dostarlimab concentrate for solution for infusion (Jemperli®)

GlaxoSmithKline

08 March 2024

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

dostarlimab (Jemperli®) is accepted for use within NHSScotland.

Indication under review: in combination with platinum-containing chemotherapy for the treatment of adult patients with mismatch repair deficient (dMMR)/microsatellite instability-high (MSI-H) primary advanced or recurrent endometrial cancer and who are candidates for systemic therapy.

In a double-blind, randomised, phase III study, progression-free survival was significantly improved with dostarlimab in combination with platinum-containing chemotherapy compared with platinum-containing chemotherapy alone in patients with dMMR/MSI-H 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.

Overleaf is the detailed advice on this product.

Chair
Scottish Medicines Consortium

1. Clinical Context

1.1. Medicine background

Dostarlimab is a humanised monoclonal antibody that binds to programmed cell death protein (PD)-1 receptors causing inhibition of PD-1 pathway-mediated immune responses that results in inhibition of T-cell function such as proliferation, cytokine production, and cytotoxic activity. Dostarlimab also potentiates T-cell responses, including anti-tumour immuno-responses through blockade of PD-1 binding to PD-ligand (L)1 and PD-L2. The recommended dose as combination therapy is dostarlimab 500 mg by intravenous infusion every 3 weeks for six cycles with chemotherapy followed by dostarlimab 1,000 mg every 6 weeks for all cycles thereafter until disease progression, unacceptable toxicity or for a duration of up to 3 years. Refer to the product information for the recommended doses of concomitantly used chemotherapeutic agents.[1]

SMC recently accepted dostarlimab on an interim basis for use as monotherapy for the treatment of adult patients with mismatch repair deficient (dMMR)/microsatellite instability-high (MSI-H) recurrent or advanced endometrial cancer (EC) that has progressed on or following prior treatment with a platinum-containing regimen (SMC2404).

1.2. Disease background

Endometrial cancer (EC) is the sixth most common cancer among females worldwide. It predominantly affects postmenopausal women and those over 50 years of age. Most cases are diagnosed at an early stage (Federation of Gynecology and Obstetrics [FIGO] stages I or II), 10% to 15% of cases recur, with 80% to 90% of recurrences within 3 years, and approximately 20% of cases are diagnosed with advanced or metastatic disease (stage III or IV).[2]

Endometrial cancer can be classified as dMMR when defective DNA MMR results in genetic hyper mutability known as MSI. The resulting accumulation of base pair mismatches interferes with normal DNA replication and drives genomic instability. Cases of dMMR/MSI-H tumours account for 25% to 30% of endometrial cancers.[3, 4]

1.3. Treatment pathway and relevant comparators

For patients with advanced or metastatic EC, surgery alone is unlikely to be curative and systemic chemotherapy becomes a key component of treatment. Carboplatin plus paclitaxel is the standard of care for patients with advanced or recurrent disease and was considered the relevant comparator in this submission. The immunotherapies, dostarlimab and pembrolizumab (that inhibit the PD-1 pathway), are licensed for use in patients with advanced or recurrent disease that has progressed on or following platinum-containing chemotherapy (that is, in the second-line setting). Currently, there are no immunotherapy medicines used routinely for the first-line treatment of these patients.[1, 3, 5]

1.4. Category for decision-making process

Eligibility for interim acceptance decision option

Dostarlimab received a positive scientific opinion under the Early Access to Medicines Scheme with the Medicines and Healthcare Products Regulatory Agency (MHRA).

Dostarlimab received an Innovation Passport allowing entry into the Innovative Licensing and Access Pathway (ILAP).

Eligibility for a PACE meeting
Dostarlimab meets SMC orphan equivalent 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 dostarlimab in combination with platinum-containing chemotherapy for primary advanced or recurrent endometrial cancer comes from the RUBY-1 study.[4] Details are summarised in Table 2.1.

