Indication	Monotherapy treatment for advanced or recurrent endometrial cancer with high microsatellite instability or mismatch repair deficiency (dMMR) who have received platinum-based chemotherapy. NB the patient must have not received any prior treatment with an anti-PD-1, anti-PD-L2, anti-CD137, or anti-Cytotoxic T-lymphocyte-associated antigen-4 (CTLA-4) antibody unless the patient has been treated with dostarlimab in a company early access scheme.
Treatment Intent	Palliative
Frequency and number of cycles	Repeat every 21 days for 4 cycles Repeat every 42 days from Cycle 5 onwards Continue until disease progression, unacceptable toxicity or patient choice. A formal medical review should occur by the end of the 2nd 3-weekly cycle of treatment to determine whether treatment with dostarlimab should continue.
Monitoring Parameters pre-treatment	• **Virology screening:** All new patients referred for systemic anti-cancer treatment should be screened for hepatitis B and C and the result reviewed prior to the start of treatment. Patients not previously tested who are starting a new line of treatment, should also be screened for hepatitis B and C. Further virology screening will be performed following individual risk assessment and clinician discretion. • FBC, U&E, LFTs and glucose at baseline and at each cycle. • Thyroid function must be assessed at baseline then at least every 6 weeks. • Cortisol monitoring should be undertaken in line with ESMO immunotherapy toxicity guidance available on KMCC website (see link below). Cortisol level should not be taken within 24hours of the last steroid dose. • **Hepatic impairment:** No recommended dose adjustment in mild hepatic impairment. Limited data in moderate impairment and no available data in severe impairment. • **Renal impairment:** No recommended dose adjustment in mild or moderate renal impairment. Limited data in severe impairment or end-stage renal disease undergoing dialysis • The use of systemic corticosteroids or immunosuppressants before starting dostarlimab should be avoided. Systemic corticosteroids or other immunosuppressants can be used after starting dostarlimab to treat immune-related adverse reactions. • **Infusion-related reactions:** ➢ For severe infusion reactions (grade 3-4), infusion should be stopped and dostarlimab permanently discontinued. ➢ Grade 2 reaction, withhold dose. If reaction resolves within 1 hour of stopping, the infusion may be restarted at 50 % of the original infusion rate, or restart when symptoms resolve with pre-medication. If grade 2 recurs with adequate premedication, permanently discontinue. • **Adverse reactions and dose modification:** • **Immune-related adverse reactions** may appear during or after treatment. The most common immune-related reactions are: anaemia (including autoimmune haemolytic anaemia), pneumonitis, colitis, hyperthyroidism, hypothyroidism and arthralgia. The following additional, immune related adverse reactions have been reported in patients receiving dostarlimab: type 1 diabetes, nephritis, hepatitis, pancreatitis, severe skin reactions, encephalitis, Guillain-Barre syndrome, myocarditis, iridocyclitis, uveitis and diabetic ketoacidosis. See guidelines for management of immune-related adverse reactions following immunotherapy https://www.kmcc.nhs.uk/medicines-and-prescribing-incorporating-sact-pathways/immunotherapy/ available on KMCC website and the SPC. • Cases of Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN), have been reported. If SJS or TEN is confirmed, dostarlimab should be permanently discontinued. Caution

	should be used when considering the use of dostarlimab in a patient who has previously experienced a severe or life-threatening skin adverse reaction on prior treatment with other immune-stimulatory anticancer agents. • **Dose Modification:** Dose reduction is not recommended. Dose delay or discontinuation may be required based on adverse reaction (see table 1). • **<u>Common drug interactions (for comprehensive list refer to BNF/SPC)</u>:** No interaction studies have been performed. • Each patient should be given a copy of the Jemperli ® patient alert card at each cycle. • Patients must be advised to contact the oncology team or the 24-hour hot-line immediately if they experience any side effect, as some side effects worsen rapidly. Prompt management of side effects can ensure that the patient continues with treatment
References	SPC accessed online 22.09.2023 KMCC protocol GYN-045 V2

NB For funding information, refer to CDF and NICE Drugs Funding List

Table 1: Dose modification

Immune-related adverse reactions	Severity grade	Dose modification
Colitis	2 or 3	Withhold dose. Restart dosing when toxicity resolves to grade 0-1.
	4	Permanently discontinue.
Hepatitis	Grade 2 with AST or ALT > 3 and up to 5 × ULN or total bilirubin > 1.5 and up to 3 × ULN	Withhold dose. Restart dosing when toxicity resolves to grade 0 to 1.
	Grade >/=3 with AST or ALT > 5 × ULN or total bilirubin > 3 × ULN	Permanently discontinue (see exception below*)
Type 1 diabetes mellitus (T1DM)	3 or 4 (hyperglycaemia)	Withhold dose. Restart dosing in appropriately managed, clinically and metabolically stable patients.
Hypophysitis or adrenal insufficiency	2,3 or 4	Withhold dose. Restart dosing when toxicity resolves to grade 0 to 1. Permanently discontinue for recurrence or worsening while on adequate hormonal therapy.
Hypothyroidism or hyperthyroidism	3 or 4	Withhold dose. Restart dosing when toxicity resolves to grade 0 to 1.
Pneumonitis	2	Withhold dose. Restart dosing when toxicity resolves to grade 0-1. If grade 2 recurs, permanently discontinue.
	3 or 4	Permanently discontinue.
Nephritis	2	Withhold dose. Restart dosing when toxicity resolves to grade 0-1.
	3 to 4	Permanently discontinue.
Exfoliative dermatologic conditions (e.g. SJS, TEN, DRESS)	suspected	Withhold dose for any grade. Restart dosing if not confirmed and when toxicity resolves to grade 0 or 1.
	confirmed	Permanently discontinue.
Myocarditis	2,3 or 4	Permanently discontinue
Severe neurological toxicities (myasthenic syndrome/myasthenia gravis, Guillain-Barré syndrome, encephalitis, transverse myelitis)	2,3 or 4	Permanently discontinue
Other immune-related adverse reactions (including but not limited to myositis, sarcoidosis, autoimmune haemolytic anaemia, pancreatitis, iridocyclitis, uveitis, diabetic ketoacidosis, arthralgia, solid organ transplant rejection, graft-versus-host disease)	3	Withhold dose. Restart dosing when toxicity resolves to grade 0-1.
	4	Permanently discontinue.
Recurrence of immune-related adverse reactions after resolution to ≤ grade 1 (except for pneumonitis, see above)	3 to 4	Permanently discontinue.

*For patients with liver metastases who begin treatment with grade 2 increase of AST or ALT, if AST or ALT increases by >/= 50 % relative to baseline and lasts for at least 1 week, then treatment should be discontinued.

Cycle 1-4 repeat every 21 days

Day	Drug	Dose	Route	Infusion Duration	Administration
1	**DOSTARLIMAB**	**500mg**	IV	30mins	In 100ml Sodium Chloride 0.9% Administered via a 0.22 micron in-line filter
TTO	Drug	Dose	Route	Directions	
Day 1	Metoclopramide	10mg	PO	10mg TDS PRN. Do not take for more than 5 days continuously.	

Cycle 5 onwards repeat every 42 days (cycle 5 to be started 21 days after cycle 4)

Day	Drug	Dose	Route	Infusion Duration	Administration
1	**DOSTARLIMAB**	**1000mg**	IV	30mins	In 100ml Sodium Chloride 0.9% Administered via a 0.22 micron in-line filter
TTO	Drug	Dose	Route	Directions	
Day 1	Metoclopramide	10mg	PO	10mg TDS PRN. Do not take for more than 5 days continuously.	