National Institute for Health and Care Excellence

Health Technology Evaluation

Pembrolizumab with platinum-based chemotherapy then pembrolizumab maintenance for treating primary advanced or recurrent endometrial cancer ID6381

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	Peaches Womb Cancer Trust	An evaluation of this topic via the single technology appraisal route is appropriate.	Comment noted. No action required
	MSD	MSD agrees the appropriate route is a single technology appraisal.	Comment noted. No action required
Wording	Peaches Womb Cancer Trust	Yes, the remit is reflective of the issues of clinical and cost effectiveness.	Comment noted. No action required
	MSD	MSD suggests a change to the remit wording to 'People with primary advanced or recurrent endometrial cancer' to reflect the anticipated licence wording.	The title and remit have been updated to include the word 'primary'. An explanation of this has also been added to the background section.

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Timing	Peaches Womb Cancer Trust	More effective treatment strategies are required for patients with advanced or recurrent endometrial cancer. Improved long term survival and quality of life are important to patients, and have the potential to reduce health care costs associated with treatment morbidity and palliative treatment. We would therefore argue that this evaluation is required urgently.	Comment noted. We aim to publish final guidance within 90 days of receiving marketing authorisation.
	MSD	The timelines proposed for this appraisal are considered suitable.	Comment noted. No action required.

Comment 2: the draft scope

Section	Consultee/ Commentator	Comments [sic]	Action
Background information	Peaches Womb Cancer Trust	The definitions and endometrial cancer statistics are correct.	Comment noted. No action required.
	MSD	MSD has no comments to make on the background section.	Comment noted. No action required.
Population	Peaches Womb Cancer Trust	Yes	Comment noted. No action required.
	MSD	MSD suggests a change to the population wording to 'People with **primary** advanced or recurrent endometrial cancer' to reflect the anticipated licence wording.	Comment noted. The population has been updated to include '**primary'**.
Subgroups	Peaches Womb Cancer Trust	Subgroups in which to consider the effectiveness of the technology - all molecular subgroups (MMRd, NSMP, *POLE* and p53abn)	Comment noted. We have updated the

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			subgroups to reflect that other molecular subgroups may also be considered, where evidence allows.
	MSD	**Mismatch repair (MMR) immunohistochemistry status:** MSD considers subgroup analyses based on MMR status to be suitable for consideration. **Local vs metastatic recurrence:** MSD does not consider this to be a subgroup of relevance. The KEYNOTE-868 (NRG-GY018) trial is not an internal MSD trial so information concerning site of recurrence may not have been collected or cleaned in a systematic way. Forest plots available in the clinical study report (CSR) make a distinction between subgroups based on whether patients had recurrent or primary advanced disease at the start of the trial, but not explicitly based on site of recurrence (local vs. metastatic). Although the CSR for KEYNOTE-868 (NRG-GY018) does have indirect data points with regards to details about the site of recurrence (including tumour [target and non-target] identification and prior therapies [radiation, etc]), which could potentially be used to assess some of the site-relevant information for recurrent patients, MSD considers that more detailed data may have gaps and will likely be subject to limitations when attempting to interpret the data. Therefore, we do not consider local vs. metastatic recurrence to be an appropriate subgroup of relevance for consideration in the planned appraisal.	Comment noted. No action required. Comment noted. The subgroups are kept inclusive at this stage. If there is insufficient evidence for them to be considered, or if they are not relevant, the company is invited to justify this in its submission. Previous debulking surgery has been added as a subgroup, for consistency with other topics in this area.

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Comparators	Peaches Womb Cancer Trust	Appropriate comparators	Comment noted. No action required.
	MSD	**Platinum based chemotherapy** MSD suggest platinum-based chemotherapy should be changed to be 'carboplatin plus paclitaxel' to reflect the recommendation in the British Gynaecological Cancer Society's Endometrial Cancer Guidelines. (1) *'Carboplatin-paclitaxel is the recommended standard first-line chemotherapy regimen for the treatment of advanced/recurrent endometrial cancer regardless of histologic subtype.'* **Hormone Therapy** We suggest that hormone therapy is removed from the comparators, as per BGCS guidelines, this treatment is used for patients not fit for chemotherapy. (1) The guidelines also state "*there is no evidence that hormonal treatment in patients with advanced or recurrent endometrial cancer improves overall survival*". Hormone therapy is used if all other treatment options are exhausted or patients cannot tolerate further lines of chemotherapy and even then it has a palliative intent rather than an expectation of clinical response. Hormone therapy was also not included as a comparator for the recent appraisal, TA963, also in this treatment setting. **Best Supportive Care** Similarly to hormone therapy MSD suggests this is removed from the scope. BSC is a palliative pathway offered to patients who are not considered suitable for active treatment.	Comments noted. Best supportive care has been removed as a subgroup because people who are able to take pembrolizumab with platinum-based chemotherapy are, by definition, able to take platinum-based chemotherapy. So best supportive care would not be suitable for this population. Hormone therapy has been retained as a comparator. The comparators are kept inclusive at this stage. If there is insufficient evidence for them to be considered, or if they are not relevant, the company is invited to justify this in its submission.