Table 2.1. Overview of relevant study[4]

Criteria	RUBY-1
Study design	Double-blind, randomised, placebo-controlled, phase III study
Eligible patients	- Aged ≥18 years with histologically or cytologically confirmed primary advanced or first recurrent endometrial cancer not treated with systemic therapy (first recurrent patients treated with prior [neo]adjuvant systemic anticancer therapy had to have progressed ≥6 months after completing this prior treatment) - FIGO stage III or IV disease not amenable to curative therapy - ECOG performance status of 0 or 1
Treatments	Dostarlimab 500 mg or placebo IV in combination with carboplatin (AUC of 5 mg/mL/min) IV and paclitaxel (175 mg/m^2 BSA) IV once every 3 weeks for the first six cycles, followed by dostarlimab 1000 mg or placebo IV once every 6 weeks for up to 3 years, or until disease progression, toxic effect of treatment, patient withdrawal, investigator decision to withdrawal or death.
Randomisation	Patients were randomised equally with stratification by MMR/MSI status (dMMR/MSI-H or pMMR/MSS), previous external pelvic radiotherapy (yes or no) and disease status (recurrent, primary stage III or primary stage IV).
Primary outcome	There were two co-primary outcomes: - PFS defined as the time from randomisation until radiographic progressed disease (investigator-assessed using RECIST v1.1) or death from any cause in the dMMR/MSI-H subpopulation and in the ITT population, which included all randomised patients. - OS defined as the time from randomisation until death from any cause in the ITT population.
Secondary outcomes	- ORR defined as the proportion of patients with a best overall response of complete or partial response (investigator-assessed using RECIST v1.1) - DOR defined as the time from first documented response until first progressive disease (investigator-assessed using RECIST v1.1) or death from any cause - DCR defined as the proportion of patients with a best overall response of complete or partial response or stable disease (investigator-assessed using RECIST v1.1) - PFS2 defined as time from randomisation to date of assessment of progression on the first subsequent anticancer therapy following study treatment or death by any cause
Statistical analysis	The co-primary outcomes were tested in the following hierarchical order: PFS in the dMMR/MSI-H subpopulation, PFS in the ITT population and OS in the ITT population. Other secondary outcomes were considered descriptive only.

AUC = area under the curve; BSA = body surface area; DCR = disease control rate; dMMR/MSI-H = mismatch repair deficient/microsatellite instability-high; DOR = duration of response; ECOG = Eastern Co-operative Oncology Group; FIGO = Federation of Gynecology and Obstetrics; ITT = intention to treat; IV = intravenous; pMMR/MSS = mismatch repair-proficient/ microsatellite-stable; OS = overall survival; ORR = objective response rate; PFS = progression-free

survival; PFS2 = time to progression on first subsequent treatment; RECIST = Response Evaluation Criteria in Solid Tumors.

A hierarchical statistical testing strategy was applied where the primary outcomes were tested in a pre-specified order: progression-free survival (PFS) in the dMMR/MSI-H subpopulation, PFS in the intention to treat (ITT) population and overall survival (OS) in the ITT population. At the interim analysis (data cut-off 28 September 2022), there was a significantly greater improvement in PFS in the dMMR/MSI-H subpopulation and the ITT population in the dostarlimab group compared with the placebo group. There was also better OS in the ITT population in the dostarlimab group compared with the placebo group; the difference did not cross the p-value stopping boundary at this first interim analysis but did reach statistical significance at the second interim analysis (further details below table 2.2).[4] In the dMMR/MSI-H subpopulation, OS was only assessed as a pre-specified subgroup analysis and results are descriptive only. RUBY-1 included a number of secondary outcomes including objective response rate (ORR), duration of response (DOR), disease control rate (DCR) and time to progression on first subsequent anticancer therapy (PFS2). Secondary outcomes were not included in the hierarchical testing and results are descriptive only.[1, 4] Details of results are presented in Table 2.2.

Table 2.2 Results for co-primary and selected secondary outcomes in RUBY-1 study at first interim analysis (data cut-off 28 September 2022)[1, 4, 6]

	dMMR/MSI-H subpopulation		**ITT population**	
	Dostarlimab (n=53)	**Placebo (n=65)**	**Dostarlimab (n=245)**	**Placebo (n=249)**
Primary outcome: PFS				
Median duration of follow-up, months	24.8		25.4	
Number of PFS events	19	47	135	177
Median PFS	Not reached	7.7	[c]	[c]
Hazard ratio (95% CI), p-value	0.28 (0.16 to 0.50) p<0.001		0.64 (0.51 to 0.80), p<0.001	
KM estimated PFS at 24-months	61%	16%	36%	18%
Primary outcome: OS				
Number of deaths	7	24	65	100
Median OS	Not reached	Not reached	[c]	[c]
Hazard ratio (95% CI), p-value	0.30 (0.13 to 0.70)		0.64 (0.46 to 0.87), p=0.0021[a,b]	
KM estimated survival at 24-months	83%	59%	71%	56%

