SMC2767

pembrolizumab concentrate for solution for infusion (Keytruda®)

Merck Sharp & Dohme (UK) Limited

06 June 2025

The Scottish Medicines Consortium (SMC) has completed its assessment of the above product and, following review by the SMC executive, advises NHS Boards and Area Drug and Therapeutics Committees (ADTCs) on its use in NHSScotland. The advice is summarised as follows:

ADVICE: following a full submission

pembrolizumab (Keytruda®) is accepted for use within NHSScotland.

Indication under review: in combination with carboplatin and paclitaxel, for the first-line treatment of primary advanced or recurrent endometrial carcinoma in adults.

In a double-blind, phase III study, addition of pembrolizumab to carboplatin plus paclitaxel chemotherapy significantly improved progression-free survival in adults undergoing first-line treatment of primary advanced or recurrent endometrial carcinoma.

This advice applies only in the context of an approved NHSScotland Patient Access Scheme (PAS) arrangement delivering the cost-effectiveness results upon which the decision was based, or a PAS/ list price that is equivalent or lower.

Chair
Scottish Medicines Consortium

1. Clinical Context

1.1. Medicine background

Pembrolizumab is a monoclonal antibody that binds to the programmed cell death-1 (PD-1) receptor and blocks its interaction with ligands PD-L1 and PD-L2, thereby enhancing T-cell anti-tumour responses. In the indication under review, it is given by intravenous (IV) infusion, 200 mg every three weeks, in combination with carboplatin and paclitaxel, for six cycles and then 400 mg every six weeks for up to 14 cycles as monotherapy.[1]

1.2. Disease background

Endometrial cancer is the fourth most common cancer in women in the UK. The incidence of endometrial cancer increases with age and is highest between the ages of 75 to 79 years in the UK. Risk factors include obesity, hypertension, hyperinsulinaemia and prolonged exposure to unopposed oestrogen. Endometrial cancer is confined to the uterus at diagnosis in about 80% of cases and often detected by post-menopausal bleeding. Survival rates are high for localised disease that is surgically removed, but poor for distant disease, with estimated survival between 18% to 25% at five years. About 25% to 30% of endometrial cancers are mismatch repair deficient (dMMR). Endometrial cancer that is dMMR is more likely to have high levels of mutations.[2-4]

1.3. Treatment pathway and relevant comparators

The 2021 British Gynaecological Cancer Society (BGCS) uterine cancer guideline recommends carboplatin plus paclitaxel as standard first-line chemotherapy for the treatment of advanced or recurrent endometrial cancer.[2] This is the current standard of care for patients with mismatch repair proficient (pMMR) tumours in Scotland. In April 2024, SMC published advice (SMC2635) that dostarlimab is accepted for use within NHSScotland in combination with platinum-containing chemotherapy for the treatment of adult patients with dMMR/microsatellite instability-high (MSI-H) primary advanced or recurrent endometrial cancer and who are candidates for systemic therapy. This is the standard of care for patients with dMMR tumours in Scotland. Subsequently, dostarlimab's licence was extended to include patients with pMMR tumours and another medicine, durvalumab, has been recently licensed for both dMMR and pMMR cohorts in this indication.[5, 6] Currently, there is no SMC advice for these new indications for dostarlimab and durvalumab. Cancer Medicines Outcome Programme Public Health Scotland (CMOP-PHS) data confirmed that the majority of patients in NHSScotland receiving first-line systemic anti-cancer therapy for advanced endometrial cancer received carboplatin plus paclitaxel or one of these medicines alone, while a smaller proportion received both in combination with dostarlimab.[7]

1.4. Category for decision-making process

Eligibility for a PACE meeting

Pembrolizumab meets SMC end of life criteria for this indication.