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		In the TA963 final scope best supportive care was not included in the comparator list.(2)	
Outcomes	Peaches Womb Cancer Trust	Yes	Comment noted. No action required.
	MSD	MSD is in agreement with the outcomes listed, apart from Disease Free Survival as this is not an outcome in the KEYNOTE-868 (NRG-GY018) trial. DFS is used in trials where patients have curative intent surgery with no residual disease. Therefore DFS should be removed.	Comment noted. Disease free-survival has been removed as an outcome.
Equality	MSD	MSD does not anticipate any equality issues.	Comment noted. No action required.
Questions for consultation	MSD	**Where do you consider pembrolizumab with chemotherapy followed by maintenance pembrolizumab will fit into the existing care pathway for endometrial cancer?** MSD considers that pembrolizumab will be used in addition to the existing standard of care, carboplatin + paclitaxel. **Would pembrolizumab plus lenvatinib be an alternate treatment option to pembrolizumab with chemotherapy followed by maintenance pembrolizumab in this patient population?** The BGCS treatment recommendation for these patients is carboplatin + paclitaxel. Pembrolizumab + lenvatinib is currently reimbursed in the UK on the basis of data from the KEYNOTE-775 trial, as reflected in TA904. While the KEYNOTE-868 (NRG-GY018) trial which informs this appraisal and KEYNOTE-775 both include a subset of patients that have progressed after receiving prior adjuvant chemotherapy, it is not possible for MSD to compare	Comment noted. No action required. Comment noted. No action required. Comment noted. No action required.

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		pembrolizumab plus chemotherapy based on KEYNOTE-868 (NRG-GY018) with pembrolizumab plus lenvatinib based on TA904. [redacted]). Additionally, MSD is currently prohibited from using unpublished KEYNOTE-775 information for the purpose of HTA submissions for KEYNOTE-868 (NRG-GY018) due to contractual obligations with a third party. **Would people with primary advanced or recurrent endometrial cancer with high microsatellite instability or mismatch repair deficiency have the same treatment options as the wider patient population at this point in the treatment pathway?** The BGCS guidelines recommend carboplatin plus paclitaxel for this setting therefore a backbone of this combination would be preferable. **For people with newly diagnosed advanced endometrial cancer with microsatellite instability or mismatch repair deficiency, would pembrolizumab with platinum-based chemotherapy be considered as an alternative treatment option to dostarlimab with platinum-based chemotherapy (subject to NICE evaluation ID3968), following surgery with curative intent?** KEYNOTE-868 (NRG GY-018) is not intended to be used in patients following surgery with curative intent. The wording of the question suggests an adjuvant treatment setting where patients have no residual disease, whereas KEYNOTE-868 (NRG GY-018) is for patients who have measurable disease.	Comment noted. No action required. Comment noted. No action required.

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		Please select from the following, will insert the technology be: C: Prescribed in secondary care with routine follow-up in secondary care	Comment noted. No action required.
		For comparators and subsequent treatments, please detail if the setting for prescribing and routine follow-up differs from the intervention. There is no difference for the comparators and subsequent treatments.	Comment noted. No action required.
		Would pembrolizumab with chemotherapy be a candidate for managed access? MSD believe this intervention is a candidate for baseline NHS funding. However, MSD remains committed to patient access as a priority, and are willing to discuss options for managed access should it prove necessary.	Comment noted. No action required.
		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? MSD does not consider that the use of pembrolizumab and chemotherapy will result in any potential substantial health-related benefits that are unlikely to be included in the QALY calculation.	Comment noted. No action required.

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

N/A