Secondary outcomes				
ORR in evaluable patients, % (n/N)	78% (38/49)	69% (40/58)	70% (149/212)	65% (142/219)
Complete response rate, % (n/N)	31% (15/49)	21% (21/58)	25% (53/212)	20% (43/219)
Partial response rate, % (n/N)	47% (23/49)	48% (28/58)	45% (96/212)	45% (99/219)
Median duration of response, months	Not reached	5.4	10.6	6.2

[a] OS was assessed in the ITT as a primary outcome. OS in the relevant dMMR/MSI-H subpopulation was assessed as a pre-specified subgroup analysis only.
[b] does not cross the pre-specified boundary for significance of 0.00177
CI = confidence interval; dMMR/MSI-H: mismatch repair deficient/microsatellite instability-high; ITT = intention to treat; KM = Kaplan Meier; ORR = objective response rate; OS = overall survival; PFS = progression-free survival.
[c]*results for median PFS and median OS in the ITT population were considered confidential by the company.*

The company has provided preliminary results for OS at the second interim analysis. The clinical study report at this data cut-off is not yet available and results are unpublished and limited but a company press release indicates that RUBY-1 has met its other primary outcome, demonstrating a statistically significant and clinically meaningful benefit in OS in the ITT population. [7, 8]

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

2.2. Health-related quality of life outcomes

Health Related Quality of Life (HRQoL) was assessed using the following questionnaires: the EuroQol five-dimensions five levels (EQ-5D-5L) visual analogue scale (VAS), the European Organisation for the Research and Treatment of Cancer Core Quality of Life Questionnaire (EORTC QLQ-C30) and the EORTC-QLQ-Endometrial Cancer (EN24). These instruments were used at baseline and at every cycle of treatment; results were not statistically tested and are descriptive only. The mean change from baseline in EORTC-QLQ-C30 and EN24 and EQ-5D-5L were similar between the treatment groups in the dMMR/MSI-H subpopulation and the ITT population.[4, 6]

3. Summary of Safety Evidence

At data cut-off (28 September 2022) in RUBY-1, the median duration of treatment with dostarlimab was 43 weeks and with placebo was 36 weeks. For patients in the dostarlimab and placebo group, respectively, AEs related to dostarlimab or placebo (that is, not chemotherapy-related) were reported in 84% and 74% of patients respectively. Patients reporting a grade 3 or higher AE were 71% and 60% respectively; 33% and 20% related to dostarlimab and placebo respectively. A serious AE was reported in 38% and 28% of patients respectively; 12% and 6.9% related to dostarlimab and placebo respectively. Adverse events led to discontinuation of dostarlimab or placebo in 17% and 9.3% of patients respectively.[4]

The most frequently reported AEs of grade 3 or higher in the dostarlimab group versus the placebo group were: anaemia (15% and 16%), neutropenia (9.5% and 9.3%), neutrophil count decreased (8.3% and 14%), lymphocyte count decreased (5.4% and 7.3%), decreased white cell

count (6.6% versus 5.3%), hypertension (7.1% versus 3.3%), pulmonary embolism (5.0% versus 4.9%) and hypokalaemia (5.0% versus 3.7%).[4]

Immune-related events were assessed during RUBY-1. The incidence of grade 2 or higher immune-related AEs was 57% in the dostarlimab group and 36% in the placebo group, with 38% and 15% of patients respectively reported as related to dostarlimab or placebo. The most frequently reported immune-related AEs of grade 2 or higher in the dostarlimab and placebo groups respectively were: hypothyroidism (11% versus 2.8%), rash (6.6% versus 2.0%), arthralgia (5.8% versus 6.5%) and increased alanine aminotransferase (5.8% versus 0.8%).[4]

Results for the dMMR/MSI-H subpopulation of the RUBY-1 study have not been published but the SPC notes that the safety profile was not different from that of the overall population.[1, 4]

Five deaths were reported due to AEs in the dostarlimab group; two were considered dostarlimab-related (one during the first six cycles due to myelosuppression and one during the 90-day safety follow-up due to hypovolemic shock). [4]