2. Summary of Clinical Evidence

2.1. Evidence for the licensed indication under review

Evidence is from the KEYNOTE-868 study, detailed in Table 2.1 below.[8 9]

Table 2.1. Overview of relevant studies.[8, 9]

Criteria	KEYNOTE-868
Study design	Double-blind, phase III study.
Eligible patients	Adults with newly diagnosed advanced (Stage III or IV) metastatic or recurrent endometrial cancer (except for carcinosarcoma) who had ECOG PS of 0 to 2.
Treatments	Placebo or pembrolizumab 200 mg IV every three weeks plus paclitaxel 175 mg/m^2 BSA IV and carboplatin AUC 5 mg/mL/minute IV for six cycles then placebo or pembrolizumab 400 mg IV every 6 weeks for up to 14 cycles.
Randomisation	Stratified by dMMR (yes versus no), ECOG performance status (0 or 1 versus 2), and receipt of previous adjuvant chemotherapy (yes or no). Patients equally assigned.
Primary outcome	Progression-free survival, defined as the time from randomisation to disease progression by investigator on RECISTv1.1 or death from any cause; assessed separately in dMMR and pMMR cohorts in ITT population (all randomised patients).
Secondary outcomes	Overall survival, defined as time from randomisation to death from any cause. Objective response rate, defined as CR or PR by investigator on RECISTv1.1.
Statistical analysis	Primary outcome controlled for multiplicity in dMMR and pMMR cohorts and across interim analyses. Secondary outcomes not controlled for multiplicity.

Abbreviations: AUC = area under curve; BSA = body surface area; CR = complete response; dMMR = mismatch repair deficient; ECOG PS = Eastern Cooperative Oncology Group (ECOG) performance status; ITT = intention-to-treat; IV = intravenous infusion; pMMR = mismatch repair proficient; PR = partial response; RECISTv1.1 = response evaluation criteria in solid tumors version 1.1.

In the pMMR and dMMR cohorts, at 6 and 16 December 2022 cutoffs, respectively, after median follow-up of 7.9 and 12 months, the primary outcome, investigator-assessed progression-free survival (PFS) significantly increased with pembrolizumab-chemotherapy compared with placebo-chemotherapy. Updated descriptive analyses at August 2023 cutoff, may be compromised by unblinding in February 2023. Results are in Table 2.2.[8-10]

Table 2.2: Results of KEYNOTE-868 study.[8-10]

	pMMR		dMMR	
	Pembrolizumab-chemotherapy	**Placebo-chemotherapy**	**Pembrolizumab-chemotherapy**	**Placebo-chemotherapy**
	N=294	**N=294**	**N=110**	**N=112**
Progression-free survival investigator-assessed on RECISTv1.1; December 2022				
Events	95	138	29	60
Median PFS, months	13.1	8.7	NR	8.3
HR (95% CI)	0.57 (0.44 to 0.74), p<0.001		0.34 (0.22 to 0.53), p<0.001	
2-year PFS	38%	14%	65%	27%
Overall survival, December 2022				
Deaths	45	54	10	17
Median OS, months	28.0	27.4	NR	NR
HR (95% CI)	0.79 (0.53 to 1.17)		0.55 (0.25 to 1.19)	
2-year OS	61%	52%	85%	73%
Overall survival, August 2023				
Deaths	77	92	17	27

Median OS, months	28.9	28.7	NR	42.7
HR (95% CI)	0.80 (0.59 to 1.08)		0.57 (0.31 to 1.04)	
3-year OS	50%	35%	81%	71%
Objective response investigator-assessed on RECISTv1.1, December 2022				
ORR, % (n)	61% (135/220)	52% (121/235)	78% (74/95)	70% (66/95)
CR, % (n)	11% (24/220)	6.8% (16/235)	28% (27/95)	12% (11/95)
Median DOR months	7.1	6.4	NR	4.4

Abbreviations: CI = confidence interval; CR = complete response; DOR = duration of response; HR = hazard ratio; NR = not reached; ORR = objective response rate; OS = overall survival; PFS = progression-free survival; RECISTv1.1 = response evaluation criteria in solid tumors version 1.1.

