National Institute for Health and Care Excellence

Health Technology Evaluation

Dostarlimab with platinum-based chemotherapy for advanced or recurrent endometrial cancer with microsatellite stability or mismatch repair proficiency

Response to stakeholder organisation comments on the draft remit and draft scope

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Comment 1: the draft remit and proposed process

Section	Stakeholder	Comments [sic]	Action
Appropriateness of an evaluation and proposed evaluation route	GSK	GSK believes it is appropriate to evaluate this technology through the NICE Single Technology Appraisal process.	Thank you for your comment. No action required.
	Peaches Womb Cancer Trust	An evaluation of this topic via the single technology route is appropriate.	Thank you for your comment. No action required.
Wording	GSK	GSK believes the proposed remit is appropriate and correctly reflects the evaluation objective.	Thank you for your comment. No action required.

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	Peaches Womb Cancer Trust	Yes	Thank you for your comment. No action required.
Timing issues	GSK	This patient population is an underserved group of patients with limited treatment options and poor prognosis. Adherence to the proposed timelines is critical to minimise any lag between marketing authorisation and patient access to new therapies.	Thank you for your comment. This topic has been scheduled into the work programme.
	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. The ability to live well for longer, with minimal and manageable side effects from treatment is very important to patients living with advanced and recurrent womb cancer. Having access to a more effective treatment would enable people with *all* molecular subtypes of advanced or recurrent endometrial cancer to live longer, fuller lives. We would therefore argue that this evaluation is required urgently.	Thank you for your comment. This topic has been scheduled into the work programme.

Comment 2: the draft scope

Section	Consultee/ Commentator	Comments [sic]	Action
Background information	GSK	The background section has omitted a description of recurrent endometrial cancer as applicable to the anticipated marketing authorisation. Recurrent endometrial cancer refers to endometrial cancer which recurs following optimal surgical intervention, which may include neo-adjuvant or adjuvant chemotherapy, which is of curative intent[1,2].	Thank you for your comment. The scope has been updated with a description of recurrent cancer. Please note that the

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		Within the description of the treatment pathway additional clarity would help to distinguish between interventions and treatments used in the adjuvant, first line, and relapsed setting of primary advanced or recurrent endometrial cancer. Adjuvant chemotherapy or chemoradiation may be considered alongside curative-intent surgery particularly in early staged cancers[3]. For primary advanced or recurrent endometrial cancer, the standard-of-care treatment consists of surgery where appropriate followed by carboplatin and paclitaxel as a first line of treatment[4]. Subsequently, for patients who then experience relapse or metastasis, despite first line chemotherapy, treatment options include hormone therapy, immunotherapy, targeted therapy and chemotherapy. 1. *Rütten H, Verhoef C, van Weelden WJ, Smits A, Dhanis J, Ottevanger N, Pijnenborg JMA. Recurrent Endometrial Cancer: Local and Systemic Treatment Options. Cancers (Basel). 2021 Dec 14;13(24):6275. doi: 10.3390/cancers13246275. PMID: 34944893; PMCID: PMC8699325.* 2. *Del Carmen, MARCELA G., I. I. DAVID M BORUTA, and JOHN O. Schorge. "Recurrent endometrial cancer." Clinical obstetrics and gynecology 54.2 (2011): 266-277.* 3. *DeLeon, Maria C., Natraj R. Ammakkanavar, and Daniela Matei. "Adjuvant therapy for endometrial cancer." Journal of gynecologic oncology 25.2 (2014): 136-147.* 4. *Morrison, Jo, et al. "British Gynaecological Cancer Society (BGCS) uterine cancer guidelines: Recommendations for practice." European Journal of Obstetrics & Gynecology and Reproductive Biology 270 (2022): 50-89.*	background section is intended as a brief overview of the condition and current treatment.
	Peaches Womb Cancer Trust	For consistency, we suggest replacing the first paragraph in the background section with the first paragraph from the background section from the final scope from TA963, since this provides more comprehensive information on the clinical presentation of recurrent or advanced stage disease: **Background**	Thank you for your comment. The scope has been updated with a description of recurrent cancer.

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		Endometrial cancer is a cancer of the lining of the womb (uterus), known as the endometrium. It is the most common type of womb cancer, often diagnosed in the earlier stages. When diagnosed, endometrial cancer is categorised between stage 1 and 4. Advanced endometrial cancer is defined as stage 3 or 4, where the cancer has spread outside the womb. In stage 3, the spread of cancer is contained within the pelvis. Once the cancer has spread into another area of the body, it is classed as stage 4 or metastatic (stages 3 and 4 are known as advanced cancer). Recurrent endometrial cancer is when the cancer returns after primary treatment. The cancer can recur anywhere, commonly in the abdominal cavity, lymph nodes, lung and vagina. The symptoms of recurrence and advanced stage disease are variable but include abdominal pain, bloating, nausea, shortness of breath, vaginal bleeding and changes in bowel or bladder habits.[1] Ref: Final scope (July 2023) https://www.nice.org.uk/guidance/ta963/history	
Population	GSK	GSK believes the population is adequately defined.	Thank you for your comment. No action required.
	Peaches Womb Cancer Trust	Yes	Thank you for your comment. No action required.
Subgroups	GSK	GSK does not believe the subgroups as suggested in the draft scope are appropriate for consideration as part of the appraisal. **Local versus metastatic recurrence**	Thank you for your comment. These subgroups have been kept in the scope. The committee will assess the available evidence

