National Institute for Health and Care Excellence

Health Technology Evaluation

Dostarlimab with carboplatin and paclitaxel for treating primary advanced or recurrent endometrial cancer (ID3968)

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	GSK	The company believes that evaluating this topic via the proposed evaluation route (single technology appraisal) is appropriate.	Comment noted. No action required.
	Peaches Womb Cancer Trust	An evaluation of this topic via the single technology appraisal route is appropriate.	Comment noted. No action required.
Wording	GSK	The anticipated indication statement to be included within the summary of product characteristics is: [redacted] Therefore, the company request the following change to the remit to accurately reflect the anticipated licensed population:	Scope has been amended as suggested.

Section	Stakeholder	Comments [sic]	Action
		"Dostarlimab with platinum-containing chemotherapy for treating adult patients with primary advanced or recurrent endometrial cancer"	
	Peaches Womb Cancer Trust	Yes	Comment noted. No action required.
Timing issues	GSK	The proposed NICE submission date of the technology is [redacted] 2023. The NHS would benefit from appraisal of this technology at this time due to a high level of unmet need driven by the lack of effective, approved treatment options in this indication. To date there has been no NICE guidance issued for a medicine in the first line treatment of advanced/recurrent endometrial cancer. The company believe it is of utmost importance that the proposed appraisal scheduling is maintained, enabling NICE to issue timely final guidance after regulatory approval. Information regarding the anticipated regulatory timelines are accurately included with UK PharmaScan to reflect current expectations.	Comments noted. NICE has scheduled this topic into its work programme. For further details, see the NICE website: https://www.nice.org.uk/guidance/indevelopment/gid-ta10850. No action required.
	Peaches Womb Cancer Trust	There is an urgent need for more effective treatments for those with advanced or recurrent endometrial cancer that are more widely accessible to all. Improved long term survival and quality of life are important to patients, and have potential to reduce health care costs associated with treatment morbidity and palliative treatments. We would therefore argue that this evaluation is required urgently.	Comments noted. NICE has scheduled this topic into its work programme. For further details, see the NICE website: https://www.nice.org.uk/guidance/indevelopment/gid-ta10850. No action required.

Section	Stakeholder	Comments [sic]	Action
Additional comments on the draft remit			

Comment 2: the draft scope

Section	Consultee/ Commentator	Comments [sic]	Action
Background information	GSK	The clinical trial mentioned when describing the technology is the RUBY trial (NCT03981796). Part I of this trial only is relevant and within scope for this appraisal. The regimen investigated in Part I of the RUBY trial is dostarlimab plus carboplatin-paclitaxel followed by dostarlimab monotherapy compared with carboplatin-paclitaxel plus placebo followed by placebo in people with recurrent or primary advanced (Stage 3 or 4) endometrial cancer.[1] Part II of the RUBY trial is not within scope for this appraisal. Part II investigates dostarlimab plus carboplatin-paclitaxel followed by dostarlimab plus niraparib compared with carboplatin-paclitaxel plus placebo followed by placebo in participants with recurrent or primary advanced (FIGO Stage 3 or 4) endometrial cancer.[1] The company therefore request that within *The Technology* section the text is amended to reflect: *"It has been studied in a clinical trial in which dostarlimab plus carboplatin-paclitaxel followed by dostarlimab monotherapy ~~plus niraparib~~ were compared with carboplatin-paclitaxel plus placebo followed by placebo in people with recurrent or primary advanced (Stage 3 or 4) endometrial cancer"*	Scope has been amended as suggested.