2.2. Health related quality of life outcomes

Health Related Quality of Life was assessed only in the pMMR cohort. Quality of life was measured on the Functional Assessment of Cancer Therapy-Endometrial Trial Outcome Index (FACT-En-TOI); neurotoxicity on the Functional Assessment of Cancer Therapy/Gynecologic Oncology Group-Neurotoxicity (FACT/GOG-Ntx subscale); fatigue on the Patient Reported Outcomes Measurement Information System (PROMIS)-Fatigue (short form), and physical function on the PROMIS-physical function (short form) at Week 0, 6, 18, 30 and 54.[8, 9]

A regulatory review noted that, within the pMMR cohort, worsening quality of life and increasing fatigue appeared more pronounced in the pembrolizumab-chemotherapy group, compared with placebo-chemotherapy, at week 18 (that is, at the end of chemotherapy). These return to baseline afterwards and appear to correspond with the increase in toxicity with the addition of pembrolizumab to chemotherapy. Both treatment groups had similar slight worsening in the FACT/GOG-Ntx subscale evaluating neurotoxicity.[8]

2.3. Indirect evidence to support clinical and cost-effectiveness comparisons

An indirect comparison of pembrolizumab plus carboplatin-paclitaxel versus dostarlimab plus carboplatin-paclitaxel in patients with dMMR, which suggested similar PFS, supported the economic analyses. This is detailed in Table 2.3 below.

Table 2.3: Summary of indirect treatment comparison

Criteria	Overview
Design	Network meta-analysis and fractional polynomial model (both fixed effects).
Population	Adults with newly diagnosed advanced endometrial cancer, mismatch repair deficient (dMMR).
Comparators	Dostarlimab plus chemotherapy (carboplatin and paclitaxel).
Studies	Mismatch repair deficient (dMMR) cohorts of KEYNOTE-868[8-10] and RUBY-1.[11]
Outcomes	Progression-free survival.
Results	Pembrolizumab-chemotherapy versus dostarlimab-chemotherapy • Analysis based on time-varying fractional polynomial model (due to violation of proportional hazard assumption): similar treatment effect. • Analysis based on network meta-analysis (assumes proportional hazards): similar treatment effect.

Abbreviations: CrI = credible interval.

*Other data were also assessed but remain confidential.**

3. Summary of Safety Evidence

A regulatory review concluded that the overall toxicity of pembrolizumab plus carboplatin-paclitaxel in this setting was in line with established safety profiles and there were no new safety signals. There was a higher incidence of adverse events in the pembrolizumab arm, as expected from an add-on treatment.[8]

At the December 2022 cut-off, in the pembrolizumab and placebo groups, 98% (376/382) and 99% (375/377) of patients had an adverse event (treatment-related in 96% and 95%, respectively). In the pembrolizumab group, compared with placebo, there was a higher incidences of adverse events that were grade ≥3, 59% versus 46% (treatment-related in 45% versus 32%); and serious, 35% versus 19% (treatment-related in 22% versus 11).[8]

At the December 2022 cut-off, within the respective pembrolizumab and placebo groups, adverse events grade ≥3 included anaemia (15% and 10%), neutrophil count decreased (13% and 13%), white blood cell count decreased (8.6% and 7.7%), lymphocyte count decreased (6.0% and 4.5%), hypertension (4.7% and 5.3%), neutropenia (3.9% and 2.7%), febrile neutropenia (3.4% and 1.1%), fatigue (1.3% and 2.7%) and thrombocytopenia (0.5% and 0.5%).[8]

There were no new immune-related adverse events identified. At the December 2022 cut-off, within the pembrolizumab and placebo groups, adverse events of special interest occurred at a higher rate, 36% versus 26%. These included hypothyroidism (12% versus 3.7%), hyperthyroidism (6.5% versus 2.7%), severe skin reactions (3.4% versus 1.6%), pneumonitis (1.0% versus 0.5%), adrenal insufficiency (1.0% versus 0.3%), colitis (1.8% versus 0.8%). Rates of infusion reactions were similar across the groups (both 18%).[8]

4. Summary of Clinical Effectiveness Considerations

4.1. Key strengths

- In a double-blind, phase III study, addition of pembrolizumab to carboplatin-paclitaxel significantly improved median PFS by about 4.4 months in the pMMR cohort, with a HR of 0.57, and in the dMMR cohort, where the HR was 0.34.[8]
- The study was designed and powered to investigate the primary outcome, PFS, separately in dMMR and pMMR cohorts. This supports decision-making separately in these groups, which have different standards of care and prognosis.

