NIHR | Innovation Observatory

Newcastle University

Health Technology Briefing
October 2025

Pembrolizumab for previously untreated advanced or recurrent endometrial cancer

Company/Developer	Merck Sharp & Dohme Ltd

☐ New Active Substance ☒ Significant Licence Extension (SLE)

NIHRIO ID: 40579	NICE ID: Not available	UKPS ID: 669249

Licensing and Market Availability Plans

Currently in phase III clinical trials.

Summary

Pembrolizumab is in development for the treatment of advanced or recurrent endometrial cancer (EC), a malignancy (cancerous growth) from the lining of the uterus. EC is one of the most common gynaecological cancers, with higher risk and poorer prognosis in cases that are diagnosed at an advanced stage or recur after initial treatment. A specific subgroup of these cancers shows deficiency (flaw) in DNA mismatch repair (dMMR), which leads to increased mutation rates and tumour aggressiveness. Standard treatment for advanced or recurrent EC typically involves platinum-based chemotherapy, which may not be effective or well tolerated in all patients. There remains an unmet need for targeted therapies that offer durable responses and are less toxic than conventional chemotherapy, particularly for patients with dMMR tumours.

Pembrolizumab is given as an intravenous infusion and belongs to a class of medicines called immune checkpoint inhibitors. It works by targeting a protein called PD-1 on immune cells, which helps to restore the immune system's ability to detect and destroy cancer cells. Pembrolizumab may be an innovative solution as it harnesses the body's natural immune defences. If licensed, pembrolizumab will offer an additional treatment option for patients with dMMR advanced or recurrent endometrial carcinoma who have not previously been treated with prior systemic chemotherapy.

Proposed Indication

Pembrolizumab for patients with dMMR advanced or recurrent endometrial carcinoma.[1]

This briefing reflects the evidence available at the time of writing and a limited literature search. It is not intended to be a definitive statement on the safety, efficacy or effectiveness of the health technology covered and should not be used for commercial purposes or commissioning without additional information. A version of the briefing was sent to the company for a factual accuracy check. The company was available to comment.

Copyright © National Institute for Health and Care Research Innovation Observatory, The University of Newcastle upon Tyne.

Technology

Description

Pembrolizumab (KEYTRUDA, MK-3475) is a humanised monoclonal anti-programmed cell death-1 (PD-1) antibody (IgG4/kappa isotype with a stabilising sequence alteration in the Fc region) produced in Chinese hamster ovary cells by recombinant DNA technology.[3] The PD-1 receptor acts as an immune checkpoint that prevents overactivation of the immune system.[4] Certain tumour types express high levels of PD-L1 (programmed death-ligand 1), while others use adaptive immune resistance by co-opting PD-L1 pathways to evade immune detection.[5] When PD-L1 engages with PD-1, the T-cell function becomes inhibited.[6] This keeps cancer cells from suppressing the immune system.[7] This allows the immune system to attack the cancer cells.[3]

Pembrolizumab is currently in development for the treatment of patients with dMMR (deficient DNA mismatch repair) cancer, and cannot be cured with surgery or radiation therapy, and has worsened after other systemic therapies.[7] In the phase III clinical trial (NCT05173987) patients receive pembrolizumab 400 mg via intravenous (IV) infusion on Day 1 of each 6-week cycle (Q6W) for up to 18 cycles (up to approximately 2 years).[2]

Key Innovation

Advanced or recurrent EC is particularly hard to treat. The presence of certain tumour cell characteristics may impact the type of treatment chosen and how well it might work; one of these characteristics is mismatch repair/microsatellite instability (MMR/MSI), which describes the process by which cells fix mistakes in their DNA.[8] Cancers that are MMR deficient tend to have a high tumour mutational load and are more responsive to PD-1–based immunotherapy. Immune checkpoint inhibitors, such as pembrolizumab, prevent tumour cells from evading the immune system; the cancer cells are then recognised by T cells and can trigger an antitumour immune response.[9] If licensed, pembrolizumab will offer an additional treatment option for patients with dMMR advanced or recurrent endometrial carcinoma who have not previously been treated with prior systemic chemotherapy.[2]

Regulatory & Development Status

Pembrolizumab is currently marketed in the EU/UK in combination with other medicinal products for the following indications:[3]

- NSCLC
- Head and neck squamous cell carcinoma
- Renal cell carcinoma
- Oesophageal carcinoma
- Triple-negative breast cancer
- Endometrial carcinoma
- Cervical cancer
- Urothelial cancer
- Gastric or gastro-oesophageal junction adenocarcinoma
- Biliary tract carcinoma

Pembrolizumab is also currently marketed in the EU/UK as a monotherapy for the following indications:[3]

Copyright © National Institute for Health and Care Research Innovation Observatory, The University of Newcastle upon Tyne.

