SMC2797

durvalumab concentrate for solution for infusion (Imfinzi®)

AstraZeneca UK Limited

05 September 2025

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

ADVICE: following a full submission assessed under the end of life and orphan equivalent medicine process

durvalumab (Imfinzi®) is accepted for use within NHSScotland

Indication under review: in combination with carboplatin and paclitaxel for the first-line treatment of adults with primary advanced or recurrent endometrial cancer who are candidates for systemic therapy, followed by maintenance treatment with:

- durvalumab as monotherapy in endometrial cancer that is mismatch repair deficient (dMMR)
- durvalumab in combination with olaparib in endometrial cancer that is mismatch repair proficient (pMMR).

In a double-blind, randomised, phase III study, progression-free survival was significantly improved with the addition of durvalumab to chemotherapy followed by durvalumab maintenance with or without olaparib compared with chemotherapy alone in patients with primary advanced or recurrent endometrial cancer.

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.

This advice takes account of the views from a Patient and Clinician Engagement (PACE) meeting.

Chair,
Scottish Medicines Consortium

1. Clinical Context

1.1. Medicine background

Durvalumab is a human monoclonal antibody which binds to programmed cell death ligand-1 (PD-L1) and inhibits the interaction of PD-L1 with PD-1 and CD80. This enhances anti-tumour immune responses and increases T-cell activation. In the indication under review, the recommended dose of durvalumab is 1,120 mg intravenously (IV) every 3 weeks in combination with carboplatin and paclitaxel for a minimum of four and up to six cycles. This is followed by durvalumab 1,500 mg IV every 4 weeks as monotherapy in mismatch repair deficient (dMMR) patients or in combination with olaparib 300 mg orally twice daily in mismatch repair proficient (pMMR) patients. Treatment is continued until disease progression or unacceptable toxicity. See Summary of Product Characteristics (SPC) for more details.[1, 2]

1.2. Disease background

Endometrial cancer is the fourth most common cancer in women in the UK. The incidence 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 5 years. About 25% to 30% of endometrial cancers are dMMR. Endometrial cancer that is dMMR is more likely to have high levels of mutations.[3-6]

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.[4] This is the current standard of care for patients with 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, pembrolizumab, has been recently licensed for both dMMR and pMMR cohorts in this indication.[7, 8] NHSScotland 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 (SACT) for advanced endometrial cancer received carboplatin plus paclitaxel or one of these medicines alone, while a smaller proportion received both in combination with dostarlimab.[9]

1.4. Category for decision-making process (if appropriate)

<u>Eligibility for a PACE meeting</u>

Durvalumab meets SMC orphan equivalent and end of life criteria for this indication.

2. Summary of Clinical Evidence

2.1. Evidence for the licensed indication under review

Evidence to support the efficacy and safety of durvalumab with or without olaparib comes from the DUO-E study. Details are summarised in Table 2.1.

Table 2.1. Overview of relevant studies[2, 10]

Criteria	DUO-E
Study design	Double-blind, randomised, placebo-controlled, phase III study.
Eligible patients	• aged 18 years or older with histologically confirmed newly diagnosed advanced (FIGO measurable stage III or stage IV) or recurrent endometrial cancer. • not treated with systemic anticancer therapy (except recurrent patients treated in the adjuvant setting at least 12 months after completing this prior treatment and relapse) • recurrent disease with poor potential for curative surgery • known MMR status • ECOG performance status of 0 or 1
Treatments	Paclitaxel 175 mg/m^2 BSA IV and carboplatin AUC5 or AUC6 mg/mL/min IV every 3 weeks for a maximum of six cycles together with one of the following three treatments: • durvalumab 1,120 mg IV every 3 weeks, followed by maintenance treatment with durvalumab 1,500 mg IV every 4 weeks and placebo orally twice daily until disease progression. • durvalumab 1,120 mg every 3 weeks, followed by maintenance treatment with durvalumab 1,500 mg IV every 4 weeks with olaparib 300 mg orally twice daily until disease progression. • placebo IV every 3 weeks, followed by maintenance treatment with placebo IV every 4 weeks and placebo orally twice daily until disease progression.
Randomisation	Patients were randomised equally with stratification by MMR status (proficient versus deficient), disease status (newly diagnosed versus recurrent) and geographic region (Asia versus non-Asia).
Primary outcome	PFS defined as time between date of randomisation to date of objective disease progression as assessed by investigator using RECIST v1.1 criteria or death due to any cause, whichever occurred first.
Secondary outcomes	• OS, defined as time from randomisation to death from any cause • ORR, defined as proportion of patients with measurable disease at baseline who achieved a complete or partial response assessed by investigator. • DoR, defined as time from first documented response until documented progression or death in absence of progression.
Statistical analysis	The primary outcome of investigator-assessed PFS was tested independently in the two treatment groups: (1) durvalumab plus chemotherapy versus placebo plus chemotherapy, and (2) durvalumab plus olaparib plus chemotherapy versus placebo plus chemotherapy. The study was also controlled for multiplicity across the analyses of the primary outcome and key secondary outcome of OS.

