National Institute for Health and Care Excellence

Single Technology Evaluation

Pembrolizumab for previously treated solid tumours with high microsatellite instability or mismatch repair deficiency [ID4036]

Response to stakeholder organisation 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 and proposed process

Section	Stakeholder	Comments [sic]	Action
Appropriateness of an evaluation and proposed evaluation route	MSD (Company)	MSD agrees that evaluation of this topic, and its routing through the single technology appraisal, is appropriate	Comment noted. Thank you.
	GSK (Comparator)	No comment	Noted. Thank you.
Wording	MSD (Company)	The wording of the remit is appropriate.	Comment noted. Thank you.
	GSK (Comparator)	No comment	Noted. Thank you
Timing	MSD (Company)	The anticipated scheduling/timing of this appraisal as communicated to us by NICE is appropriate.	Comment noted. Thank you.

Section	Stakeholder	Comments [sic]	Action
	GSK (Comparator)	No comment	Noted. Thank you.

Comment 2: the draft scope

Section	Consultee/ Commentator	Comments [sic]	Action
Background information	MSD (Company)	The background information is suitably accurate and complete.	Comment noted. Thank you.
	GSK (Comparator)	No comment	Noted. Thank you.
Population	MSD (Company)	The population has been defined appropriately.	Comment noted. Thank you.
	GSK (Comparator)	No comment	Noted. Thank you.
Subgroups	MSD (Company)	We do not anticipate that there are any groups within the population that should be considered separately, or that there are subgroups in which the technology is expected to be more clinically or cost effective. MSD acknowledge that NICE have recommended exploring subgroups by tumour type and previous therapy. MSD will explore whether this is feasible, appropriate, and if patient numbers allow.	Comment noted. Thank you.
	GSK (Comparator)	No comment	Noted. Thank you.

Section	Consultee/ Commentator	Comments [sic]	Action
Comparators	MSD (Company)	The treatment options used in established clinical practice in the NHS for this indication are: • *For relevant endometrial tumours*: chemotherapy (paclitaxel, doxorubicin, gemcitabine). • *For relevant gastric tumours*: chemotherapy (taxane or irinotecan and/or 5-fluorouracil-based). • *For relevant small intestine tumours*: chemotherapy (taxane based). • *For relevant biliary tumours*: chemotherapy (irinotecan and/or 5-fluorouracil-based, pemigatinib. • *For colorectal tumours*: chemotherapy (irinotecan and/or 5-fluorouracil-based), TAS-102 (after other chemotherapy options exhausted), nivolumab + ipilimumab (2L only)	Comment noted. Thank you. The comparators in the scope have been aligned to established management. The comparators for endometrial tumours have been aligned to those included in the final scope for dostarlimab for previously treated advanced or recurrent endometrial cancer with high microsatellite instability or mismatch repair deficiency (TA779)
	GSK (Comparator)	As per NICE health technology evaluations, process and methods manual, 2022, dostarlimab is not an appropriate comparator for people with previously treated advanced or recurrent MSI-H or dMMR endometrial cancer. Section 2.2.15 of the manual states '*technologies that NICE has recommended with managed access are not considered established practice in the NHS and are not considered suitable comparators*.'. As per TA779, dostarlimab is recommended for use within the Cancer Drugs Fund, via a managed access agreement.	Comment noted. Thank you. Dostarlimab has been removed from the comparators list. The comparators for endometrial cancer have been updated to align with those included in the final scope for TA779.

Section	Consultee/ Commentator	Comments [sic]	Action
		The other comparator listed for people with previously treated advanced or recurrent MSI-H or dMMR endometrial cancer is *'established management without pembrolizumab'*. The final scope for the dostarlimab appraisal, TA779, outlined a specific list of comparator treatment options in this setting which may be appropriate for consideration for this appraisal: *'Chemotherapy, including:* *- Carboplatin and paclitaxel* *- Paclitaxel monotherapy* *- Doxorubicin monotherapy* *- Carboplatin monotherapy* *Hormone therapy (such as medroxyprogesterone acetate and megestrol)* *Best supportive care'*	
Outcomes	MSD (Company)	The outcomes listed are appropriate and will capture the most important health-related benefits and harms of the technology.	Comment noted. Thank you.
	GSK (Comparator)	No comment	Noted. Thank you.
Equality	MSD (Company)	We do not anticipate the draft remit and scope to raise any equality issues.	Comment noted. Thank you.
	GSK (Comparator)	No comment	Noted. Thank you.
Other considerations	MSD (Company)	None.	Comment noted. Thank you.
	GSK (Comparator)	No comment	Noted. Thank you.

Section	Consultee/ Commentator	Comments [sic]	Action
Questions for consultation	MSD (Company)	**Question:** What is the population size for unresectable or metastatic solid tumours with MSI-H or dMMR in England? MSD response: We currently expect that there will be approximately 500 new patients each year in England with previously treated solid tumours with high microsatellite instability or mismatch repair deficiency in the indication of relevance to this appraisal. **Question:** Which solid tumour sites are most commonly associated with MSI-H or dMMR? MSD response: dMMR/MSI-H biomarkers are associated with colorectal cancer, endometrial cancer, and gastrointestinal cancers (pancreatic, oesophageal, gastric, small bowel, biliary tract cancer [cholangiocarcinoma]). Other solid tumours such as breast, prostate and bladder cancers can also be MSI-H but it is far less common than for the GI/CRC/endo tumours. **Question:** Are screening strategies for MSI-H and dMMR in solid tumours routinely available and established in NHS practice? MSD response: NICE currently recommends that microsatellite instability (MSI) testing or immunohistochemistry (IHC) should be used on all colorectal cancers, when first diagnosed, to detect abnormalities that might mean the presence of Lynch Syndrome. NICE also recommends the centres offer testing for Lynch syndrome to people who are diagnosed with	Thank you for providing your response to these questions. Comment noted. Thank you. Comment noted. Thank you. We have aligned the scope with the solid tumour sites that are included in the marketing authorisation for MSI-H or dMMR Comment noted. Thank you.