4.2. Key uncertainties

- KEYNOTE-868 was unblinded in February 2023 based on interim analyses (December 2022), which became the primary analyses of PFS. At this cut-off, in the pMMR and dMMR cohorts, the numbers of PFS events correspond to 39% and 40% of data maturity respectively. Regulators considered these data immature. Updated analyses are difficult to interpret as most patients in the placebo group discontinued soon after unblinding, including those who had not yet had progressive disease, with some subsequently receiving immunotherapy. This may confound the updated analysis.

- At the interim analyses (December 2022), OS data were immature. Updated analyses (August 2023) are limited by unblinding of the study in February 2023 and discontinuation issues leading to interpretation difficulties.[8]
- To address the lack of direct comparative evidence in dMMR patients against dostarlimab in combination with chemotherapy, an indirect comparison was provided. The indirect comparison was limited by some heterogeneity in age and clinical factors across the KEYNOTE-868 and RUBY study populations. The likely confounding of the PFS data from KEYNOTE-868, due to unblinding and subsequent pre-progression treatments in the placebo group, increases the uncertainty of the comparison. This potential confounding may underestimate the magnitude of benefit observed for pembrolizumab in the network meta-analysis for the comparison with the dostarlimab regimen. Despite these limitations, the conclusion suggesting similar PFS appears reasonable. The indirect comparison did not include assessments of OS, safety and quality of life.

4.3. Clinical expert input

Clinical experts consulted by SMC considered that pembrolizumab in combination with carboplatin and paclitaxel fills an unmet need in patients with pMMR, as there is currently no first-line treatment option in this population that includes an immunotherapy in combination with chemotherapy.

4.4. Service implications

Clinical experts consulted by SMC considered that the introduction of this medicine may impact on service delivery with up to 14 additional visits for pMMR patients for pembrolizumab administration following the six cycles of chemotherapy. For dMMR patients there may be fewer visits as the maximum duration of treatment with pembrolizumab is shorter than with dostarlimab: 2 years versus 3 years.

5. Summary of Patient and Carer Involvement

The following information reflects the views of the specified Patient Group.

- We received a patient group submission from Peaches Womb Cancer Trust, which is a registered charity.
- Peaches Womb Cancer Trust has received 28% pharmaceutical company funding in the past two years, including from the submitting company.
- A diagnosis of advanced endometrial cancer has a substantial impact on every aspect of women's lives. Physical symptoms such as vaginal bleeding, pain and discomfort, incontinence, nausea, fatigue and abdominal swelling are highly impactful on quality of life, socialising and being able to work. Many will require care around the clock, resulting in carers having to take time off work, impacting financially, but also resulting in fatigue, burnout, guilt, frustration and grief.
- There are limited effective treatment options for women with primary advanced endometrial cancer. The limited first-line treatment options for people with advanced or recurrent pMMR endometrial cancer is devastating. People with pMMR cancers represent

70-80% of all endometrial cancer cases, meaning that the majority still lack access to effective first-line therapies.

- Patients with primary stage 3 disease are fearful of recurrence and want a treatment that prevents it or stops it progressing to an incurable state. For stage 4 cancer, pembrolizumab offers the opportunity for women to potentially live longer, fuller lives.
- Women want treatment options that will increase life expectancy and offer hope of a longer, meaningful life, with many willing to accept some increase in treatment-related side effects for improved long-term survival.

6. Summary of Comparative Health Economic Evidence

6.1. Economic case

The details of the submitted economic case are presented in Table 6.1.