Abbreviations: AUC = area under the curve; BSA = body surface area; dMMR = mismatch repair deficient; DoR = duration of response; ECOG = Eastern Co-operative Oncology Group; FIGO = International Federation of Gynecology and Obstetrics; IV = intravenous; ORR = objective response rate; OS = overall survival; PFS = progression-free survival; pMMR = mismatch repair proficient; RECIST = Response Evaluation Criteria in Solid Tumors.

At the time of the primary progression-free survival (PFS) analysis (data cut-off 12 April 2023), there were significant improvements in investigator-assessed PFS in both the durvalumab (plus chemotherapy) and durvalumab plus maintenance olaparib (plus chemotherapy) groups compared

with placebo (plus chemotherapy). The interim analyses of overall survival (OS) performed at this time did not meet the predefined thresholds for superiority of either durvalumab group over placebo. Details are presented in Table 2.2.

Table 2.2: Results for primary and selected secondary outcomes in ITT population of DUO-E[1, 2, 10]

	Durvalumab plus chemotherapy (n=238)	**Durvalumab plus olaparib plus chemotherapy (n=239)**	**Placebo plus chemotherapy (n=241)**
Primary outcome: investigator-assessed PFS			
Median follow-up, months	15.4	15.4	12.6
Number of PFS events	139	126	173
Median PFS, months	10.2	15.1	9.6
HR (95% CI), p-value versus placebo	0.71 (0.57 to 0.89), p=0.003	0.55 (0.43 to 0.69), p<0.001	-
18-month PFS rate	38%	46%	22%
Secondary outcome: OS			
Median follow-up, months	18.4	18.7	18.6
Number of deaths	65	52	82
Median OS, months	NR	NR	25.9
HR (95% CI) versus placebo	0.77 (0.56 to 1.07)[A]	0.59 (0.42 to 0.83)[A]	-
18-month OS rate	75%	79%	69%
Secondary outcome: ORR	**n=202**	**n=184**	**n=198**
Patients with ORR, %	62% (125/202)	64% (117/184)	55% (109/198)
OR (95% CI) versus placebo	1.32 (0.89 to 1.90)	1.44 (0.95 to 2.18)	-
Median duration of response, months	13.1	21.3	7.7

[A] p=value did not meet the predefined level for statistical significance (stopping boundary of p<0.0011 for durvalumab plus chemotherapy versus chemotherapy and p<0.0006 for durvalumab, olaparib plus chemotherapy versus chemotherapy).
Abbreviations: CI = confidence interval; HR = hazard ratio; ITT = intention-to-treat; NR = not reached; OR = odds ratio; ORR = objective response rate; OS = overall survival; PFS = progression-free survival

Subgroup analyses were performed according to MMR status and the results for durvalumab (plus chemotherapy) versus placebo (plus chemotherapy) support the licensed indication in the dMMR subgroup; while results for durvalumab plus maintenance olaparib (plus chemotherapy) versus placebo (plus chemotherapy) support the licensed indication in the pMMR subgroup. Only the subgroup analyses of PFS were prespecified with those for other outcomes assessed post hoc. The study was not powered for subgroup analyses and results are considered descriptive only. Details are presented in Table 2.3.

