Dostarlimab Therapy

INDICATIONS FOR USE:

INDICATION	ICD10	Regimen Code	HSE approved reimbursement status*
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.	C54	00819a	N/A

*This is for post 2012 indications only

TREATMENT:

The starting dose of the drugs detailed below may be adjusted downward by the prescribing clinician, using their independent medical judgement, to consider each patients individual clinical circumstances.

Dostarlimab is administered as a 500mg dose every 3 weeks for four cycles, followed by 1000mg every 6 weeks for all subsequent cycles. Cycle 5 should be given 3 weeks after cycle 4. Treatment is administered until disease progression or unacceptable toxicity occurs.

Facilities to treat anaphylaxis MUST be present when systemic anti-cancer therapy (SACT) is administered.

Cycles 1-4

Day	Drug	Dose	Route	Diluent & Rate	Cycle
1	Dostarlimab	500mg	IV infusion	100mL NaCl 0.9% over 30 minutes	Every 21 days
The final concentration of the diluted solution should be between 2 mg/mL and 10 mg/mL					

Note: Administration volumes and fluids have been standardised to facilitate electronic prescribing system builds.

Cycle 5 onwards

Day	Drug	Dose	Route	Diluent & Rate	Cycle
1	Dostarlimab	1000mg	IV infusion	100mL NaCl 0.9% over 30 minutes	Every 42 days
Dostarlimab must not be administered as an intravenous push or bolus injection					
The final concentration of the diluted solution should be between 4 mg/mL and 10 mg/mL					

Note: Administration volumes and fluids have been standardised to facilitate electronic prescribing system builds.

ELIGIBILITY:

- Indication as above
- Histologically confirmed endometrial cancer
- Confirmation of dMMR/MSI-H tumour status by a validated test
- Adequate haematological, hepatic and renal function
- ECOG 0-2
- Age ≥18 years

CAUTIONS:

- History of serious autoimmune disease

EXCLUSIONS:

- Hypersensitivity to dostarlimab or any of the excipients
- Information regarding prior therapy with an anti PD-1 or anti PD-L1 antibody is available here
- Any medical condition that requires immunosuppressive doses of systemic corticosteroids or other immunosuppressive medication(s) (defined as >10mg prednisolone/daily (or steroid equivalent, excluding inhaled or topical steroids)
- History of interstitial lung disease
- Untreated brain metastases
- Any active clinically significant infection requiring therapy
- Pregnancy/Breastfeeding

PRESCRIPTIVE AUTHORITY:

- The treatment plan must be initiated by a Consultant Medical Oncologist

TESTS:

Baseline tests:

- FBC, renal and liver profile
- Glucose
- Thyroid function tests.
- Virology screen: Hepatitis B (HBsAg, HBcoreAb) and Hepatitis C

Regular tests:

- FBC, renal and liver profile prior to each cycle
- Glucose prior to each cycle
- TSH every 3 to 6 weeks.

Disease monitoring:

Disease monitoring should be in line with the patient's treatment plan and any other test/s as directed by the supervising Consultant.

DOSE MODIFICATIONS:

- Dose modification is not recommended
- Dosing delay or discontinuation may be required based on individual safety and tolerability
- Recommended modifications to manage adverse reactions are provided in table 2.

Renal and Hepatic Impairment:

Table 1: Dose modification in renal and hepatic impairment

Renal Impairment		**Hepatic Impairment**	
No dose adjustment is needed		**Mild/Moderate**	No dose adjustment is needed
Haemodialysis	No need for dose adjustment is expected	**Severe**	No need for dose adjustment is expected

Management of adverse events:

Table 2: Dose Modification for Adverse Events

Immune-related adverse reactions	**Severity[a]**	**Recommended dose modification**
Colitis	2 or 3	Withhold dose. Restart dosing when toxicity resolves to grade 0 or 1.
	4	Permanently discontinue.
Hepatitis	Grade 2 with AST[b] or ALT[c] >3 and up to 5 × ULN[d] or total bilirubin > 1.5 and up to 3 × ULN	Withhold dose. Restart dosing when toxicity resolves to grade 0 or 1.
	Grade ≥3 with AST or ALT >5 × ULN or total bilirubin >3 × ULN	Permanently discontinue. (Exception: 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).
Type 1 diabetes mellitus	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 or 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 or 1.
Pneumonitis	2	Withhold dose. Restart dosing when toxicity resolves to grade 0 or 1. If grade 2 recurs, permanently discontinue.
	3 or 4	Permanently discontinue.