The SPC recommends monitoring for immune-related AEs including pneumonitis, colitis, hepatitis, hypothyroidism, hyperthyroidism, nephritis, rash, arthralgia and adrenal insufficiency. Details of management of immune-related AEs are outlined in the SPC.[1]

4. Summary of Clinical Effectiveness Considerations

4.1. Key strengths

- Direct evidence from a randomised, double-blind, phase III study (RUBY-1) demonstrated a significant improvement in PFS versus a relevant comparator in patients with dMMR/MSI-H primary advanced or recurrent endometrial cancer.[1, 4] In this setting, dostarlimab is added to carboplatin plus paclitaxel which is generally considered standard of care.
- There was a significant improvement in investigator-assessed PFS in the dMMR/MSI-H subpopulation and ITT population. At the data cut-off (28 September 2022), the addition of dostarlimab was associated with a 72% relative reduction in the risk of progression or death and an apparent 70% relative reduction in the risk of death compared with placebo in the dMMR/MSI-H subpopulation (OS for these patients was not formally tested). The size of the treatment effect was larger in this licensed dMMR/MSI-H subpopulation, with predominantly endometrioid histology, than in the overall study population and appears to be clinically relevant.[4]
- Other secondary outcomes including ORR, DOR and DCR numerically favoured the addition of dostarlimab compared with placebo to carboplatin plus paclitaxel.[1, 4]

4.2. Key uncertainties

- Results for the dMMR/MSI-H subpopulation (24% [118/494] of RUBY-1 study patients) support this licensed indication. However, analysis of PFS in these patients was a primary outcome included in the hierarchical testing and the results were statistically and clinically significant; HR 0.28 (95% CI 0.16 to 0.50). OS in the relevant dMMR/MSI-H subpopulation was not included in the hierarchy. This was performed as a pre-specified subgroup analysis; results

favoured dostarlimab over placebo (HR 0.30 [95% CI 0.13 to 0.70]) but are considered descriptive only.[1, 4]

- At the data cut-off (28 September 2022), the median duration of follow-up was approximately 2 years. However, only seven patients in the dostarlimab group and 24 patients in the placebo group of the dMMR/MSI-H subpopulation had died and median OS had not been reached in either group. Preliminary results from the second interim analysis of OS in the ITT population indicate a significant survival benefit with dostarlimab. However further OS analyses are awaited to determine the treatment effect of dostarlimab on OS in the relevant dMMR/MSI-H subpopulation but may be confounded by subsequent treatment. At the 28 September 2022 data cut-off, 28% (15/53) of patients in the dostarlimab group and 58% (38/65) of patients in the placebo group in the dMMR/MSI-H subpopulation had received any subsequent anticancer therapy; 15% and 38% respectively had received immunotherapy.[1, 4, 7]
- The licensed indication is for the use of dostarlimab in combination with platinum-containing chemotherapy. In RUBY-1 dostarlimab was added to carboplatin plus paclitaxel. There is no evidence to support the use of dostarlimab in combination with other platinum-containing chemotherapy regimens. However, carboplatin plus paclitaxel appears to be current standard of care for these patients.[3, 4, 10, 11]
- Study patients had an ECOG performance status of 0 or 1 and there are no data to support the use of dostarlimab in patients who may have poorer performance status in clinical practice.[4]

4.3. Ongoing studies

The ongoing RUBY-1 study may address some of the key uncertainties in the clinical evidence.

4.4. Clinical expert input

Clinical experts consulted by SMC considered that dostarlimab fills an unmet need in this therapeutic area offering improvements over chemotherapy alone.

Clinical experts consulted by SMC considered that dostarlimab was a therapeutic advancement due to improved PFS and OS in patients with dMMR/MSI-H primary advanced or recurrent endometrial cancer. This would be added to current standard of care with carboplatin plus paclitaxel.

4.5. Service implications

The continued use of dostarlimab for up to 3 years may have service implications for administration but may in part displace the use of immunotherapy in the second-line setting after chemotherapy.

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

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 the Peaches Womb Cancer Trust, which is a registered charity.