Table 2.3: Results for subgroup analyses of primary and selected secondary outcomes according to MMR population and licensed treatment from DUO-E.[1, 2, 10]

	dMMR		pMMR	
	Durvalumab plus chemotherapy (n-46)	**Placebo plus chemotherapy (n=49)**	**Durvalumab plus olaparib plus chemotherapy (n=191)**	**Placebo plus chemotherapy (n=192)**
Primary outcome: investigator-assessed PFS				
Median follow-up, months	15.5	10.2	15.2	12.8
Number of PFS events	15	25	108	148
Median PFS, months	NR	7.0	15.0	9.7
HR (95% CI) versus placebo	0.42 (0.22 to 0.80)		0.57 (0.44 to 0.73)	
18-month PFS rate	68%	32%	42%	20%
Secondary outcome: OS				
Median follow-up, months	19.1	18.4	18.4	18.6
Number of deaths	7	18	46	64
Median OS, months	NR	23.7	NR	25.9
HR (95% CI) versus placebo	0.34 (0.13 to 0.79)		0.69 (0.47 to 1.00)	
12-month OS rate	91%	74%	87%	81%
Secondary outcome: ORR				
Patients with ORR, %	71% (30/42)	40% (17/42)	61% (90/147)	59% (92/156)
OR (95% CI) versus placebo	3.68 (1.51 to 9.39)		1.10 (0.69 to 1.74)	
Median duration of response, months	NR	10.5	18.7	7.6

Abbreviations: CI = confidence interval; dMMR = mismatch repair deficient; HR = hazard ratio; MMR = mismatch repair; NR = not reached; OR = odds ratio; ORR = objective response rate; OS = overall survival; PFS = progression-free survival; pMMR = mismatch repair proficient.

2.2. Health-related quality of life outcomes

Health-Related Quality of Life (HRQoL) was assessed using the European Organisation for Research and Treatment of Cancer (EORTC) Core Quality of Life Questionnaire (EORTC QLQ-C30) and the EORTC Quality of Life Questionnaire-Endometrial Cancer Module (EORTC QLQ-EN24) as secondary outcomes. These instruments were used at baseline, every 3 weeks for six cycles and then every 4 weeks until second disease progression. The EORTC QLQ-C30 is a generic cancer assessment comprising five functional scales and three symptom scales and global health status (score range 0 to 100 with higher scores indicating better functioning or worse symptoms). The EORTC QLQ-EN24 is an endometrial cancer specific assessment of symptoms and functioning (score range 0 to 100 with higher scores indicating better functioning or worse symptoms).

There was an initial decrease (worsening) in overall EORTC QLQ-C30 from baseline during the chemotherapy period in all three treatment groups which improved once chemotherapy was stopped. The changes from baseline to data cut-off 12 April 2023 are small and slightly worse in the durvalumab plus olaparib group compared with the other two treatment groups during the maintenance period. However, differences between treatments were not considered clinically

meaningful. There were no clinically meaningful differences in the EORTC QLQ-EN24 key symptoms between groups with the exception of taste change.[2]

The EQ-5D-5L index score and visual analogue scale were assessed as exploratory outcomes. There was little difference between the three treatment groups over the study period.[2, 10]

Subgroup analyses of HRQoL outcomes based on MMR status were not performed.

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

In the absence of direct evidence versus dostarlimab in the dMMR subpopulation, the submitting company performed anchored indirect comparisons using data for the dMMR/microsatellite instability-high subgroups of DUO-E and RUBY-1. Details are presented in Table 2.4.

Table 2.4: Summary of indirect treatment comparison[10, 11]

Criteria	Overview
Design	Anchored MAIC (for PFS only) and unadjusted indirect comparison (for OS and safety).
Population	Adults with primary advanced or recurrent endometrial cancer that is dMMR and/or MSI-H.
Comparators	Dostarlimab plus SoC (carboplatin plus paclitaxel).
Studies included	DUO-E for durvalumab plus SoC (n=55 in a post hoc subpopulation with dMMR and/or MSI-H status) and RUBY-1 for dostarlimab plus SoC (n=53 in the dMMR/MSI-H subpopulation). Safety analyses were based on the full safety analysis populations (n=235 for durvalumab plus SoC and n=241 for dostarlimab plus SoC respectively).
Outcomes	PFS, OS and safety (grade 3 or higher AEs, AEs leading to discontinuation of immunotherapy or placebo and any SAE).
Results	There was no evidence of a difference in efficacy (PFS and OS) with durvalumab plus SoC compared with dostarlimab plus SoC: confidence intervals were very wide. Based on an unadjusted indirect comparison, durvalumab plus SoC may perform better in terms of grade 3 or higher AEs compared with dostarlimab plus SoC but there was no evidence of a difference in other safety outcomes.