Table 6.1 Description of economic analysis

Criteria	Overview
Analysis type	Cost-utility analysis
Time horizon	A lifetime horizon of 35 years with 1-week cycle lengths
Population	Adult patients with untreated primary advanced or recurrent endometrial carcinoma
Comparators	The primary comparator in the analysis for the all-comer population was platinum-based chemotherapy (CT), specifically carboplatin and paclitaxel. A second comparator of dostarlimab in combination with platinum-based CT was applied in subgroup analysis for dMMR cohort.
Model description	A three-state partitioned survival model was used, with health states of PFS, progressed disease (PD) and death. All patients entered the model in the PFS state and remained in this health state until disease progression, following which, patients either transitioned into the PD health state or entered the absorbing health state of Death. The occupancy of health states over time was derived from the survival curves from the KEYNOTE-868 study.[9, 10] The proportion of patients occupying each health state was calculated using the PFS and OS survival curves.
Clinical data	The key effectiveness data for pembrolizumab came from the KEYNOTE-868 study.[9, 10] Clinical data for the pMMR and dMMR subgroups in KEYNOTE-868 was retrospectively combined to generate a combined all-comer population, to provide greater statistical power for survival modelling. This included input parameters for PFS, OS, time to treatment discontinuation (TTD) and patient utilities Since there was no head-to-head data available for pembrolizumab + CT versus dostarlimab + CT, an indirect comparison was conducted between the KEYNOTE-868 study[9, 10] and the RUBY-1 study[11] for the dMMR subgroup analysis.
Extrapolation	The model used independently fitted parametric curves using patient-level data to estimate PFS and OS as the proportional hazards assumption was violated. For extrapolation PFS in both arms, the company argued the spline and two-piece models provided better fit to the observed data compared with the standard parametric models; they more closely captured the observed hazard profiles and they generally provided more plausible long-term extrapolations. The 1-knot hazard spline was selected as the base case for the CT arm and the two-piece log-normal curve was selected as the base case for pembrolizumab + CT.

	For OS, standard parametric models were deemed to be suitable for modelling the CT arm but were inappropriate to estimate long-term outcomes in the pembrolizumab + CT arm due to poor visual fit. The standard log-logistic curve was selected for CT in the modelled base case. This curve had the best fit to the observed data, aligned the closest with the UK and Scottish clinicians' long-term estimates, and reflected the possibility of survival at 20 years and beyond. Selection of the pembrolizumab + CT curve was done by considering the relative benefit over the preferred CT curve. Based on the visual and statistical fit, clinical plausibility and representation of the observed HR, the 3-knot odds spline curve was selected as the base case for the pembrolizumab + CT arm. For the dMMR cohort, the standard log-logistic and standard exponential curves were chosen for the pembrolizumab + CT and CT arms, respectively. The company also provided details of long-term extrapolation applied in the exploratory scenario restricted to the pMMR patient subgroup. This was based on individual patient data from the pMMR cohort analysis of KEYNOTE-868.[9, 10] For PFS, the company selected a two-piece generalised gamma model for pembrolizumab + CT and a 1-knot odds spline model for the CT. For OS, in the CT arm clinical experts supported the standard gamma curve as most clinically plausible and representative of expectations. In the pembrolizumab + CT arm, clinical experts supported the two-piece log-normal curve as most clinically plausible and representative of expectations.
Quality of life	Health state utility scores applied in the base case were not derived from KEYNOTE-868.[9, 10] Instead, utility values were based on EQ5D-5L data from the KEYNOTE-158 study[12] of pembrolizumab in participants with dMMR/MSI-H cancers across different tumour types, including endometrial carcinoma, and who have failed at least one line of therapy. The utility values were health state dependent and were the same for all patients with endometrial carcinoma regardless of subgroup status. Adverse event disutilities were applied and the utilities were adjusted for age.
Costs and resource use	Costs included in the model were medicine acquisition, administration, monitoring, adverse events, subsequent treatments and end of life. A price year of 2023/24 was used and costs and benefits were discounted at 3.5%
PAS	A Patient Access Scheme (PAS) was submitted by the company and assessed by the Patient Access Scheme Assessment Group (PASAG) as acceptable for implementation in NHSScotland. Under the PAS, a discount was offered on the list price. A PAS discount is in place for dostarlimab and this is included in the results used for decision-making by using estimates of the comparator PAS price.