Nephritis	2	Withhold dose. Restart dosing when toxicity resolves to grade 0 or 1.
	3 or 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 or 1.
	4	Permanently discontinue
Recurrence of immune-related adverse reactions after resolution to ≤ grade 1 (except for pneumonitis, see above)	3 or 4	Permanently discontinue
Other adverse reactions	**Severity[a]**	**Dose modification**
Infusion-related reactions	2	Withhold dose. If resolved within 1 hour of stopping, 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.
	3 or 4	Permanently discontinue.

[a] Toxicity graded per National Cancer Institute Common Terminology Criteria for Adverse Events (CTCAE) version 5.0.

[b] AST = aspartate aminotransferase

[c] ALT = alanine aminotransferase

[d] ULN = upper limit of normal

SUPPORTIVE CARE:

EMETOGENIC POTENTIAL:

- As outlined in NCCP Classification Document for Systemic AntiCancer Therapy (SACT) Induced Nausea and Vomiting linked here

Minimal (**Refer to local policy).**

For information:
Within NCIS regimens, antiemetics have been standardised by the Medical Oncologists and Haemato-oncologists and information is available in the following documents:

- NCCP Supportive Care Antiemetic Medicines for **Inclusion in NCIS** (Medical Oncology) - link here
- NCCP Supportive Care Antiemetic Medicines for **Inclusion in NCIS** (Haemato-oncology) - link here

PREMEDICATIONS: No specific recommendations

OTHER SUPPORTIVE CARE:

- Women of childbearing potential must use effective contraception during treatment with dostarlimab and until 4 months after the last dose of dostarlimab.

ADVERSE EFFECTS

- Please refer to the relevant Summary of Product Characteristics (SmPC) for details. This medicinal product is subject to additional monitoring. Healthcare professionals are asked to report any suspected adverse reactions.

DRUG INTERACTIONS:

- Current SmPC and drug interaction databases should be consulted for information

REFERENCES:

1. Oaknin A, et al. Safety and antitumour activity of dostarlimab in patients with advanced or recurrent DNA mismatch repair deficient/microsatellite instability-high (dMMR/MSI-H) or proficient/stable (MMRp/MSS) endometrial cancer: interim results from GARNET – a phase I, single-arm study. J Immunother Cancer 2022;10:e003777
2. Giraud E L, Lijster B D, et al. Dose recommendations for anticancer drugs in patients with renal or hepatic impairment: an update. Available at: https://pubmed.ncbi.nlm.nih.gov/37269847/
3. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®). Antiemesis Version 1.2024 – December 13, 2023. Accessed June 2024. Available at https://www.nccn.org/professionals/physician_gls/pdf/antiemesis.pdf
4. Herrstedt J et al. 2023 MASCC and ESMO guideline update for the prevention of chemotherapy and radiotherapy induced nausea and vomiting. ESMO Open. 2024;9(2):102195. Accessed June 2024. Available at https://www.esmo.org/guidelines/guidelines-by-topic/esmo-clinical-practice-guidelines-supportive-and-palliative-care/prevention-of-chemotherapy-and-radiotherapy-induced-nausea-and-vomiting

5. Dostarlimab (Jemperli®) Summary of Product Characteristics. Accessed June 2024. Available at https://www.ema.europa.eu/en/documents/product-information/jemperli-epar-product-information_en.pdf

Version	Date	Amendment	Approved By
1	14/06/2024		Prof Maccon Keane

Comments and feedback welcome at oncologydrugs@cancercontrol.ie.