Abbreviations: AE = adverse event; CI = confidence interval; dMMR = mismatch repair deficient; HR = hazard ratio; ITC = indirect treatment comparison; MAIC = matching adjusted indirect comparison; MSI-H = microsatellite instability-high; OR = odds ratio; OS = overall survival; PFS = progression-free survival; SAE = serious adverse event; SoC = standard of care.

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

3. Summary of Safety Evidence

The company submission has included safety data from DUO-E for the safety analysis set (n=709) during the overall treatment period (chemotherapy plus maintenance periods). The overall safety profile of durvalumab with chemotherapy followed by durvalumab with or without olaparib as maintenance therapy was generally consistent with the established safety profiles of the individual medicines. There was an increased incidence of grade 3 or 4 and serious adverse events (AEs) when olaparib was added to durvalumab during maintenance therapy. At data cut-off 12 April 2023, the median duration of treatment with carboplatin plus paclitaxel was six cycles across all three treatment groups. The median overall duration of treatment was 9.9 months in the durvalumab monotherapy group (n=235), 13.1 months of durvalumab and 9.2 months of olaparib in the durvalumab plus olaparib group (n=238) and was 9.0 months of IV placebo and 5.7 months of oral placebo in the placebo group (n=236). In the durvalumab, durvalumab plus olaparib and

placebo groups respectively, patients reporting a grade 3 or higher AE were 55%, 67% and 56%, patients reporting a serious AE were 31%, 36% and 31% and patients discontinuing durvalumab or placebo therapy due to an AE was 11%, 9.2% and 8.1%. Details of AEs in the dMMR and pMMR subpopulations were generally consistent with the overall safety population.[2, 10]

During the overall treatment period, the most frequently reported treatment-emergent AEs related to chemotherapy.[2, 10] Following chemotherapy during the maintenance period, frequently reported treatment-emergent AEs of any grade in the durvalumab, durvalumab plus olaparib and placebo groups of the full safety analysis set were: anaemia (8.7%, 36% and 10%), nausea (12%, 41% and 15%), fatigue or asthenia (10%, 32% and 12%), alopecia (1.1%, 2.6% and 0.6%), neutropenia (7.1%, 18% and 4.1%), constipation (7.1%, 6.8% and 5.3%), thrombocytopenia (3.3%, 14% and 5.3%), diarrhoea (15%, 18% and 12%), vomiting (7.1%, 20% and 9.5%) and peripheral neuropathy (2.7%, 6.3% and 3.0%).[10]

In the overall treatment period, immune-related AEs were reported in 28% of the durvalumab group, 24% of the durvalumab plus olaparib group and 6.8% of the placebo group. Those affecting more than 5% of the population included hypothyroid events in 14%, 12% and 2.5%; dermatitis or rash in 6.4%, 6.3% and 3.4%.[10]

An AE led to death in 1.7% (4/235) of patients in the durvalumab group, 2.1% (5/238) of patients in the durvalumab plus olaparib group and 3.4% (8/236) of patients in the placebo group. None of these events were considered related to study medication by the investigator.[2, 10]

A new AE of pure red cell aplasia was observed in three patients in the durvalumab plus olaparib group. The SPCs for both medicines have been updated to add this and to recommend that both medicines are discontinued if this AE is confirmed.[1, 2, 12]

4. Summary of Clinical Effectiveness Considerations

4.1. Key strengths

- The addition of durvalumab to carboplatin plus paclitaxel followed by maintenance durvalumab with or without olaparib significantly improved investigator-assessed PFS in patients with advanced or recurrent endometrial cancer and these improvements were considered clinically relevant. Carboplatin plus paclitaxel alone is a relevant comparator in the pMMR population.[2, 10]
- Available PFS results are supported by a trend in improvements in OS at the first interim analysis.[2, 10]
- The addition of durvalumab with or without olaparib maintenance to standard chemotherapy did not have a clinically meaningful detrimental effect on quality of life.[2]

4.2. Key uncertainties

- The evidence for the addition of durvalumab to chemotherapy in the dMMR population and of durvalumab plus maintenance olaparib in the pMMR population comes from subgroup analyses of DUO-E.[1, 2, 10] Subgroup analyses were only pre-specified for the primary outcome of PFS. In addition, subgroup analyses were not powered or controlled for type I error and should be interpreted with caution.[2, 10]

