National Institute for Health and Care Excellence

Single Technology Appraisal (STA)

Pembrolizumab with chemotherapy for treating HER2 negative advanced gastric or gastro-oesophageal junction adenocarcinoma

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

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
Appropriateness of an evaluation and proposed evaluation route	Merck Sharp & Dohme (company)	Yes, the remit is appropriate	Thank you for your comment. No action required.
	Together Support Group	Evaluation and route is considered appropriate.	Thank you for your comment. No action required.
Wording	Merck Sharp & Dohme (company)	Yes, the wording is appropriate.	Thank you for your comment. No action required.
	Together Support Group	Yes	Thank you for your comment. No action required.

Section	Consultee/ Commentator	Comments [sic]	Action
Timing Issues	Merck Sharp & Dohme (company)	There is currently a high unmet need in this patient population, therefore scheduling an appraisal in line with the regulatory submission timelines would be appropriate.	Thank you for your comment. NICE has scheduled this topic into its work programme. No action required.
	Together Support Group	We do feel it is urgent due to the large number of patients unable to have curative treatment	Thank you for your comment. NICE has scheduled this topic into its work programme. No action required.
Additional comments on the draft remit		No comments	Noted.

Comment 2: the draft scope

Section	Consultee/ Commentator	Comments [sic]	Action
Background information	Merck Sharp & Dohme (company)	Background information is accurate and complete.	Thank you for your comment. No action required.
	Together Support Group	We feel the information is complete and accurate.	Thank you for your comment. No action required.

Section	Consultee/ Commentator	Comments [sic]	Action
Population	Merck Sharp & Dohme (company)	The population is defined appropriately.	Thank you for your comment. No action required.
	Together Support Group	Yes, but we are seeing younger patients of both gender being diagnosed at later stage.	Thank you for your comment. No action required.
Subgroups	Merck Sharp & Dohme (company)	Subgroup data based on PD-L1 status is expected to be available.	Thank you for your comment. No action required.
	Together Support Group	Subgroup is younger patients, this technology may be clinically more effective because of their fitness at a younger age and generally in better health than an older patient Often diagnosed at a more advanced stage due to the vague symptoms not being recognised or considered a cancer risk, outside of the known age group.	NICE cannot make recommendations which group people on the basis of age because this is a protected characteristic under the Equalities Act 2010. This suggested subgroup has not been added to the scope.The generalisability of the trial population to the population which will have pembrolizumab in clinical practice will be taken into account.

Section	Consultee/ Commentator	Comments [sic]	Action
Comparators	Merck Sharp & Dohme (company)	NG83 clinical guidance recommends that patients with untreated HER-2 negative gastric and gastro-oesophageal junction cancer should be offered doublet and triplet chemotherapy regimens. However clinical advice to MSD suggests that triplet chemotherapy regimens are not used in clinical practice in the UK. During NICE's recent appraisals in the same therapy area, resulting in publication of TA737 and TA857, the NICE appraisal committee concluded that doublet chemotherapy is the standard of care in clinical practice. Therefore, MSD proposes that triplet chemotherapy regimens are not relevant comparators for this appraisal.	Thank you for your comment. Triplet chemotherapy has been removed from the list of comparators.
	Together Support Group	yes	Thank you for your comment. No action required.
Outcomes	Merck Sharp & Dohme (company)	MSD considers that the outcome measures listed are appropriate.	Thank you for your comment. No action required.
	Together Support Group	yes	Thank you for your comment. No action required.
Equality	Merck Sharp & Dohme (company)	No additional comments.	Thank you for your comment. No action required.
	Together Support Group	None that I can see	Thank you for your comment. No action required.