- Endometrial carcinoma: microsatellite instability high (MSI-H) or dMMR, advanced or recurrent and progressing on or after platinum containing therapy in any setting and who are not candidates for curative surgery or radiation.
- Melanoma
- NSCLC
- Urothelial carcinoma
- Classical Hodgkin lymphoma
- Head and neck squamous cell carcinoma
- Renal cell carcinoma
- Colorectal cancer (MSI-H or dMMR)
- Gastric cancer (MSI-H or dMMR)
- Small intestine cancer (MSI-H or dMMR)
- Biliary cancer (MSI-H or dMMR)

Pembrolizumab is currently in Phase II or III clinical development for various types of cancer, including, but not limited to:[10]

- Head and neck squamous cell carcinomas
- Urothelial cancer
- Bladder cancer
- Metastatic non-small cell lung cancer
- Metastatic cutaneous melanoma
- Nasopharyngeal carcinoma
- Sarcoma
- Selected types of solid tumour

Patient Group

Disease Area and Clinical Need

Endometrial cancer (EC), also known as uterine or womb cancer, starts in the lining of the womb (the endometrium).[11] It is the most common type of womb cancer. The most common symptom of womb cancer is abnormal bleeding from the vagina. Other symptoms of womb cancer include bleeding after the menopause, bleeding that is unusually heavy or persistent between periods, and an abnormal vaginal discharge that might be pink. Less common symptoms can include low red blood cell level (anaemia), high platelet count (thrombocytosis) or high blood sugar level. Further symptoms may include abdominal pain, a swollen stomach, bloating, a change in bowel or bladder habits and/or a new cough.[12] Factors that increase the risk of EC include changes in the balance of hormones in the body, more years of menstruation, never having been pregnant, older age, obesity, hormone therapy for breast cancer, or genetics and inherited syndromes.[13] Recurrent EC is diagnosed when cancer returns after the patient has been in remission.[14] Remission is a decrease in or disappearance of signs and symptoms of cancer.[15] EC may return to the same area as before or may have metastasised (spread to other areas).[14] Further EC classifications are made on type and stage. Specifying subtype of EC enables doctors to understand the likelihood of the cancer recurring after treatment, and as well which treatment would be most effective. There are 4 molecular subtypes of EC, which are DNA polymerase epsilon (POLE)-mutated; Mismatch repair-deficient (dMMR); No specific molecular profile; and P53 abnormal.[16] Patients with advanced or recurrent EC typically have limited treatment options and poor long-term survival outcomes following first-line therapy. Real-world treatment patterns and survival outcomes data are limited for patients in this setting.[17]

Copyright © National Institute for Health and Care Research Innovation Observatory, The University of Newcastle upon Tyne.

EC typically occurs in women who have stopped having periods (post-menopausal women).[12] It is the 4th most common cancer in females in the UK. In the UK, the prevalence of advanced or recurrent EC is estimated to be 8,140 per 100,000 female population.[18] In England, in 2024-2025, the finished consultant episodes (FCE) and finished admission episodes for EC (ICD code C51-C58) is 82,295 and 80,568 respectively, resulting in 115,880 bed days and 59,882 day cases.[19]

Recommended Treatment Options

The National Institute for Health and Care Excellence (NICE) recommend the following treatments for advanced or recurrent endometrial cancer:[20,21]

- Pembrolizumab with carboplatin and paclitaxel for untreated primary advanced or recurrent endometrial cancer
- Dostarlimab with platinum-based chemotherapy for treating primary advanced or recurrent endometrial cancer with high microsatellite instability or mismatch repair deficiency