- In the dMMR subpopulation, the addition of durvalumab alone or with olaparib maintenance improved PFS over placebo to a similar extent. In the pMMR subpopulation, the addition of durvalumab alone to chemotherapy improved PFS and there was further improvement with the addition of maintenance olaparib.[2, 10]
- At the primary PFS analysis, the results for OS were immature (28% maturity with 199 deaths across all three groups). Median OS has not been reached in either the durvalumab or durvalumab plus olaparib groups.[2, 10]
- At baseline, just over half of study patients (53%) had recurrent disease and only a small proportion of patients had newly diagnosed stage III disease (5.7%) probably due to the requirement to have measurable disease at baseline. There were no UK study centres and a relatively high proportion of study patients were Asian (30%). These factors may affect the generalisability of study results to Scottish clinical practice.[2, 10]
- There are no direct comparative data versus dostarlimab plus chemotherapy which is the most relevant comparator in the dMMR subpopulation. The submitting company provided indirect comparisons using the dMMR/MSI-H subpopulations of the DUO-E and RUBY-1 studies which indicated similar efficacy and safety.[10, 11] There are a number of limitations which affect the robustness of these results including differences in patient characteristics, use of a small post hoc subgroup of dMMR/MSI-H patients from DUO-E and immature OS data from both studies with different durations of follow-up. The resulting between treatment hazard ratios had wide confidence intervals which included 1 suggesting no evidence of a difference but indicating uncertainty in the relative efficacy and safety. Despite these limitations, the results are considered reasonable.

4.3. Clinical expert input

Clinical experts consulted by SMC considered that durvalumab, when used in combination with olaparib and chemotherapy in patients with pMMR disease, fills an unmet need and provides a therapeutic advancement over chemotherapy alone, due to significant improvements in PFS.

4.4. Service implications

Clinical experts consulted by SMC considered that the introduction of the durvalumab plus olaparib regimen may impact on service delivery with additional visits for pMMR patients for administration and management following the six cycles of chemotherapy.

Diagnostic test required to identify patients eligible for treatment: contact local laboratory for information**.**

5. Patient and clinician engagement (PACE)

A patient and clinician engagement (PACE) meeting with patient group representatives and clinical specialists was held to consider the added value of durvalumab, as an orphan-equivalent and end of life medicine, in the context of treatments currently available in NHSScotland.

The key points expressed by the group were:

- Primary advanced or recurrent endometrial cancer is an incurable and life-limiting disease with debilitating physical symptoms, including pain and fatigue that limit the patient's ability to work and care for themselves or family. The patient's family may be required to support them and help them attend healthcare appointments. This disease has an immense psychological impact on patients and their family who can suffer anxiety and grief.
- There is the potential for healthcare inequality as Black women may be more likely to be diagnosed with pMMR endometrial cancer and more often with mutations and at a later stage.
- In this clinical setting, there are a limited number of immunotherapy-containing regimens, with this only recently being introduced for pMMR disease. For patients with dMMR and pMMR disease, the durvalumab regimen provides an additional treatment option that allows care to be individualised with respect to comorbidities and effects of previous treatments. In pMMR disease, it offers a regimen containing a class of medicine not previously available in this setting.
- The durvalumab regimens may provide patients with an extended time when their cancer is controlled, and they feel well. It may reduce their reliance on family and carers. Accessing this treatment may provide reassurance that they are receiving optimal therapy and give them hope that they may be able to continue to work, to enjoy life with their family, and to plan. It is possible that durvalumab may extend their life to a time when other new treatments become available. Overall, it may have a positive impact on patients' mental health, giving them hope and optimism for the future, and allowing them to lead a more meaningful and fuller life.
- Clinical experts advised that durvalumab would be used in line with its licence. Compared with other immunotherapies, it would require a similar number of hospital visits for administration, monitoring and management of side effects. There may be additional visits for management of side effects associated with olaparib.
- Patients noted that immunotherapies such as durvalumab may be associated with side effects, but they are happy to risk or to endure these to gain the substantial benefits in progression-free survival.

Additional Patient and Carer Involvement

We received a patient group submission from Peaches Womb Cancer Trust, which is a registered charity. Peaches Womb Cancer Trust has received 26.2% pharmaceutical company funding in the past two years, with none from the submitting company. A representative from Peaches Womb Cancer Trust participated in the PACE meeting. The key points of their submission have been included in the full PACE statement considered by SMC.

6. Summary of Comparative Health Economic Evidence

6.1. Economic case

The economic case is summarised in Table 6.1.