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		1. *A Study to Evaluate Dostarlimab Plus Carboplatin-paclitaxel Versus Placebo Plus Carboplatin-paclitaxel in Participants With Recurrent or Primary Advanced Endometrial Cancer - Full Text View - ClinicalTrials.gov* *Accessed 07/02/23*	
	Peaches Womb Cancer Trust	Whilst the definitions and endometrial cancer statistics are correct, we feel that there are some gaps in the background information. • The background correctly states the symptoms of endometrial cancer recurrence, however does not explicitly state that these are also the clinical presentation of advanced stage disease. • The background covers the treatment of advanced endometrial cancer accurately and in much detail, however does not describe the treatment options available to those with recurrence. This is important, as treatment options in recurrence are extremely limited and we feel this should be highlighted. • The background does not indicate the number/ incidence of people diagnosed with advanced and recurrent endometrial cancer. This is important to highlight to understand the scale of the issue and how many people it affects.	Scope has been amended as suggested regarding clinical presentation of advanced stage disease and incidence of recurrent endometrial cancer. Treatment options recommended by NICE for advanced/recurrent endometrial cancer are already included in scope.
Population	GSK	The company suggests alternative wording based on the anticipated indication statement: *"People with primary advanced or recurrent endometrial cancer"*	Scope has been amended as suggested.
	Peaches Womb Cancer Trust	Yes	Comments noted. No action required.
Subgroups	GSK	Within the RUBY trial Part 1 (NCT03981769), patients with primary advanced/recurrent endometrial cancer were eligible for inclusion, as per the trial inclusion and exclusion criteria, and irrespective of their biomarker	Subgroups added to the scope.

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		status.[1] Patients DNA mismatch repair deficiency (dMMR) status was considered during sample size calculations and as a stratification factor to ensure the trial population contained a representative mixture of patients whose disease was dMMR/Microsatellite instability high (MSI-H) and DNA mismatch repair proficient (MMRp), as seen in real world clinical practice. The trial's hypothesis for evaluating the primary efficacy parameters [redacted] As per the trial design, the populations for consideration are: [redacted] 1. *A Study to Evaluate Dostarlimab Plus Carboplatin-paclitaxel Versus Placebo Plus Carboplatin-paclitaxel in Participants With Recurrent or Primary Advanced Endometrial Cancer - Full Text View - ClinicalTrials.gov Accessed 07/02/23* 2. *RUBY trial protocol (GSK data on file) 31/03/2022*	
	Peaches Womb Cancer Trust	Subgroups in which to consider the effectiveness of the technology: • People with mismatch repair deficient tumours • Local vs metastatic recurrence • People who have had primary debulking surgery vs those who have not had surgery	Subgroups added to the scope.
Comparators	GSK	– Carboplatin with paclitaxel Guidelines suggest carboplatin-paclitaxel doublet should be considered the first-line therapy for advanced (stage 3 or 4) or recurrent endometrial cancer.[1,2] UK experts suggest carboplatin-paclitaxel doublet is the primary	Comments noted. Hormone therapy and best supportive care have been removed from the final scope.

Section	Consultee/ Commentator	Comments [sic]	Action
		first line systemic therapy used in the population relevant to this appraisal.[3] In a recent study of patients with recurrent or advanced endometrial cancer in England, the majority of patients (77.8% [n=1,824]) in a cohort of patients eligible for immune checkpoint inhibitor (ICI) trials who were treated with first line systemic chemotherapy (n=2,345) received carboplatin-paclitaxel.[4] Finally, carboplatin-paclitaxel was chosen as the comparator for the RUBY trial as it is the first line systemic treatment which, to date, has demonstrated the best survival outcomes in this population and is the guidelines recommended standard of care.[1,2] The RUBY trial therefore provides direct comparative data versus the most efficacious, and most broadly used, available treatment option for the relevant patient population. – Hormone therapy (such as medroxyprogesterone acetate and megestrol) The company request that hormone therapy is removed as a comparator. Hormone therapy is used in a limited patient population in the first line treatment of advanced/recurrent endometrial cancer; disease which is hormone receptor positive, low-grade carcinoma, endometrioid histology with indolent disease, in patients who are not fit/suitable for primary surgery.[1,2,3] Patients who are not fit for surgery (reasons often include extreme obesity and medical comorbidities[3]), or not fit for first line carboplatin-paclitaxel doublet, are not fit enough to receive the RUBY treatment regimen (platinum containing chemotherapy in combination with dostarlimab). Patients who are not appropriate candidates for carboplatin-paclitaxel doublet are not the appropriate population for this appraisal. - Paclitaxel monotherapy The company request that paclitaxel monotherapy is removed as a comparator. Paclitaxel monotherapy is not a standard of care treatment for	The list of chemotherapies has been updated to "*platinum-based doublet chemotherapy*". It has also been specified that pembrolizumab plus lenvatinib is only a comparator in people who had neoadjuvant or adjuvant platinum-based doublet chemotherapy.