Section	Consultee/ Commentator	Comments [sic]	Action
		endometrial cancer. We are aware that the majority of centres will do Lynch (or MSI-H) testing for CRC and endometrial cancers as per the guidelines. Currently, several genetic tests specific to MSI status (including MLH1 promoter hypermethylation) in solid tumours are commissioned by the NHS as specified in the national genomic test directory for cancer. In larger centres it is common to test the MSI-H status of other GI tumours. In smaller centres, while such testing are available to them, MSI-H/dMMR testing of tumours other than in colorectal or endometrial sites tend not to be implemented as there is currently no treatment option reimbursed specifically for patients who have MSI-H/dMMR tumours of these sites (i.e. these test are not conducted as the test results would currently have no impact on how the patients would be treated). **Question:** Which treatments are considered to be established clinical practice in NHS for MSI-H or dMMR unresectable or metastatic tumours in people who have progressed following prior therapies? MSD response: The treatment options used in established clinical practice in the NHS for this indication are: • *For relevant endometrial tumours*: Chemotherapy (paclitaxel, doxorubicin, gemcitabine). • *For relevant gastric tumours*: chemotherapy (taxane or irinotecan and/or 5-fluorouracil-based).	Comment noted. Thank you. The comparators listed in the scope aims to be inclusive. The comparators have therefore been updated to reflect established clinical practice in the NHS. The comparators listed in the

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		• *For relevant small intestine tumours*: chemotherapy (taxane based). • *For relevant biliary tumours*: chemotherapy (irinotecan and/or 5-fluorouracil-based, pemigatinib. • *For colorectal tumours*: chemotherapy (irinotecan and/or 5-fluorouracil-based), TAS-102 (after other chemotherapy options exhausted), nivolumab + ipilimumab (2L only) **Question:** Would pembrolizumab be used differently based on tumour site?	scope for endometrial tumours have been updated to align with those included in the final scope for TA779.
		MSD response: No, there would be no difference for the use of pembrolizumab (dose/method of administration) between tumour sites.	Comment noted. Thank you.
		Question: Are the outcomes listed appropriate? MSD response: Yes.	Comment noted. Thank you.
		Question: Are the subgroups suggested in 'other considerations appropriate? Are there any other subgroups of people in whom pembrolizumab is expected to be more clinically effective and cost effective or other groups that should be examined separately?	Comment noted. Thank you.

Section	Consultee/ Commentator	Comments [sic]	Action
		MSD response: We do not anticipate that there are any groups within the population that should be considered separately, or that there are subgroups in which the technology is expected to be more clinically or cost effective. MSD acknowledge that NICE have recommended exploring subgroups by tumour type and previous therapy. MSD will explore whether this is feasible, appropriate, and if patient numbers allow. **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? MSD response: No. **Question:** NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others. Please let us know if you think that the proposed remit and scope may need changing in order to meet these aims. MSD response: No changes to the proposed remit and scope are needed in order to meet these aims. **Question:** Do you consider pembrolizumab to be innovative in its potential to make a significant and substantial impact on health-related benefits and how it might improve the way that current need is met (is this a 'step-change' in the management of the condition)?	Comment noted. Thank you. Comment noted. Thank you.

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		MSD response: Pembrolizumab is innovative in its potential to make a significant and substantial impact on health-related benefits as it will be the first immune-oncologic monotherapy available for the treatment of previously treated solid tumours with MSI-H or dMMR, and so will be a step change from the current chemotherapy options that are used in clinical practice. **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? MSD response: The use of pembrolizumab may result in potential substantial health-related quality of life benefits in patients' caregivers that are unlikely to be included in the QALY calculation. It has been demonstrated that for patients with cancer, their cancer and its associated treatment can be associated with significant health-related quality of life impact in their caregivers. One of the tumour types included in this indication is that of endometrial tumours, therefore there are likely to be additional quality of life impact particularly on women on child-bearing age with such tumours as well as on their partners/families that may not be captured in the QALY calculation. As the indication to be appraised is in tumours where previous treatments have failed and where the disease may be progressing rapidly, the speed of progression of the cancer can make collection of nuanced quality of life and health-utility data in these patients challenging both practically and ethically.	Comment noted. Thank you. Comment noted. Thank you.

Section	Consultee/ Commentator	Comments [sic]	Action
	GSK (Comparator)	Which treatments are considered to be established clinical practice in NHS for MSI-H or dMMR unresectable or metastatic tumours in people who have progressed following prior therapies? The company would like to highlight the final scope agreed recently for appraisal TA779; a specific list of comparator treatment options were provided in this setting which may be appropriate for consideration for this appraisal: Chemotherapy, including: - Carboplatin and paclitaxel - Paclitaxel monotherapy - Doxorubicin monotherapy - Carboplatin monotherapy Hormone therapy (such as medroxyprogesterone acetate and megestrol) Best supportive care'	Comment noted. Thank you. The scope has been updated to align with the comparators included in the final scope for TA779.
Additional comments on the draft scope	MSD (Company)	None.	Comment noted. Thank you.
	GSK (Comparator)	No comment	Noted. Thank you.