6.2. Results

The submitting company presented base case results for the all-comer population, with the comparator of platinum-based CT, as well as separate subgroup analysis results by MMR status using the comparator of platinum-based CT for patients in the pMMR subgroup and dostarlimab in combination with platinum-based CT for the dMMR subgroup. SMC considered results for decision-making that took into account all relevant PAS. SMC is unable to present these results due to competition law issues.

6.3. Sensitivity analyses

The company provided probabilistic sensitivity analysis, deterministic sensitivity analysis (DSA) and scenario analysis. In the DSA, parameters relating to 2L immunotherapy in the CT arm and utility values had the greatest effect on the incremental cost-effectiveness ratio.

The company also conducted scenario analyses to test the impact of several assumptions provided in Table 6.3 below.

Table 6.3 Range of scenarios explored within sensitivity analyses

#	Category	Base case value	Scenario value
Base case vs CT (all comer population)			
1	Time horizon	35	10
2			20
3	Discount rate (costs and utilities)	3.5%	1.5%
4	Impact of AE (cost and disutilities)	Include	Exclude
5	Utility values	KEYNOTE-158 (2L EC cohort, UK value set): progression-based	KEYNOTE-826 (1L cervical cancer, UK value set): Time to death
6			KEYNOTE-826 (1L cervical cancer, UK value set): progression-based
7			KEYNOTE-158 (full 2L+ EC cohort, UK value set): progression-based
8			KEYNOTE-775 (2L EC, Australian value set): progression-based
9	Subsequent treatment	Re-weighted trial-based treatment mix based on Scottish clinician input; no IO rechallenge	Alternative re-weighted trial-based treatment mix based on Scottish clinician input, also assuming equal radiotherapy use between arms; no IO rechallenge
10			Re-weighted trial-based treatment mix based on UK advisory board clinician input; no IO rechallenge
11			Treatment mix as per KEYNOTE-868 (NRG-GY018); no IO rechallenge
12			Treatment mix as per KEYNOTE-868 (NRG-GY018); includes IO rechallenge
13	Healthcare resource utilisation	UK clinician inputs	Healthcare resource use reported in TA963
14	OS extrapolation	Pembrolizumab + CT: 3-knot odds CT: standard log-logistic	CT: standard generalised gamma
15			CT: standard log-normal
16			Pembrolizumab + CT: two-piece log-normal
17			Pembrolizumab + CT: 2-knot (odds)
18	PFS extrapolation	Pembrolizumab + CT: two-piece log-normal CT: 1-knot (hazard)	Pembrolizumab + CT: two-piece log-logistic CT: two-piece log-normal
19	PFS extrapolation (dMMR)	Time-varying hazard ratio from NMA applied to selected pembrolizumab curve to estimate	Apply hazard ratio of 1 for dostarlimab + CT vs pembrolizumab + CT (i.e. assume equivalent efficacy)

		dostarlimab efficacy	
20	Treatment waning	No waning applied	Applied to a proportion of pembrolizumab + CT patients. Assumed start at 7 years (post treatment initiation) for 2 years before efficacy of CT is assumed
21	TTD extrapolation	Pembrolizumab + CT: Observed KM CT: Observed KM	Pembrolizumab + CT: Standard generalised gamma CT: Standard Weibull

Abbreviations: 2L, second-line; AE, adverse event; CT, paclitaxel + carboplatin; EC, endometrial carcinoma; IO, immunotherapy; ICER, incremental cost effectiveness ratio; ITT, intention to treat; KM, Kaplan–Meier; NICE, National Institute of Health and Care Excellence; NMA, network meta-analysis; OS, overall survival; PFS, progression-free survival; TOT, time on treatment; TTD, time to treatment discontinuation; TVHR, time-varying hazard ratio.