Clinical Trial Information

Trial	**KEYNOTE-C93/GOG-3064/ENGOT-en15; NCT05173987; 2021-003185-12;** A Phase 3 Randomized, Open-label, Active-comparator Controlled Clinical Study of Pembrolizumab Versus Platinum Doublet Chemotherapy in Participants With Mismatch Repair Deficient (dMMR) Advanced or Recurrent Endometrial Carcinoma in the First-line Setting **Phase III –** Active, not recruiting **Location(s):** 13 EU countries, UK, USA, Canada and other countries **Primary completion date:** May 2027
Trial Design	Randomised, parallel assignment, open-label
Population	N=280 (estimated); patients with inoperable stage 3 or 4 Endometrial Carcinoma or carcinosarcoma with confirmed dMMR; aged 18 years and above
Intervention(s)	Pembrolizumab administered by intravenous infusion
Comparator(s)	Carboplatin and paclitaxel administered by intravenous infusion
Outcome(s)	Primary outcome measure: Progression-Free Survival (PFS) per Response Evaluation Criteria in Solid Tumors Version 1.1 (RECIST 1.1) as Assessed by Blinded Independent Central Review (BICR) [Time Frame: Up to approximately 45 months] See trial record for list of other outcomes
Results (efficacy)	-
Results (safety)	-

Estimated Cost

Copyright © National Institute for Health and Care Research Innovation Observatory, The University of Newcastle upon Tyne.

Pembrolizumab is already marketed in the UK; the NHS indicative price (hospital only) of one 100mg/4ml vial of concentrate for solution for infusion is £2,630.[22]

Relevant Guidance

NICE Guidance

- NICE technology appraisal awaiting development. Lenvatinib with pembrolizumab for untreated recurrent or advanced endometrial cancer (GID-TA10851). Expected date of issue to be confirmed.
- NICE technology appraisal awaiting development. Endometrial cancer (high risk, newly diagnosed) - pembrolizumab (with chemotherapy, adjuvant) (GID-TA11235). Expected date of issue to be confirmed.
- NICE technology appraisal guidance. Pembrolizumab with carboplatin and paclitaxel for untreated primary advanced or recurrent endometrial cancer (TA1092). Published August 2025.
- NICE technology appraisal in development. Dostarlimab with platinum-containing chemotherapy for treating primary advanced or recurrent endometrial cancer with high microsatellite instability or mismatch repair deficiency (GID-TA10850). Expected publication date February 2024.
- NICE guideline. Suspected cancer: recognition and referral (NG12). June 2015. Last updated: August 2023.
- NICE technology appraisal guidance. Dostarlimab for previously treated advanced or recurrent endometrial cancer with high microsatellite instability or mismatch repair deficiency (TA779). Published March 2022.

NHS England (Policy/Commissioning) Guidance

- NHS England. 2013/14 NHS Standard Contract for Complex Gynaecology – Specialist Gynaecological Cancers. E10/S/f.
- NHS England. 2013/14 NHS Standard Contract for Cancer: Chemotherapy (Adult). B14/S/a.
- NHS England. 2013/14 NHS Standard Contract for Cancer: Radiotherapy (All Ages). B01/S/a

Other Guidance

- Sznurkowski et al. Updated Guidelines for the Diagnosis and Treatment of Endometrial Carcinoma: The Polish Society of Gynecological Oncology. 2025.[23]
- My Endometrial Cancer Team. 8 Treatments for Advanced Endometrial Cancer. 2025.[24]
- American Cancer Society. Treatment Choices for Endometrial Cancer, by Stage.[25]
- Restaino et al. Management of Patients Diagnosed with Endometrial Cancer: Comparison of Guidelines. 2023.[26]
- Heffernan et al. Previously treated recurrent or advanced endometrial cancer in England: A real-world observational analysis. 2022.[27]
- European Society for Medical Oncology (ESMO). Endometrial cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment, and follow-up. 2022.[28]
- Spanish Society of Medical Oncology. SEOM-GEICO clinical guidelines for endometrial cancer (2021). 2022.[29]
- British Gynaecological Cancer Society (BGCS) Uterine Cancer Guidelines: Recommendations for Practice. 2021.[30]
- European Society of Gynaecological Oncology (ESGO). ESGO/ESTRO/ESP guidelines for the management of patients with endometrial carcinoma. 2021.[31]

Copyright © National Institute for Health and Care Research Innovation Observatory, The University of Newcastle upon Tyne.