- Peaches Womb Cancer Trust has received 19% 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 a woman's life. The biggest challenges of living with this condition are managing the short- and long-term side effects of current treatments and (for some) poor control of symptoms that adversely impact quality of life, combined with the psychological impact of living with the fear of recurrence and/or progression.
- Current first-line treatments for advanced or recurrent endometrial cancer are inadequate because options are limited, and they offer little hope to those affected of prolonging life expectancy.
- This new medicine is important to patients and carers because it promises improved survival over current treatments without substantially increasing overall treatment burden. The potential for improved progression free survival of the patient due to dostarlimab brings hope to the family or carers of leading a relatively normal life and spending precious time together, which has a positive emotional and psychological impact on them.

6. Summary of Comparative Health Economic Evidence

6.1. Economic case

Table 6.1 Description of economic analysis

Criteria	Overview
Analysis type	The submitting company presented a cost-utility analysis.
Time horizon	The time horizon was a lifetime horizon.
Population	Adult patients with dMMR/ MSI-H primary advanced or recurrent endometrial cancer and who are candidates for systemic therapy.
Comparators	Dostarlimab in combination with platinum-containing chemotherapy (PCC) was compared with PCC alone.
Model description	The submitting company used a partitioned survival model (PSM) with three health states; progression-free disease (PFD), progressed disease (PD) and death. PFD was estimated by extrapolating progression-free survival (PFS) curves, PD was estimated as the difference between overall survival (OS) and PFS. Death was estimated by extrapolating OS curves and then calculating death = 1 – OS. The model had a cycle length of one week.
Clinical data	Clinical evidence came from the RUBY-1 study. The primary outcomes were PFS and OS. There was a significant improvement in investigator-assessed PFS in the dMMR/MSI-H subpopulation and ITT population. The submitting company applied data form the ITT population in the model, as this had more observations. Adverse events were also taken from the ITT population in the RUBY-1 study.
Extrapolation	For PFS, a flexible spline approach was taken. For the dostarlimab arm the Odds k=1 was selected and for the PCC arm, the Odds k=2 was selected for the base case. For OS a piecewise approach was taken. For the dostarlimab arm the piecewise approach consisted of Kaplan Meier (KM) followed by unstratified hazard ratio (HR) approach applied to the PCC log-logistic extrapolation. The PCC arm had the KM followed by the log-logistic extrapolation. General population mortality was applied to the OS ratio. For time to treatment discontinuation (TTD), rates from RUBY-1 were applied for the first six treatment cycles in the dostarlimab arm, followed by the KM for the follow-up period and further continued by the Weibull standard parametric curve. A stopping rule of three years was applied to dostarlimab.

Quality of life	Health benefits were measured using EQ-5D-5L during the RUBY-1 study. Disutilities from adverse events were also applied.
Costs and resource use	The model included medicine acquisition, administration, subsequent treatment and adverse event costs. Other costs included in the model were monitoring and end of life costs. Quantities for both subsequent treatment and monitoring costs were sourced from clinical experts only.
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.

6.2. Results

The base case results predicted the outcomes as an incremental life year gain and incremental QALY gain for dostarlimab of 5.85 and 4.18 respectively. SMC would wish to present the with PAS cost-effectiveness estimates that informed the SMC decision. However, owing to the commercial in confidence concerns regarding the PAS, SMC is unable to publish these results.

6.3. Sensitivity analyses

Key scenario analyses that were tested are described below in Table 6.3.1. The results of these analyses cannot be published due to them being classed as commercial in confidence by the company.

Table 6.3.1 Key scenario analyses

No.	Category	Base case value	Scenario value
1	Base case	-	-
2	Time horizon	Lifetime	20 years
3	Utility values source	Utility scores ITT	Utility scores dMMR/MSI-H
4	Treatment wastage	Wastage on	Wastage off
5	PFS source	PFS IA (dostarlimab in combination with PCC Odds k=1 and PCC Odds k=2)	PFS BICR (dostarlimab in combination with PCC Odds k=1 and PCC Odds k=2)
6	PFS extrapolation	Flexible dostarlimab in combination with PCC Odds k=1 and PCC Odds k=2	Flexible Odds k=1 for both arms
7	PFS extrapolation	Flexible dostarlimab in combination with PCC Odds k=1 and PCC Odds k=2	Flexible Odds k=2 for both arms
8	OS extrapolation	Dostarlimab extrapolated using unstratified HR. PCC extrapolated using log-logistic	OS HR unstratified with full parametric extrapolation
9	PFS treatment risk waning	No treatment risk waning of PFS	PFS curves as per base case, treatment waning from years 6-9

No.	Category	Base case value	Scenario value
10	OS treatment risk waning	No treatment risk waning of OS	OS curves log-logistic for both arms and treatment risk convergence from years 6-9
11	Subsequent treatment distribution	Subsequent treatment distribution (UK expert opinion (including two Scottish clinicians))	Subsequent treatment distribution (RUBY-1 trial)
12	OS treatment risk waning	No treatment risk waning of OS and no new data.	As scenario 10 - PFS curves as per base case and OS curves log-logistic for both arms and treatment risk convergence from years 6-9 with new data.