Table 6.1 Description of economic analysis

Criteria	Overview
Analysis type	Cost utility analysis
Time horizon	37.4 years based on a starting age of 62.6 years
Population	The analysis population matched the licensed population. The modelling was conducted separately for the dMMR and pMMR subgroups.
Comparators	Within the dMMR subgroup, durvalumab plus SoC was compared with dostarlimab plus SoC and SoC alone. In the pMMR subgroup, durvalumab plus olaparib plus SoC was compared against SoC alone. In all cases SoC was assumed to comprise of carboplatin plus paclitaxel.
Model description	The model was a three-state partitioned survival model. The three included states were progression-free, progressed disease and death.
Clinical data	The main source of clinical data was the DUO-E study.[1, 2, 10] This provided PFS and OS data in the durvalumab plus SoC arm (dMMR), durvalumab plus olaparib plus SoC (pMMR) and SoC (both dMMR and pMMR). The company identified dostarlimab plus SoC as a relevant comparator in the dMMR population, but this was not included in the DUO-E study. The submitting company based their assumptions regarding the efficacy of dostarlimab plus SoC on an indirect treatment comparison (ITC) (details of which are provided in Section 2.3).
Extrapolation	The submitting company fitted independent parametric curves to the treatment arms in the DUO-E study. In the dMMR subgroup PFS was extrapolated using 2-knot spline model in the durvalumab plus SoC arm, and a 1-knot spline model in the SoC arm. A log-normal curve was used for OS across both durvalumab plus SoC and SoC. In the pMMR subgroup a log-logistic curve was used to extrapolate PFS and OS in both the durvalumab plus olaparib plus SoC and SoC arms. Based on the results of the ITC, the company assumed that in the dMMR population that dostarlimab plus SoC and durvalumab plus SoC had identical clinical outcomes.
Quality of life	Quality of life data were collected in the DUO-E study using the EQ-5D-5L instrument, which was mapped to the 3L values using Hernández Alava et al. (2017)[13] and Hernández Alava et al. (2020)[14]. State utility values were consistent across the dMMR and pMMR populations. Age adjustment was applied. A one-off AE disutility was included in the first model cycle.
Costs and resource use	Medicine costs included in the model were acquisition costs (including subsequent treatments), administration costs and adverse events costs. No cost for MMR type testing was included as this was assumed standard practice for endometrial cancer patients in Scotland. Wider NHS costs included in the model were health state resource costs and an end of life cost. The sub-elements of the health state resource costs were outpatient visits, CT scan, complete blood counts, specialist nurse visits, GP visits, cancer antigen-125 tests, and thyroid function tests.
PAS	Patient Access Schemes (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 of durvalumab and olaparib. A PAS discount is in place for dostarlimab and this was included in the results used for decision-making by using estimates of the comparator PAS price. 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.

6.2. Results

The company presented economic analysis which compared the costs and health outcomes between the various treatment options. SMC is unable to present decision-making results due to the confidential PAS discounts on durvalumab, olaparib and dostarlimab.

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

6.3. Sensitivity analyses

A range of sensitivity and scenario analyses were considered and descriptions of these key scenarios are provided in Table 6.2.

Table 6.2. Scenario analysis

				dMMR		pMMR
No.	**Parameter**	**Base case**	**Scenario**	**SoC + dostarlimab–ICER (£/QALY)**	**SoC–ICER (£/QALY)**	**SoC–ICER (£/QALY)**
	Base case	-	-	**CiC**	**CiC**	**CiC**
1	Time horizon	Lifetime (37.4 years)	25 years	**CiC**	**CiC**	**CiC**
2	Efficacy of dostarlimab	Dostarlimab PFS = durvalumab PFS	Dostarlimab PFS set to ITC upper 95% CI limit	**CiC**	**N/A**	**N/A**
3			Dostarlimab PFS set to ITC lower 95% CI limit	**CiC**	**N/A**	**N/A**
4		Dostarlimab OS = durvalumab OS	Dostarlimab PFS set to ITC upper 95% CI limit	**CiC**	**N/A**	**N/A**
5			Dostarlimab PFS set to ITC lower 95% CI limit	**CiC**	**N/A**	**N/A**
6	PFS parametric curve	Various–See Table 6.1 for details	Weibull	**CiC**	**CiC**	**CiC**
7			Spline, 1 knot	**CiC**	**CiC**	**N/A**
8	OS parametric curve	Various – See Table 6.1 for details	Weibull	**CiC**	**CiC**	**CiC**
9			Log-normal	**CiC**	**CiC**	**CiC**
10			Log-logistic	**CiC**	**CiC**	**CiC**
11	Durvalumab (and olaparib where relevant) stopping rule	Treatment duration 3 years	Treatment duration 5 years	**CiC**	**CiC**	**CiC**
12			Stopping rule removed, no drop off	**CiC**	**CiC**	**CiC**
13	RDI	Include	Exclude	**CiC**	**CiC**	**CiC**