References

1 UK PharmaScan. *Technology Summary (669249) KEYTRUDA, Pembrolizumab dMMR advanced or recurrent endometrial cancer*. Available from: https://www.ukpharmascan.org.uk/HS/technology/669249 [Accessed 24 October 2025].

2 ClinicalTrials.gov. *Study of Pembrolizumab (MK-3475) Versus Chemotherapy in Mismatch Repair Deficient (dMMR) Advanced or Recurrent Endometrial Carcinoma (MK-3475-C93/ KEYNOTE-C93/GOG-3064/ENGOT-en15). Trial ID: NCT05173987*. Available from: https://clinicaltrials.gov/study/NCT05173987?term=NCT05173987&rank=1#study-overview [Accessed 21 August 2025].

3 Electronic Medicines Compendium. *KEYTRUDA 25 mg/mL concentrate for solution for infusion*. 2025. Available from: https://www.medicines.org.uk/emc/product/2498/smpc (login required) [Accessed 20 August 2025].

4 Flynn P and Gerriets V. *Pembrolizumab*. 2023. Available from: https://www.ncbi.nlm.nih.gov/books/NBK546616/ [Accessed 21 August 2025].

5 Francisco LM, Sage Pt Fau - Sharpe AH, Sharpe AH. The PD-1 pathway in tolerance and autoimmunity. 2010. https://pubmed.ncbi.nlm.nih.gov/20636820/.

6 Pardoll DM. The blockade of immune checkpoints in cancer immunotherapy. https://pubmed.ncbi.nlm.nih.gov/22437870/.

7 National Cancer Institute. *Pembrolizumab*. 2025. Available from: https://www.cancer.gov/about-cancer/treatment/drugs/pembrolizumab [Accessed 20 August 2025].

8 Chase DM, Kobayashi M, Gomez P, Lubinga SJ, Chan JK. Treatment patterns and outcomes by mismatch repair/microsatellite instability status among patients with primary advanced or recurrent endometrial cancer in the United States. 2025. https://pmc.ncbi.nlm.nih.gov/articles/PMC12323428/.

9 Canadian Agency for Drugs and Technologies in Health. Pembrolizumab (Keytruda): Therapeutic area: Unresectable or metastatic microsatellite instability-high or mismatch repair deficient solid tumours: Reimbursement Review [Online]. Ottawa (ON); 2025.

10 ClinicalTrials.gov. *Search for Pembrolizumab, Phase II and III*. 2025. Available from: https://clinicaltrials.gov/search?intr=Pembrolizumab&aggFilters=phase:2%203&viewType=Table [Accessed 05 September 2025].

11 Cancer Research UK. *Womb (uterine) cancer including endometrial cancer*. 2024. Available from: https://www.cancerresearchuk.org/about-cancer/womb-cancer [Accessed 22 August 2025].

12 Cancer Research UK. *Symptoms of womb cancer*. 2024. Available from: https://www.cancerresearchuk.org/about-cancer/womb-cancer/symptoms [Accessed 22 August 2025].

13 Mayo Clinic. *Endometrial cancer: Overview*. Available from: https://www.mayoclinic.org/diseases-conditions/endometrial-cancer/symptoms-causes/syc-20352461 [Accessed 22 August 2025].

14 My Endometrial Cancer Team. *Recurrent Endometrial Cancer: Treatments, Life Expectancy, and More*. 2025. Available from: https://www.myendometrialcancerteam.com/resources/advanced-or-recurrent-endometrial-cancer-when-it-spreads-or-returns [Accessed 22 August 2025].

15 National Cancer Institute. *NCI Dictionary of Cancer Terms: remission*. Available from: https://www.cancer.gov/publications/dictionaries/cancer-terms/def/remission [Accessed 22 August 2025].

Copyright © National Institute for Health and Care Research Innovation Observatory, The University of Newcastle upon Tyne.