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		Within the pivotal RUBY trial which evaluated dostarlimab within the proposed indication, recurrence was captured as a yes/no binary variable and the location of recurrence was not recorded. Subgroup analysis has been performed on patients with recurrent disease but, within this subgroup, further analysis based on location of recurrence is not feasible. In addition, guidelines recommend carboplatin-paclitaxel for first line treatment regardless of recurrence location. Therefore, GSK do not believe it is informative for subgroups based on local or metastatic recurrence to be considered as part of this technology appraisal. **People who had primary debulking surgery vs people who have not:** GSK do not believe this to be a subgroup of relevance. All patients typically undergo surgery to debulk primary advanced endometrial cancer unless the patient is insufficiently fit. The RUBY trial recruited patients regardless of prior surgical status, however the majority had undergone prior surgery for MMRp EC ([redacted]). The small number of patients not receiving surgery would likely prevent any meaningful conclusions from being drawn from a subgroup analysis. Furthermore, it is also unlikely to be feasible to carry out this analysis given how information relating to surgery was collected as part of the RUBY trial. Within the clinical study report prior anti-cancer surgery for endometrial cancer is captured as a 'yes/no' variable and therefore the type and/or outcome of surgery is not readily available.	and determine the relevant subgroups.
	Peaches Womb Cancer Trust	Since the microsatellite stable or mismatch repair proficient group includes the molecular subgroups NSMP, POLE and p53abn, which may respond differently to the technology, these subgroups may need to be considered separately.	Thank you for your comment. The committee will assess

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			evidence on molecular subgroups if available. The scope has been updated to include this.
Comparators	GSK	**Hormone therapy** As recognised within national BGCS guidelines, platinum containing chemotherapy (namely carboplatin-paclitaxel doublet) is the standard-of-care treatment for patients with primary advanced or recurrent endometrial cancer[1]. The evidence supporting the use of hormone therapy in endometrial cancer is sparse, with variable response rates reported[2]. The absence of evidence to support a survival benefit result in this being cited as a palliative systemic therapy in this setting within guidelines[1]. It is considered for use in only a subset of primary advanced or recurrent cancer patients based on grading, hormone receptor status and primarily for those unsuitable for treatment with cytotoxic chemotherapy[1,3]. Therefore, patients requiring treatment with hormone therapy would be unsuitable for dostarlimab *in combination chemotherapy*, precluding it from being considered a relevant comparator. This has been acknowledged previously as part of TA963 which has recommended dostarlimab in combination with platinum-based chemotherapy in an analogous setting for patients who are MMR deficient[4]. **Durvalumab with platinum-based chemotherapy, followed by durvalumab with or without olaparib maintenance (subject to NICE appraisal)** Durvalumab with platinum-based chemotherapy, followed by durvalumab with or without olaparib maintenance is an inappropriate comparator, as it is not established standard of care in the NHS and therefore should not be included	Thank you for your comment. The scope intends to be inclusive at this stage. The committee will determine the relevant comparators. Durvalumab and pembrolizumab may become established NHS practice by the time of the first committee meeting for dostarlimab.

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		in the scope, per the NICE methods. This is yet an unlicensed treatment and not routinely available within the NHS. As described in the NICE manual under Sections 2.2.12 and 2.6.1, comparators considered at the scoping stage are required to be established practice in the NHS[5]. GSK are aware this treatment is undergoing a NICE technology appraisal however a recommendation is not expected until 21st May 2025. GSK do not consider it appropriate or reasonable to include a comparator subject to a NICE appraisal outcome which may occur only after the submission date of the proposed dostarlimab indication. Furthermore, the clinical trial within which this treatment was investigated has been reviewed by both the FDA in the United States and by the EMA in Europe however there have been significant divergences in the indication statements in each case. Notably, this regimen is not recommended for patients with MMRp/MSS endometrial cancer in the United States and within Europe the use of olaparib is mandated per the SmPC posology[6,7]. **Pembrolizumab with platinum-based chemotherapy, followed by pembrolizumab maintenance (subject to NICE appraisal)** Pembrolizumab with platinum-based chemotherapy is an inappropriate comparator per the NICE methods and should be removed from the appraisal scope. As described above, it is prescribed in the NICE manual under Sections 2.2.12 and 2.6.1 that comparators considered at the scoping stage are required to be established practice in the NHS[5]. Pembrolizumab with platinum-based chemotherapy, followed by pembrolizumab maintenance is not currently licensed for the treatment of primary advanced or recurrent endometrial cancer, nor is it routinely available for use within the NHS and so cannot be considered part of established practice.	

