NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Evaluation

Dostarlimab for previously treated advanced or recurrent endometrial cancer with high microsatellite instability or mismatch repair deficiency (MA review of TA779) [ID6326]

Final scope

Final remit/evaluation objective

To appraise the clinical and cost effectiveness of dostarlimab within its marketing authorisation for previously treated advanced or recurrent endometrial cancer with high microsatellite instability (MSI-H) or mismatch repair deficiency (dMMR).

Background

Endometrial cancer is a cancer of the lining of the womb (uterus), known as the endometrium. It is the most common type of uterine 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. 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. The mismatch repair (MMR) system recognises and repairs genetic mismatches generated during DNA replication in cells. Around 26% of endometrial tumours have a defect in the MMR system.¹ Tumours with MMR deficiency can develop microsatellite instability. which is a change in the length of repetitive sequences in tumour DNA compared with normal DNA.

In 2022, there were 8,556 new cases of endometrial cancer in England.² Around 79% of people have early-stage disease and around 21% have advanced or metastatic disease on diagnosis.³ Around 13% of people with early-stage disease have a recurrence after initial treatment.⁴

In advanced or recurrent endometrial cancer, initial treatment may include a combination of surgery, radiation and chemotherapy. Hormone therapy may also be used, usually in a palliative setting.⁵⁻⁷ Standard chemotherapy options for advanced or recurrent endometrial cancer are platinum-containing regimens, the most common is carboplatin plus paclitaxel. NICE technology appraisal guidance 963 recommends dostarlimab with platinum-based chemotherapy for use in the Cancer Drugs Fund (CDF) as an option for treating advanced or recurrent endometrial cancer with high microsatellite instability or mismatch repair deficiency in adults who are candidates for systemic therapy. This appraisal is currently under review. Other immunotherapy-containing systemic therapies may be used after chemotherapy:

 NICE technology appraisal guidance 904 recommends pembrolizumab with lenvatinib for treating advanced or recurrent endometrial cancer in adults

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whose cancer has progressed on or after a platinum-based therapy and who cannot have curative surgery or radiotherapy.

 NICE technology appraisal guidance 914 recommends pembrolizumab for treating advanced or recurrent endometrial cancer with high microsatellite instability or mismatch repair deficiency in adults whose cancer has progressed during or after a platinum-based therapy, who cannot have curative surgery or radiotherapy.

Currently dostarlimab is recommended for use in the Cancer Drugs Fund as an option for treating advanced or recurrent endometrial cancer with high microsatellite instability or mismatch repair deficiency in adults who have had platinum-based chemotherapy (NICE technology appraisal guidance 779). This appraisal will update and replace technology appraisal 779.

The technology

Dostarlimab (Jemperli, GlaxoSmithKline) as monotherapy has a marketing authorisation for treating adults with mismatch repair deficiency (dMMR) or high microsatellite instability (MSI-H) primary advanced or recurrent endometrial cancer that has progressed on or following a platinum-containing therapy.

Intervention(s)	Dostarlimab
Population(s)	People with advanced or recurrent MSI-H or dMMR endometrial cancer, whose disease has progressed on or following treatment with a platinum-containing therapy
Comparators	 Chemotherapy, which may include: Carboplatin and paclitaxel Paclitaxel monotherapy Doxorubicin monotherapy Carboplatin monotherapy Pembrolizumab with lenvatinib
	 Pembrolizumab

Outcomes	The outcome measures to be considered include:
	progression-free survival
	overall survival
	response rates
	duration of response
	time to treatment discontinuation
	adverse effects of treatment
	health-related quality of life.
Economic analysis	The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year.
	The reference case stipulates that the time horizon for estimating clinical and cost effectiveness should be sufficiently long to reflect any differences in costs or outcomes between the technologies being compared.
	Costs will be considered from an NHS and Personal Social Services perspective.
	The availability of any commercial arrangements for the intervention, comparator and subsequent treatment technologies will be taken into account.
Other considerations	Guidance will only be issued in accordance with the marketing authorisation. Where the wording of the therapeutic indication does not include specific treatment combinations, guidance will be issued only in the context of the evidence that has underpinned the marketing authorisation granted by the regulator.
Related NICE recommendations	Related technology appraisals:
	Dostarlimab for previously treated advanced or recurrent endometrial cancer with high microsatellite instability or mismatch repair deficiency (2022) NICE technology appraisal guidance 779.
	Pembrolizumab with lenvatinib for previously treated advanced or recurrent endometrial cancer (2023) NICE technology appraisal guidance 904.
	Pembrolizumab for previously treated endometrial, biliary, colorectal, gastric or small intestine cancer with high microsatellite instability or mismatch repair deficiency (2023) NICE technology appraisal guidance 914.
	Related technology appraisals in development:
	Dostarlimab with platinum-based chemotherapy for treating advanced or recurrent endometrial cancer with high

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	microsatellite instability or mismatch repair deficiency (MA review of TA963). NICE technology appraisal guidance [ID6426] Publication expected May 2025.
	Durvalumab with platinum-based chemotherapy, then with or without olaparib, for treating newly diagnosed advanced or recurrent endometrial cancer. NICE technology appraisal guidance [ID6317] Publication expected May 2025.
	Pembrolizumab with carboplatin and paclitaxel for untreated advanced or recurrent endometrial cancer. NICE technology appraisal guidance [ID6381] Publication expected July 2025.
	Related interventional procedures:
	Laparoscopic hysterectomy (including laparoscopic total hysterectomy and laparoscopically assisted vaginal hysterectomy) for endometrial cancer (2010) NICE interventional procedures guidance 356.
	Related diagnostic guidance:
	Testing strategies for Lynch syndrome in people with endometrial cancer (2020) NICE diagnostics guidance 42.
Related National Policy	The NHS Long Term Plan (2019) NHS Long Term Plan. NHS England (2018) NHS manual for prescribed specialist services (2018/2019). Chapter 105

References

- 1. Ryan NAJ, McMahon R, Tobi S et al. (2020) <u>The proportion of endometrial tumours associated with Lynch syndrome (PETALS): A prospective cross-sectional study.</u> PLOS Medicine 17(9):e1003263.
- 2. NHS Digital (2024). Cancer registration statistics 2022. Accessed October 2024.
- 3. Cancer Research UK (2024). Early Diagnosis Data Hub. Accessed October 2024.
- 4. NICE TA963 (2024). Resource Impact Template. Accessed October 2024.
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- 6. NICE TA904 (2023). <u>Pembrolizumab with lenvatinib for previously treated</u> advanced or recurrent endometrial cancer. Accessed May 2025.
- 7. Morrison J, Balega J, Buckley L, et al. <u>British Gynaecological Cancer Society</u> (<u>BGCS</u>) <u>Uterine Cancer Guidelines</u>: Recommendations for Practice. Eur J Obstet Gynecol Reprod Biol 2022:270:50-89.

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