Section	Consultee/ Commentator	Comments [sic]	Action
Other considerations		No comments	
Questions for consultation	Merck Sharp & Dohme (company)	**Where do you consider pembrolizumab with chemotherapy will fit into the existing care pathway for HER2 negative advanced gastric or gastro-oesophageal junction adenocarcinoma?** MSD expects that the combination of pembrolizumab with chemotherapy will be used in line with its expected marketing authorisation in advanced metastatic settings: [redacted] **Given that pembrolizumab with chemotherapy is already recommended for people with previously untreated HER2-negative advanced gastro-oesophageal junction adenocarcinoma with a PDL1 CPS of over 10 in NICE Technology Appraisal 737, should this appraisal be limited to people with previously untreated advanced HER2-negative gastric cancer?** MSD considers that there is still an unmet need in patients with GOJ adenocarcinoma. NICE TA737 recommends pembrolizumab with platinum- and fluoropyrimidine-based chemotherapy for untreated HER2-negative advanced oesophageal and GOJ cancer in adults whose tumours express PD-L1 with a combined positive score (CPS) ≥ 10 and NICE's TA857 recommends nivolumab in patients with platinum- and fluoropyrimidine-based chemotherapy for untreated HER2-negative advanced gastric, GOJ or oesophageal adenocarcinoma whose tumours express PD-L1 with a CPS ≥ 5. Consequently, we believe that there remains an unmet need in people with gastric and GOJ cancer and a CPS < 5 who are not currently eligible for treatment with pembrolizumab (TA737) or nivolumab (TA857) as per NICE	Comments noted.

Section	Consultee/ Commentator	Comments [sic]	Action
		guidance. This proposed appraisal will address the remaining unmet need and potentially offer the first IO treatment option for patients in the above mentioned GOJ subgroups and would broaden the available treatment options for clinicians across all GOJ patients. As a result, patients with GOJ adenocarcinoma should be included in the appraisal. Also, MSD considers that pembrolizumab should be appraised within the full marketing authorisation (wording is provided in the table below). **Are the comparators appropriate? Are both doublet and triplet chemotherapy combinations used in clinical practice?** NG83 clinical guidance recommends that patients with untreated HER-2 negative gastric and gastro-oesophageal junction cancer should be offered doublet and triplet chemotherapy regimens. NICE's TA857 recommends nivolumab with platinum- and fluoropyrimidine-based chemotherapy for people with untreated HER2-negative advanced or metastatic gastric or gastro-oesophageal junction adenocarcinoma whose tumours express PD-L1 with a CPS ≥5. ESMO guidance recommends only doublet chemotherapy regimens and nivolumab for patients whose tumours express PD-L1 CPS ≥5. During NICE's recent appraisals in the same therapy area, resulting in publication of TA737 and TA857, the NICE appraisal committee concluded that doublet chemotherapy is the standard of care in clinical practice. Therefore, MSD proposes that triplet chemotherapy regimens are not relevant comparators for this appraisal. **Are the subgroups suggested in 'other considerations' appropriate? Are there any other subgroups of people in whom pembrolizumab with chemotherapy is expected to be more clinically effective and cost effective or other groups that should be examined separately?**	

Section	Consultee/ Commentator	Comments [sic]	Action
		MSD considers pembrolizumab in combination with chemotherapy to offer clinical benefit within the ITT population of patients with HER2 negative advanced gastric or GOJ adenocarcinoma, as per the expected results from KEYNOTE-859 trial. **Would pembrolizumab with chemotherapy be a candidate for managed access?** The submission to NICE will be made based on data from an interim analysis of KEYNOTE-859. Further follow-up date will become available in the future, which may mean it is appropriate to consider this technology as a candidate for managed access. **Do you consider that the use of pembrolizumab with chemotherapy can result in any potential substantial health-related benefits that are unlikely to be included in the QALY calculation?** **Please identify the nature of the data which you understand to be available to enable the committee to take account of these benefits.** MSD does not consider that the use of pembrolizumab with chemotherapy will result in any potential substantial health-related benefits that are unlikely to be included in the QALY calculation.	
Additional comments on the draft scope		No comments	Noted.

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