#### NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

## **Health Technology Evaluation**

Dostarlimab with platinum-containing chemotherapy for treating primary advanced or recurrent endometrial cancer with high microsatellite instability or mismatch repair deficiency

## Final scope

# Final remit/evaluation objective

To appraise the clinical and cost effectiveness of dostarlimab with platinum-containing chemotherapy within its marketing authorisation for treating primary advanced or recurrent endometrial cancer with high microsatellite instability (MSI-H) or mismatch repair deficiency (dMMR) in adults.

# **Background**

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.<sup>1</sup>

In 2019, there were about 8,200 new cases of endometrial cancer in England.<sup>2</sup> It is estimated that about 18% of people with endometrial cancer experience recurrence.<sup>3</sup> In the UK, around 2,500 deaths occurred in 2017-2019 accounting for 3% of all cancer deaths in females. About 15% of women diagnosed with advanced or recurrent endometrial cancer at late stage survive for 5 or more years, compared to 92% of women diagnosed at early stage. About 3% of endometrial cancers occur in women under 45 years of age.<sup>4</sup>

The first treatment for endometrial cancer is usually to remove the womb (hysterectomy) and both the fallopian tubes and ovaries (bilateral salpingo-oophorectomy). In advanced endometrial cancer, debulking surgery may be carried out to remove as much of the cancer as possible. Fadiotherapy may be used for people who cannot have surgery, or alongside surgical treatment. Chemotherapy can be used adjunct to surgery for people with stage 2-4 disease. Hormone therapy or chemotherapy may be used for cancer that has metastasised or relapsed. NICE technology appraisal guidance 779 recommends dostarlimab for use within the Cancer Drugs Fund to treat advanced or recurrent endometrial cancer with high microsatellite instability or mismatch repair deficiency in people who have had platinum-based chemotherapy.

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## The technology

Dostarlimab (Jemperli, GlaxoSmithKline) with platinum-containing chemotherapy does not currently have a marketing authorisation in the UK for endometrial cancer. It has been studied in a clinical trial in which dostarlimab plus carboplatin-paclitaxel followed by dostarlimab monotherapy were compared with carboplatin-paclitaxel plus placebo followed by placebo in people with recurrent or primary advanced (Stage 3 or 4) endometrial cancer. It is administered intravenously.

Dostarlimab as monotherapy has a marketing authorisation in the UK for the treatment of people with mismatch repair deficient (dMMR)/microsatellite instability-high (MSI-H) recurrent or advanced endometrial cancer that has progressed on or following prior treatment with a platinum-containing regimen.

Intervention	Dostarlimab with platinum-containing chemotherapy
Population	People with primary advanced or recurrent endometrial cancer with high microsatellite instability (MSI-H) or mismatch repair deficiency (dMMR)
Subgroups	If the evidence allows the following subgroups will be considered:
	<ul> <li>local vs metastatic recurrence</li> </ul>
	<ul> <li>people who had primary debulking surgery vs people who have not</li> </ul>
Comparators	platinum-based doublet chemotherapy
	For people who had neoadjuvant or adjuvant platinum-based doublet chemotherapy:
	<ul> <li>pembrolizumab plus lenvatinib (subject to ongoing NICE appraisal)</li> </ul>
Outcomes	The outcome measures to be considered include:
	<ul> <li>progression-free survival</li> </ul>
	overall survival
	response rates
	<ul> <li>duration of response</li> </ul>
	<ul> <li>adverse effects of treatment</li> </ul>
	<ul> <li>health-related quality of life.</li> </ul>

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	Related technology appraisals:
recommendations	Dostarlimab for previously treated advanced or recurrent
	endometrial cancer with high microsatellite instability or mismatch repair deficiency (2022) NICE technology appraisal guidance 779.
	mismatch repair deficiency (2022) NICE technology appraisal
	mismatch repair deficiency (2022) NICE technology appraisal guidance 779.
	mismatch repair deficiency (2022) NICE technology appraisal guidance 779.  Related technology appraisals in development:  Pembrolizumab with lenvatinib for previously treated advanced, metastatic or recurrent endometrial cancer. NICE technology appraisal guidance [ID3811] Publication expected
	mismatch repair deficiency (2022) NICE technology appraisal guidance 779.  Related technology appraisals in development:  Pembrolizumab with lenvatinib for previously treated advanced, metastatic or recurrent endometrial cancer. NICE technology appraisal guidance [ID3811] Publication expected June 2023.
	mismatch repair deficiency (2022) NICE technology appraisal guidance 779.  Related technology appraisals in development:  Pembrolizumab with lenvatinib for previously treated advanced, metastatic or recurrent endometrial cancer. NICE technology appraisal guidance [ID3811] Publication expected June 2023.  Related interventional procedures:  Laparoscopic hysterectomy (including laparoscopic total hysterectomy and laparoscopically assisted vaginal hysterectomy) for endometrial cancer (2010) NICE
	mismatch repair deficiency (2022) NICE technology appraisal guidance 779.  Related technology appraisals in development:  Pembrolizumab with lenvatinib for previously treated advanced, metastatic or recurrent endometrial cancer. NICE technology appraisal guidance [ID3811] Publication expected June 2023.  Related interventional procedures:  Laparoscopic hysterectomy (including laparoscopic total hysterectomy and laparoscopically assisted vaginal hysterectomy) for endometrial cancer (2010) NICE interventional procedures guidance 356.
Related National	mismatch repair deficiency (2022) NICE technology appraisal guidance 779.  Related technology appraisals in development:  Pembrolizumab with lenvatinib for previously treated advanced, metastatic or recurrent endometrial cancer. NICE technology appraisal guidance [ID3811] Publication expected June 2023.  Related interventional procedures:  Laparoscopic hysterectomy (including laparoscopic total hysterectomy and laparoscopically assisted vaginal hysterectomy) for endometrial cancer (2010) NICE interventional procedures guidance 356.  Related diagnostics guidance:  Testing strategies for Lynch syndrome in people with
Related National Policy	mismatch repair deficiency (2022) NICE technology appraisal guidance 779.  Related technology appraisals in development:  Pembrolizumab with lenvatinib for previously treated advanced, metastatic or recurrent endometrial cancer. NICE technology appraisal guidance [ID3811] Publication expected June 2023.  Related interventional procedures:  Laparoscopic hysterectomy (including laparoscopic total hysterectomy and laparoscopically assisted vaginal hysterectomy) for endometrial cancer (2010) NICE interventional procedures guidance 356.  Related diagnostics guidance:  Testing strategies for Lynch syndrome in people with endometrial cancer (2020) NICE diagnostics guidance 42.

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#### References

- 1. Murali R, Soslow RA, Weigelt B (2014) <u>Classification of endometrial carcinoma:</u> more than two types. The Lancet. Oncology 15(7): 268-278.
- 2. NHS Digital (2021) Cancer registration statistics, 2019. Accessed April 2023.
- 3. Siegenthaler F, Lindemann K, Epstein E, et al. (2022) <u>Time to first recurrence</u>, <u>pattern of recurrence</u>, <u>and survival after recurrence in endometrial cancer according to the molecular classification</u>. Gynecologic Oncology 165(2):230-8.
- 4. Cancer Research UK (2021) Uterine cancer statistics. Accessed April 2023.
- 5. NHS (2021) Treatment: womb (uterus) cancer. Accessed April 2023.