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 ID6415

Draft scope

Draft remit/evaluation objective

To appraise the clinical and cost effectiveness of dostarlimab with platinum-based chemotherapy within its marketing authorisation for treating primary advanced or recurrent endometrial cancer with microsatellite stable (MSS) or mismatch repair proficient (pMMR) tumours in adults.

Background

Endometrial cancer is a cancer of the lining of the womb (uterus), known as the endometrium. Over 95% of womb cancers are endometrial cancer.[1] The most common symptom of endometrial cancer is abnormal vaginal bleeding, especially in people who have stopped having periods (post menopausal). When diagnosed, endometrial cancer is categorised between stage 1 and 4. In stages 1 and 2, the cancer is contained within the uterus and cervix. 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. Advanced endometrial cancer is defined as stages 3 or 4. The majority of endometrial cancer is diagnosed at stage 1.[2] Primary endometrial cancer means that the lining of the uterus is the first place in the body where the cancer began to grow.

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.[3] 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. Conversely, tumours with MMR proficiency do not have a defect in the MMR system and do not usually have microsatellite instability.

In 2021, there were 8,264 new cases of endometrial cancer in England.[4] It is most common in older women, with only 3% of cases occurring in women under 45 years of age.[5] Diagnosis at an early stage of the cancer's development leads to improved survival chances. About 92% of people diagnosed with stage 1 endometrial cancer survive for 5 or more years. This decreases to 15% for people diagnosed with stage 4 endometrial cancer.[5] Around 2,000 people die from uterine cancer in England each year.[6]

The first treatment for endometrial cancer is usually to remove the womb (hysterectomy) and 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.[7] Radiotherapy may be used alongside surgical treatment, or for people who cannot have surgery. In addition, chemotherapy, usually consisting of carboplatin and paclitaxel, can be used adjunct

to surgery. For cancer that has metastasised or relapsed, treatment options include hormone therapy, immunotherapy, targeted therapy and chemotherapy.

The technology

Dostarlimab (Jemperli, GlaxoSmithKline) does not currently have a marketing authorisation for treating adults with mismatch repair proficient or microsatellite stable primary advanced or recurrent endometrial cancer. It has been studied in clinical trials in combination with carboplatin plus paclitaxel compared to placebo (with carboplatin plus paclitaxel).

Dostarlimab has marketing authorisations for the following indications:

- in combination with platinum-containing chemotherapy for the treatment of adult patients with mismatch repair deficient (dMMR)/microsatellite instability-high (MSI-H) primary advanced or recurrent endometrial cancer and who are candidates for systemic therapy.
- as monotherapy for the treatment of adult patients with dMMR/MSI-H recurrent or advanced endometrial cancer that has progressed on or following prior treatment with a platinum-containing regimen.

Intervention(s)	Dostarlimab with platinum-based chemotherapy followed by dostarlimab maintenance
Population(s)	People with primary advanced or recurrent endometrial cancer with microsatellite stable (MSS) or mismatch repair proficient (pMMR) tumours who are candidates for systemic treatment
Subgroups	If the evidence allows the following subgroups will be considered: • Local vs metastatic recurrence • People who have had primary debulking surgery vs those who have had not had surgery
Comparators	• Platinum-based chemotherapy (such as paclitaxel, carboplatin, cisplatin, doxorubicin and cyclophosphamide) followed by routine surveillance • Hormone therapy (such as medroxyprogesterone acetate and megestrol) followed by routine surveillance • Durvalumab with platinum-based chemotherapy, followed by durvalumab with or without olaparib maintenance (subject to NICE appraisal) • Pembrolizumab with platinum-based chemotherapy, followed by pembrolizumab maintenance (subject to NICE appraisal)
Outcomes	The outcome measures to be considered include: • progression-free survival

	• overall survival • response rates • duration of response • 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 with platinum-based chemotherapy for treating advanced or recurrent endometrial cancer with high microsatellite instability or mismatch repair deficiency. (2024) NICE technology appraisal 963 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 Pembrolizumab with lenvatinib for previously treated advanced or recurrent endometrial cancer (2023) NICE technology appraisal guidance 904 Dostarlimab for previously treated advanced or recurrent endometrial cancer with high microsatellite instability or mismatch repair deficiency (2022) NICE technology appraisal guidance 779 **Related technology appraisals in development:** Dostarlimab with platinum-based chemotherapy for treating advanced or recurrent endometrial cancer with high microsatellite instability or mismatch repair deficiency

	(managed access review of TA963). NICE technology appraisal guidance ID6426. Expected publication date TBC. Pembrolizumab with platinum-based chemotherapy then pembrolizumab maintenance for treating advanced or recurrent endometrial cancer. NICE technology appraisal guidance ID6381. Expected publication date 16 April 2025. Durvalumab with platinum-based chemotherapy, then with or without olaparib, for untreated advanced or recurrent endometrial cancer. NICE technology appraisal guidance ID6317. Expected publication date TBC. Lenvatinib with pembrolizumab for untreated recurrent or advanced endometrial cancer. NICE technology appraisal guidance ID3966. Suspended. Pembrolizumab with chemotherapy for adjuvant treatment of newly diagnosed high-risk endometrial cancer after surgery with curative intent. NICE technology appraisal guidance [ID6207] Expected publication date TBC. **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.
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.

Questions for consultation

Where do you consider dostarlimab will fit into the existing care pathway for MMRp/MSS endometrial cancer?

Please select from the following, will dostarlimab be:
A. Prescribed in primary care with routine follow-up in primary care
B. Prescribed in secondary care with routine follow-up in primary care
C. Prescribed in secondary care with routine follow-up in secondary care
D. Other (please give details):
For comparators and subsequent treatments, please detail if the setting for prescribing and routine follow-up differs from the intervention.

Would dostarlimab be a candidate for managed access?

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?

Please identify the nature of the data which you understand to be available to enable the committee to take account of these benefits.

NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others. Please let us know if you think that the proposed remit and scope may need changing in order to meet these aims. In particular, please tell us if the proposed remit and scope:

- could exclude from full consideration any people protected by the equality legislation who fall within the patient population for which dostarlimab will be licensed;
- could lead to recommendations that have a different impact on people protected by the equality legislation than on the wider population, e.g. by making it more difficult in practice for a specific group to access the technology;
- could have any adverse impact on people with a particular disability or disabilities.

Please tell us what evidence should be obtained to enable the committee to identify and consider such impacts.

NICE intends to evaluate this technology through its Single Technology Appraisal process. (Information on NICE's health technology evaluation processes is available at https://www.nice.org.uk/about/what-we-do/our-programmes/nice-guidance/nice-technology-appraisal-guidance/changes-to-health-technology-evaluation).

References

1. Cancer Research UK. Uterine cancer incidence by anatomical site. Accessed August 2024.
2. Cancer Research UK. Early Diagnosis Data Hub. Accessed August 2024.
3. Ryan NAJ et al. The proportion of endometrial tumours associated with Lynch syndrome (PETALS): A prospective cross-sectional study. Accessed July 2024.
4. NHS Digital (2024). Cancer registration statistics 2021. Accessed August 2024.
5. ONS (2019) Cancer survival by stage at diagnosis for England, 2019. Accessed August 2024.
6. Cancer Research UK. Uterine cancer mortality by UK country. Accessed August 2024.
7. NHS (2024) Treatment: womb (uterus) cancer. Accessed August 2024.