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		Furthermore, undertaking a comparison to a technology not yet licensed and without a NICE recommendation until after GSK submission date is impractical. GSK is aware pembrolizumab has been investigated in this setting and is undergoing a NICE technology appraisal. Per information available on the NICE project page, it will be April 2025 at the earliest when NICE will make a recommendation on whether, and under what circumstances, it is made available within the NHS[8]. 1. *Morrison, Jo, et al. "British Gynaecological Cancer Society (BGCS) uterine cancer guidelines: Recommendations for practice." European Journal of Obstetrics & Gynecology and Reproductive Biology 270 (2022): 50-89.* 2. *Kokka, Fani, et al. "Hormonal therapy in advanced or recurrent endometrial cancer." Cochrane Database of Systematic Reviews 12 (2010).* 3. *Wagner, Vincent M., and Floor J. Backes. "Do not forget about hormonal therapy for recurrent endometrial cancer: A review of options, updates, and new combinations." Cancers 15.6 (2023): 1799.* 4. *National Institute for Health and Care Excellence, TA963 Dostarlimab with platinum-based chemotherapy for treating advanced or recurrent endometrial cancer with high microsatellite instability or mismatch repair deficiency, 2024* 5. *National Institute for Health and Care Excellence. (2022). NICE health technology evaluations: the manual (NICE process and methods [PMG36]).* 6. *European Medicines Agency 2024, Imfinzi EPAR, https://www.ema.europa.eu/en/medicines/human/EPAR/imfinzi* 7. *FDA 2024, IMFINZI prescribing information, https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm* 8. *National Institute for Health and Care Excellence, ID6381 Pembrolizumab with platinum-based chemotherapy then pembrolizumab maintenance for treating primary advanced or recurrent endometrial cancer, 2024, https://www.nice.org.uk/guidance/indevelopment/gid-ta11461*	
	Peaches Womb Cancer Trust	-	Thank you.

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Outcomes	GSK	The endpoints listed are all considered appropriate. PFS and OS, being the primary endpoints of the RUBY trial, as well as being well recognised endpoints within oncology trials are well placed to capture the most important health related benefits (and harms) of the technology. Time to the second progression event or death (PFS2) is also a clinically important endpoint to consider as part of this appraisal.	Thank you for your comment. No action required.
	Peaches Womb Cancer Trust	Yes	Thank you for your comment. No action required.
Equality	GSK	There are no equality issues identified at this stage.	Thank you for your comment. No action required.
	Peaches Womb Cancer Trust	-	Thank you.
Other considerations	GSK	-	Thank you.
	Peaches Womb Cancer Trust	None	Thank you.
Questions for consultation	GSK	Dostarlimab is currently prescribed in secondary care followed by routine follow-up in secondary care for its existing indications within endometrial cancer. This is not expected to change for the proposed indication:	Thank you for your comment. No action required.

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		dostarlimab with platinum-based chemotherapy for advanced or recurrent endometrial cancer with microsatellite stability or mismatch repair proficiency **Where do you consider of dostarlimab with carboplatin and paclitaxel will fit into the existing care pathway for recurrent or advanced endometrial cancer?** GSK expects dostarlimab to be used as an add-on therapy to carboplatin and paclitaxel, the current standard-of-care for patients with MMRp primary advanced or recurrent endometrial cancer[1]. **Would dostarlimab with carboplatin and paclitaxel be a candidate for managed access?** GSK expects there to be limited uncertainty in the clinical and cost-effectiveness of dostarlimab with carboplatin and paclitaxel and so should be considered for baseline funding. However, managed access may be considered should significant areas of uncertainty be identified during the appraisal process. **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?** GSK anticipates the health-related quality-of-life benefits of dostarlimab are likely to be captured within the QALY calculation.	Thank you for your comment. No action required. Thank you for your comment. No action required. Thank you for your comment. No action required.

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		Morrison, Jo, et al. "British Gynaecological Cancer Society (BGCS) uterine cancer guidelines: Recommendations for practice." European Journal of Obstetrics & Gynecology and Reproductive Biology 270 (2022): 50-89.	
	Peaches Womb Cancer Trust	**Where do you consider dostarlimab will fit into the existing care pathway for MMRp/MSS endometrial cancer?** *C. Prescribed in secondary care with routine follow-up in secondary care* *For comparators and subsequent treatments, the setting for prescribing and routine follow-up **would not differ** from the intervention.* **Would dostarlimab be a candidate for managed access?** *Yes* **Do you consider that the use of dostarlimab can result in any potential substantial health-related benefits that are unlikely to be included in the QALY calculation?** *No*	Thank you for your comment. No action required. Thank you for your comment. No action required. Thank you for your comment. No action required.