14	Combined	• Stopping rule at 5 years, no drop off • Removal of RDI	**CiC**	**CiC**	**CiC**

Abbreviations: SoC, standard of care; QALY, quality adjusted life year; Incr., incremental; LYG, life year gained; ICER, incremental cost-effectiveness ratio; ITC, indirect treatment comparison; CI, confidence interval; PFS, progression-free survival; OS, overall survival, RDI, relative dose intensity

6.4. Key strengths

- The choice of comparators was appropriate, and matched the treatments highlighted as standard practice in Scotland by experts consulted by SMC.
- The modelling approach was reasonable and similar to that used in other HTA submissions for related indications.
- Quality of life data came from the central clinical study and appeared to align well with external sources.

6.5. Key uncertainties

- There was no directly comparable data between durvalumab plus SoC and dostarlimab plus SoC. This meant the submitting company relied on an ITC. The ITC concluded that there was no statistical difference between durvalumab and dostarlimab and the company used this as justification to assume identical clinical outcomes across the two treatments. The company argued that because durvalumab and dostarlimab have the same mechanism of action, it was reasonable to assume a similar treatment effect, despite the wide confidence intervals generated in the ITC. However, this was still an area of uncertainty. Should the efficacy of durvalumab not match that of dostarlimab, it could have a large impact upon the economic results (see Scenarios 2 to 5 in Table 6.3).
- The analysis within the dMMR population applies a relative dose intensity to durvalumab, matched to the observed rate of missed doses in the DUO-E study. The company assumed that all doses of dostarlimab were administered, which may have artificially increased the costs within that treatment arm. This assumption was favourable to durvalumab and may have exaggerated the cost-effectiveness of durvalumab treatment (Scenario 13).
- The submitting company applied a 3-year stopping rule for durvalumab treatment. This is not specified in the SPC and was viewed as uncertain. The submitting company received clinical feedback which stated that almost all patients would finish treatment within 5 years. A scenario testing treatment to a maximum of 5 years increased the ICER (Scenario 11).

7. Conclusion

The Committee considered the benefits of durvalumab in the context of the SMC decision modifiers that can be applied when encountering high cost-effectiveness ratios and agreed that as durvalumab is an orphan equivalent medicine, SMC can accept greater uncertainty in the economic case.

After considering all the available evidence and the output from the PACE process, the Committee accepted durvalumab for use in NHSScotland.

8. Guidelines and Protocols

The British Gynaecological Cancer Society (BGCS) published guidelines on the recommendations for practice of uterine cancer in November 2021.[4]

The European Society for Medical Oncology (ESMO) published guidelines on the diagnosis, treatment and follow-up of endometrial cancer in June 2022.[5]

The European Society of Gynaecological Oncology (ESGO), the European Society for Radiotherapy and Oncology (ESTRO) and the European Society of Pathology (ESP) published updated guidelines for the management of patients with endometrial cancer in December 2020.[15]

9. Additional Information

9.1. Product availability date

9 December 2024

Table 9.1 List price of medicine under review

Medicine	Dose regimen	Cost per cycle (£)
durvalumab + carboplatin + paclitaxel	1,120 mg IV every 3 weeks for four to six cycles AUC 5 or 6 mg/ml/min IV every 3 weeks for four to six cycles 175 mg/m^2 IV every 3 weeks for four to six cycles	5,524 338 668 = 6,530 per 3-week cycle
followed by maintenance durvalumab (+ olaparib in pMMR only)	1,500 mg IV every 4 weeks (300 mg orally twice daily) until disease progression	7,398 (+ 4,635) per 4-week cycle

AUC = area under the curve; IV = intravenous.

Costs from BNF online on 31 March 2025. Costs calculated using the full cost of vials/ampoules assuming wastage. Costs for carboplatin are based on up to maximum dose of 900 mg; costs for paclitaxel are based on body surface area of 1.8 m^2. 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 or PAS associated with medicines used in a combination regimen.

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

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This assessment is based on data submitted by the applicant company up to and including 25 July 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.