerations	Roche	No comment	Thank you.
	Merck Sharp & Dohme	No additional comments.	Thank you.
Innovation	Roche	No comment	Thank you.
	Merck Sharp & Dohme	MSD considers pembrolizumab to be innovative in its potential to make a significant and substantial impact on health-related benefits. Pembrolizumab has the potential to improve outcomes for oesophageal patients, being a step-change in the management of locally advanced unresectable or metastatic carcinoma of the oesophagus or HER-2 negative gastroesophageal junction adenocarcinoma.	Thank you for your comment. The committee will consider the innovation of this technology during the appraisal. No changes to the scope have been made.
Questions for consultation	Roche	No additional comments	Thank you.
Additional comments on the draft scope	Merck Sharp & Dohme	**Question:** Is oesophageal cancer clinically distinct to gastroesophageal junction cancer? **Answer**: In oesophago-gastric cancers, the main clinically relevant factor is the histology (adenocarcinoma vs squamous cell carcinoma [SCC]), rather	Thank you for your comment.

Section	Consultee/ Commentator	Comments [sic]	Action
		than the location (oesophagus, junction, stomach). However, there is a correlation between location of the tumour and histology. Cancers located in the proximal oesophagus tend to be more SCC, whereas junction and stomach cancers are more adenocarcinoma. At the metastatic stage, the location does not influence treatment for systemic therapy (except for symptoms control), but histology does. At earlier stage, location will influence treatment, with regards to surgery and radiotherapy. **Question:** Have all relevant comparators for pembrolizumab with platinum-based chemotherapy been included in the scope? **Answer**: Yes, all relevant comparators have been included in the scope. **Question:** Which treatments are considered to be established clinical practice in the NHS for untreated unresectable locally advanced, or metastatic oesophageal cancer? **Answer**: The established clinical practice in the NHS is platinum-based chemotherapy including doublet (cisplatin or oxaliplatin with fluorouracil or capecitabine) and triplet treatments (cisplatin or oxaliplatin with fluorouracil or capecitabine plus epirubicin). **Question:** Are the outcomes listed appropriate? **Answer**: We consider the listed outcomes to be appropriate. An additional comment has been added in the relevant section above. **Question:** Are there any subgroups of people in whom pembrolizumab with platinum-based chemotherapy is expected to be more clinically effective and cost effective or other groups that should be examined separately?	Subgroups based on PDL1 status and histology have been added to the scope.

Section	Consultee/ Commentator	Comments [sic]	Action
		• If evidence allows, should squamous cell carcinoma, adenocarcinoma and adenosquamous cell carcinoma be considered separately? **Answer**: MSD considers pembrolizumab in combination with platinum-based chemotherapy to offer clinical benefit within the ITT population of patients with advanced or metastatic untreated oesophageal cancer, as per the results from KEYNOTE-590. MSD recognises the sub-groups of importance are according to histology and PD-L1 expression and, if the data allows, will investigate these subgroups if appropriate. **Question:** Where do you consider pembrolizumab with platinum-based chemotherapy will fit into the existing NICE pathway, oesophageal and gastric cancer? **Answer**: We consider that pembrolizumab with platinum-based chemotherapy will fit into the existing NICE pathway as a first-line treatment option in patients with advanced/metastatic oesophageal carcinoma.	

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

Pfizer