6.4. Key strengths

- There was a significant improvement in investigator-assessed PFS in the dMMR/MSI-H subpopulation and ITT population.
- Following feedback from the NDC statistical advisor, the extrapolations of clinical outcomes were reasonable.
- New data from the second interim analysis of the RUBY-1 trial support the findings in the company submission.

6.5. Key uncertainties

- There was little available evidence to corroborate the RUBY-1 QoL outcomes.
- The quantities of resources used are a source of uncertainty as they are largely based on expert opinions.

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

7. Conclusion

After considering all the available evidence, the Committee accepted dostarlimab 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. [10]

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

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.[11]

9. Additional Information

9.1. Product availability date

2 October 2023

Table 9.1 List price of medicine under review

Medicine	Dose regimen	Cost per cycle/year (£)
dostarlimab + carboplatin + paclitaxel	**500 mg IV every 3 weeks for six cycles** **AUC 5 mg/ml/min every 3 weeks for six cycles** **175 mg/m^2 of body surface area every 3 weeks for six cycles**	**5,887** **+283** **+228** **=6,398 per cycle**
followed by dostarlimab	**1,000 mg every 6 weeks for up to 3 years**	**102,041 per year**

Costs from BNF online on 15 January 2024. Costs calculated using the full cost of vials/ampoules assuming wastage. Costs for carboplatin are based on up to maximum dose of 750mg; 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.

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

References

1. GlaxoSmithKline UK. Dostarlimab 500 mg concentrate for solution for infusion (Jemperli®) Summary of product characteristics. Electronics Medicines Compendium https://www.medicines.org.uk/. Last updated 03 October 2023.
2. European Medicines Agency (EMA). European Public Assessment Report. Dostarlimab (Jemperli®). 25/02/2021, EMEA/H/C/005204/0000. www.ema.europa.eu.
3. 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. Ann Oncol. 2022;33:860-77.
4. Mirza MR, Chase DM, Slomovitz BM, dePont Christensen R, Novak Z, Black D*, et al.* Dostarlimab for Primary Advanced or Recurrent Endometrial Cancer. N Engl J Med. 2023;388:2145-58.
5. Merck Sharp Dohme Ltd. Pembrolizumab concentrate for solution for infusion (Keytruda) Summary of product characteristics. Electronic Medicines Compendium www.medicines.org.uk/emc/ Last updated 3 January 2024.
6. Data on file, GlaxoSmithKline UK. Dostarlimab (Jemperli). A Phase 3, Randomized, Double-blind, Multicenter Study of Dostarlimab (TSR-042) plus Carboplatin-paclitaxel versus Placebo plus Carboplatin-paclitaxel in Patients with Recurrent or Primary Advanced Endometrial Cancer (RUBY). Clinical Study Report 07/03/2023 (data cut off: 28/09/2022).
7. GlaxoSmithKline UK. Phase III RUBY trial of Jemperli (dostarlimab) plus chemotherapy meets endpoint of overall survival in patients with primary advanced or recurrent endometrial cancer. 30/10/2023, GSK. https://www.gsk.com/en-gb/.
8. Data on File, GlaxoSmithKline UK. 1 December 2023.
9. Powell M, Hietanen S, Coleman RL, Monk BJ, Zub O, O'Malley M et al. Dostarlimab for primary advanced or recurrent (A/R) endometrial cancer (EC): Outcomes by blinded independent central review (BICR) of the RUBY trial (ENGOT-EN6-NSGO/GOG-3031/RUBY). Abstract presented at American Society of Oncology 2023. J Clin Oncol 2023; 41 (suppl 16): 5503.
10. 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. Eur J Obstet Gynecol Reprod Biol. 2022;270:50-89.
11. 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. Int J Gynecol Cancer. 2021;31:12-39.

This assessment is based on data submitted by the applicant company up to and including 16 February 2024.

**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.