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		first line treatment of advanced/recurrent endometrial cancer as per guidelines.[1,2] Guidelines note the use of monotherapy chemotherapies as an option for the treatment of patients with advanced/recurrent EC whose disease has relapsed following first line treatment (second line treatment). [1,2] This is not the line of treatment relevant to this appraisal. UK experts consulted by GSK stated that paclitaxel monotherapy would only be considered in the first line setting when relapse occurs within six months following adjuvant treatment.[3] Within the RUBY trial exclusion criteria, patients who had recurrence within six months of completing adjuvant systemic anticancer therapy treatment were not eligible for inclusion.[5] Patients who are not appropriate candidates for carboplatin-paclitaxel doublet are not the appropriate population for this appraisal. – Doxorubicin monotherapy The company request that doxorubicin monotherapy is removed as a comparator. Doxorubicin monotherapy is not a standard of care treatment for first line treatment of advanced/recurrent endometrial cancer per guidelines.[1,2] Guidelines and UK clinical experts note the use of monotherapy chemotherapies as an option for the treatment of patients with advanced/recurrent EC whose disease has relapsed following first line treatment (second line treatment). [1,2,3] Doxorubicin in combination with other chemotherapies was also noted as a treatment option in the relapsed disease setting by UK clinical experts. This is not the line of treatment relevant to this appraisal. Patients who are not appropriate candidates for carboplatin-paclitaxel doublet are not the appropriate population for this appraisal.	

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		– Carboplatin monotherapy The company request that carboplatin monotherapy is removed as a comparator. Carboplatin monotherapy is not included as a first line systemic treatment option within guidelines or by UK experts. [1,2,3] Guidelines note the use of monotherapy chemotherapies as an option for the treatment of patients with advanced/recurrent EC whose disease has relapsed following first line treatment (second line treatment). [1,2] This is not the line of treatment relevant to this appraisal. Patients who are not appropriate candidates for carboplatin-paclitaxel doublet are not the appropriate population for this appraisal. – Best supportive care The company request that best supportive care is removed as a comparator. Best supportive care is not an appropriate first line treatment option for fit patients with advanced/recurrent endometrial cancer. Patients who are not appropriate candidates for carboplatin-paclitaxel doublet are not the appropriate population for this appraisal. - Pembrolizumab plus lenvatinib Lenvatinib with pembrolizumab for untreated recurrent or advanced endometrial cancer (ID3966) is currently awaiting development within the NICE guidance development process. This combination of treatments does not currently have a first line licence, it is not recommended by NICE or within any guidance, and there is no available published data from the Phase III pivotal trial (NCT04776148). Therefore, this is not an appropriate comparator at this time for consideration within this appraisal.	

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		1. *British Gynaecological Cancer Society (BGCS) Uterine Cancer Guidelines: Recommendations for Practice. Morrison et al (2021)* 2. *Endometrial cancer: ESMO Clinical Practice Guideline for diagnosis, treatment and follow-up. Oaknin et al (2022)* 3. *Advanced/Recurrent endometrial cancer treatment pathway clinical advisory board (GSK data on file) – July 2022* 4. *Demographic and survival outcomes in patients with advanced or recurrent endometrial cancer in the English real-world setting. Ingles Russo Garces et al (2023) [poster presentation at ESMO-Gyn]* 5. *RUBY trial protocol (GSK data on file) 31/03/2022*	
	Peaches Womb Cancer Trust	Yes	Comment noted. Hormone therapy and best supportive care have been removed from the final scope. The list of chemotherapies has been updated to "*platinum-based doublet chemotherapy*". It has also been specified that pembrolizumab plus lenvatinib is only a comparator in people who had neoadjuvant or adjuvant platinum-based doublet chemotherapy.