16 American Cancer Society. *What Is Endometrial Cancer?* Available from: https://www.cancer.org/cancer/types/endometrial-cancer/about/what-is-endometrial-cancer.html [Accessed 22 August 2025].
17 Coleman RLA-Ooo, Garside JA-Ooo, Hurteau JA-Ooo, Nguyen JA-Ooo, Kobayashi MA-Ooo. Treatment Patterns and Outcomes Among Patients With Advanced or Recurrent Endometrial Cancer Initiating First-Line Therapy in the United States. 2023. https://pubmed.ncbi.nlm.nih.gov/37905183/.
18 Cancer Research UK. *Uterine cancer incidence statistics*. Available from: https://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/uterine-cancer/incidence?utm_source=chatgpt.com#heading-Zero [Accessed 22 August 2025].
19 NHS Digital. *Hospital Admitted Patient Care Activity, 2024-25*. Available from: https://digital.nhs.uk/data-and-information/publications/statistical/hospital-admitted-patient-care-activity/2024-25 [Accessed 30 September 2025].
20 National Institute for Health and Care Excellence (NICE). *Dostarlimab for previously treated advanced or recurrent endometrial cancer with high microsatellite instability or mismatch repair deficiency*. Available from: https://www.nice.org.uk/guidance/ta779 [Accessed 21 August 2025].
21 National Institute for Health and Care Excellence (NICE). *Pembrolizumab with carboplatin and paclitaxel for untreated primary advanced or recurrent endometrial cancer* (*TA1092)*. Available from: https://www.nice.org.uk/guidance/ta1092 [Accessed 24 October 2025].
22 British National Formulary (BNF): National Institute for Health and Care Excellence (NICE). *Pembrolizumab [Specialist drug]: Medicinal forms*. 2025. Available from: https://bnf.nice.org.uk/drugs/pembrolizumab-specialist-drug/medicinal-forms/ (login required) [Accessed 21 August 2025].
23 Sznurkowski JA-O, Bodnar LA-O, Dańska-Bidzińska A, Marszałek A, Blecharz P, Chudecka-Głaz A, et al. Updated Guidelines for the Diagnosis and Treatment of Endometrial Carcinoma: The Polish Society of Gynecological Oncology. 2025. https://www.mdpi.com/3349804.
24 My Endometrial Cancer Team. *8 Treatments for Advanced Endometrial Cancer*. 2025. Available from: https://www.myendometrialcancerteam.com/resources/treatments-for-advanced-endometrial-cancer [Accessed 20 August 2025].
25 American Cancer Society. *Treatment Choices for Endometrial Cancer, by Stage*. Available from: https://www.cancer.org/cancer/types/endometrial-cancer/treating/by-stage.html [Accessed 21 August 2025].
26 Restaino SA-O, Paglietti C, Arcieri MA-O, Biasioli A, Della Martina M, Mariuzzi L, et al. Management of Patients Diagnosed with Endometrial Cancer: Comparison of Guidelines. 2023.
27 Heffernan K, Nikitas FS, Shukla U, Camejo HS, Knott C. Previously treated recurrent or advanced endometrial cancer in England: A real-world observational analysis. *Gynecologic Oncology*. 2022;166(2):317-25. Available from: https://doi.org/10.1016/j.ygyno.2022.06.011.
28 Oaknin A, Bosse TJ, Creutzberg CL, Giornelli G, Harter P, Joly F, et al. Endometrial cancer: ESMO Clinical Practice Guideline for diagnosis, treatment and follow-up. 2022. https://pubmed.ncbi.nlm.nih.gov/35690222/.
29 Barretina-Ginesta MA-O, Quindós M, Alarcón JD, Esteban C, Gaba L, Gómez C, et al. SEOM-GEICO clinical guidelines on endometrial cancer (2021). 2022.
30 Morrison J, Balega J, Buckley L, Clamp A, Crosbie E, Drew Y, et al. British Gynaecological Cancer Society (BGCS) uterine cancer guidelines: Recommendations for practice. 2021;(1872-7654 (Electronic)). https://pubmed.ncbi.nlm.nih.gov/35065448/.
31 Concin N, Matias-Guiu X, Vergote I, Cibula D, Mirza MR, Marnitz S, et al. ESGO/ESTRO/ESP guidelines for the management of patients with endometrial carcinoma. *International*

Copyright © National Institute for Health and Care Research Innovation Observatory, The University of Newcastle upon Tyne.

Journal of Gynecological Cancer. 2021;31(1):12-39. Available from: https://doi.org/https://doi.org/10.1136/ijgc-2020-002230.

NB: This briefing presents independent research funded by the National Institute for Health and Care Research (NIHR). The views expressed are those of the author and not necessarily those of the NHS, the NIHR or the Department of Health.

Copyright © National Institute for Health and Care Research Innovation Observatory, The University of Newcastle upon Tyne.