6.4. Key strengths

The economic model was comprehensive and structurally sound. Appropriate sources were selected to inform the model parameters and results were based on the latest available data-cut from KEYNOTE-868.[8, 10]

6.5. Key uncertainties

There were some limitations with the analysis which include the following:

- There were concerns about the economic analysis being based on the all-comer population rather than dMMR and pMMR groups separately. Treatment options and clinical management of endometrial cancer patients varies based on dMMR or pMMR subtype. The prognosis of these two subgroups also varies substantially. KEYNOTE-868, was designed and powered to assess the primary outcome, PFS, separately in the dMMR and pMMR cohorts.[8-10] It is therefore unclear if retrospectively combining the two subgroups is entirely appropriate and does not bias results in any meaningful way. The two subgroups should ideally have been considered separately in the base case.
- An analytical limitation of pembrolizumab's effectiveness is the immaturity of the OS data. The robustness of the model essentially relies on parametric extrapolation of OS outcomes validated by expert opinion. This is compounded by the uninterpretable later analyses due to unblinding and discontinuation in the placebo arm. OS is likely to be different in the dMMR and pMMR subgroups which increases the uncertainty around the combined OS of the all-comer population.
- There is substantial uncertainty associated with the utility values applied in the analysis. Utilities from KEYNOTE 868 were not available, hence values from the endometrial cancer subgroup of patients in KEYNOTE 158 were adopted for the all-comer population.[12] These utilities may not be generalisable due to the small sample size of the endometrial cancer subgroup and the exclusion of any pMMR patients from KEYNOTE 158. It is plausible that dMMR patients may have higher utility scores compared to pMMR patients as they respond differently to immunotherapy. Hence having a single progression-based utility score for the all-comer population is likely to be biased.
- dMMR and pMMR patients are treated differently in clinical practice and there are

differences in types of subsequent treatments available to the two subgroups.[2, 3, 12] Hence, the application of a combined treatment mix for the all-comer population in the base case may not be entirely appropriate.

*Other data were also assessed but remain confidential.**

7. Conclusion

After considering all the available evidence, the Committee accepted pembrolizumab for use in NHSScotland.

8. Guidelines and Protocols

In November 2021, the BGCS published 'Uterine cancer guidelines: recommendations for practice.'[2]

In June 2022, the European Society for Medical Oncology (ESMO) published 'Guidelines on the diagnosis, treatment and follow-up of endometrial cancer.'[3]

9. Additional Information

9.1. Product availability date

19 February 2025

Table 9.1 List price of medicine under review

Medicine	Dose regimen	Cost per course (£)
Pembrolizumab Carboplatin Paclitaxel	200 mg IV every three weeks for six doses then 400 mg IV every six weeks for 14 doses AUC 5 mg/mL/minute IV every three weeks for six doses 175 mg/m^2 BSA IV every three weeks for six doses	184,544

AUC = area under the curve, BSA = body surface area, IV = intravenous; Costs based on body surface area of 1.8 m^2. Costs from BNF online on 26 March 2025. Costs calculated using the full cost of vials/ampoules assuming wastage. Costs do not take any patient access schemes into consideration.

10. Company Estimate of Eligible Population and Estimated Budget Impact

SMC is unable to publish the with PAS budget impact due to commercial in confidence issues. A budget impact template is provided in confidence to NHS health boards to enable them to estimate the predicted budget with the PAS. This template does not incorporate any PAS discounts associated with comparator medicines.