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Outcomes	GSK	The company agrees with the proposed outcome measures. Also, to be included: - Disease control rate - Time to second objective disease progression (PFS2)	Comments noted. 'Disease control rate' and 'Time to second objective disease progression' would be covered by the outcome 'response rates' included in the scope. No action required.
	Peaches Womb Cancer Trust	Yes	Comment noted. No action required.
Equality	GSK	There are no equality issues identified at this stage.	Comment noted. No action required.
	Peaches Womb Cancer Trust	No changes required.	Comment noted. No action required.
Other considerations	GSK	No additional comments	Comment noted. No action required.
	Peaches Womb Cancer Trust	None identified.	Comment noted. No action required.
Questions for consultation	GSK	**Where do you consider dostarlimab with carboplatin and paclitaxel will fit into the existing care pathway for recurrent or advanced endometrial cancer?**	Comments noted. No action required.

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		For patients with recurrent or primary advanced endometrial cancer, platinum-based chemotherapy, whilst not specifically licensed, is considered a standard of care for front-line treatment, with the most common regimen being carboplatin-paclitaxel. As outlined previously, carboplatin-paclitaxel is recommended as first line treatment in this indication in relevant UK clinical guidelines.[1,2] The use of carboplatin-paclitaxel as standard of care in this population was validated by UK clinicians at a 2022 advisory board and aligns with recent English real-world data on treatments used in this population.[3,4] The anticipated dostarlimab indication is in combination with the current standard of care. Patients who are clinically appropriate to receive the carboplatin-paclitaxel regimen as first line treatment would have the addition of dostarlimab as a third component in the regimen. As per the anticipated dosage regimen, dostarlimab would be [redacted][5] Dostarlimab is administered by intravenous infusion using an intravenous infusion pump over 30 minutes.[6] During the combination phase dostarlimab and platinum chemotherapy would be administered during the same appointment. IV administration of dostarlimab during the monotherapy phase is not displacing any treatments within the existing care pathway. **Would dostarlimab with carboplatin and paclitaxel be a candidate for managed access?** GSK is [redacted]	

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		Do you consider that the use of dostarlimab with carboplatin and paclitaxel can result in any potential substantial health-related benefits that are unlikely to be included in the QALY calculation? Health related quality of life from the RUBY trial Part 1 (NCT03981769) will be included within the submission to demonstrate the quality-of-life benefits associated with the use of dostarlimab with platinum containing chemotherapy. While the trial will aim to accurately capture this benefit during the available follow up period, it is possible that the impact to health-related quality of life will not be sufficiently captured due to limited duration of follow up. The QALY calculation should accurately capture the health-related quality of life experienced by the patient over the lifetime time horizon. **Please identify the nature of the data which you understand to be available to enable the committee to take account of these benefits.** Clinical data related to long term health-related quality of life and clinical expert opinion will be explored to ensure all health-related quality of life benefits are accounted for. 1. *British Gynaecological Cancer Society (BGCS) Uterine Cancer Guidelines: Recommendations for Practice. Morrison et al (2021)* 2. *Endometrial cancer: ESMO Clinical Practice Guideline for diagnosis, treatment and follow-up. Oaknin et al (2022)* 3. *Advanced/Recurrent endometrial cancer treatment pathway clinical advisory board (GSK data on file) – July 2022* 4. *Demographic and survival outcomes in patients with advanced or recurrent endometrial cancer in the English real-world setting. Ingles Russo Garces et al (2023) [poster presentation at ESMO-Gyn]* 5. *RUBY trial protocol (GSK data on file) 31/03/2022* 6. *JEMPERLI 500 mg concentrate for solution for infusion summary pf product characteristics https://www.medicines.org.uk/emc/product/12669/smpc (accessed 07/02/2023)*	

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	Peaches Womb Cancer Trust	***1.*** *Where do you consider dostarlimab with carboplatin and paclitaxel will fit into the existing care pathway for recurrent or advanced endometrial cancer?* As both a primary treatment and potentially a maintenance treatment. ***2.*** *Would dostarlimab with carboplatin and paclitaxel be a candidate for managed access?* Yes ***3.*** *Do you consider that the use of dostarlimab with carboplatin and paclitaxel can result in any potential substantial health-related benefits that are unlikely to be included in the QALY calculation?* No ***4.*** *Please identify the nature of the data which you understand to be available to enable the committee to take account of these benefits.* N/A	Comments noted. No action required.

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

Endometriosis UK (not taking part)