*Other data were also assessed but remain confidential.**

References

1. Merck Sharp and Dohme. Pembrolizumab (Keytruda®) Summary of Product Characteristics. Electronic Medicines Compendium www.medicines.org.uk/emc/ Last updated 25 February 2025.
2. Morrison J, Balega J, Buckley L, et al. British Gynaecological Cancer Society (BGCS) uterine cancer guidelines: Recommendations for practice. European journal of obstetrics, gynecology, and reproductive biology 2022; 270: 50-89.
3. Oaknin A, Bosse TJ, Creutzberg CL, et al. Endometrial cancer: ESMO Clinical Practice Guideline for diagnosis, treatment and follow-up. Ann Oncol 2022; 33(9): 860-77.
4. Corr BR, Erickson BK, Barber EL, et al. Advances in the management of endometrial cancer. BMJ 2025; 388: e080978.
5. GlaxoSmithKline. Dostarlimab (Jemperli®) Summary of Product Characteristics. Electronic Medicines Compendium www.medicines.org.uk/emc/ Last updated 23 December 2024.
6. AstraZeneca. Durvalumab (Imfinzi®) Summary of Product Characteristics. Electronic Medicines Compendium www.medicines.org.uk/emc/ Last updated 29 January 2025.
7. Public Health Scotland. Cancer Medicines Outcome Programme (CMOP) report, first-line treatment for primary advanced or recurrent endometrial cancer, 29 April 2025
8. European Medicines Agency (EMA). European public assessment report for pembrolizumab (Keytruda®), EMEA/H/C/003820/II/0153, 19 September 2024.
9. Eskander RN, Sill MW, Beffa L, et al. Pembrolizumab plus chemotherapy in advanced endometrial cancer. N Engl J Med 2023; 388(23): 2159-70.
10. Eskander RN, Sill MW, Beffa L, et al. Pembrolizumab plus chemotherapy in advanced or recurrent endometrial cancer: overall survival and exploratory analyses of the NRG GY018 phase 3 randomized trial. Nat Med 2025, https://doi.org/10.1038/s41591-025-03566-1.
11. Powell M, Bjorge L, Willmott L, et al. Overall survival in patients with endometrial cancer treated with dostarlimab plus carboplatin-paclitaxel in the randomized ENGOT-EN6/GOG-3031/RUBY trial. Ann Oncol 2024; 35(8): 728-38.
12. Marabelle A, Le DT, Ascierto PA, et al. Efficacy of pembrolizumab in patients with noncolorectal high microsatellite instability/mismatch repair-deficient cancer: results from the phase II KEYNOTE-158 Study. J Clin Oncol 2020; 38(1): 1-10.

This assessment is based on data submitted by the applicant company up to and including 14 May 2025.

**Agreement between the Association of the British Pharmaceutical Industry (ABPI) and the SMC on guidelines for the release of company data into the public domain during a health technology appraisal:*https://www.scottishmedicines.org.uk/about-us/policies-publications/

Medicine prices are those available at the time the papers were issued to SMC for consideration. SMC is aware that for some hospital-only products national or local contracts may be in place for comparator products that can significantly reduce the acquisition cost to Health Boards. These contract prices are commercial in confidence and cannot be put in the public domain, including via the SMC Detailed Advice Document. Area Drug and Therapeutics Committees and NHS Boards are therefore asked to consider contract pricing when reviewing advice on medicines accepted by SMC.

Patient access schemes: A patient access scheme is a scheme proposed by a pharmaceutical company in order to improve the cost-effectiveness of a medicine and enable patients to receive

access to cost-effective innovative medicines. A Patient Access Scheme Assessment Group (PASAG), established under the auspices of NHS National Services Scotland reviews and advises NHSScotland on the feasibility of proposed schemes for implementation. The PASAG operates separately from SMC in order to maintain the integrity and independence of the assessment process of the SMC. When SMC accepts a medicine for use in NHSScotland on the basis of a patient access scheme that has been considered feasible by PASAG, a set of guidance notes on the operation of the scheme will be circulated to Area Drug and Therapeutics Committees and NHS Boards prior to publication of SMC advice.

Advice context:

No part of this advice may be used without the whole of the advice being quoted in full.

This advice represents the view of the Scottish Medicines Consortium and was arrived at after careful consideration and evaluation of the available evidence. It is provided to inform the considerations of Area Drug & Therapeutics Committees and NHS Boards in Scotland in determining medicines for local use or local formulary inclusion. This advice does not override the individual responsibility of health professionals to make decisions in the exercise of their clinical judgement in the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.