

Dostarlimab-gxly (JEMPERLI) National Drug Monograph January 2026

VA Pharmacy Benefits Management Services and National Formulary Committee

The purpose of VA National Formulary Committee drug monographs is to provide a focused drug review for making formulary decisions. Updates will be made if new clinical data warrant additional formulary discussion. The Product Information or other resources should be consulted for detailed and most current drug information.

FDA APPROVAL INFORMATION	Description / MOA	Programmed death receptor-1 (PD-1)–blocking antibody
	Indication Under Review¹	<ul style="list-style-type: none"> • Primary advanced or recurrent endometrial cancer (EC) <ul style="list-style-type: none"> ○ In combination with paclitaxel/carboplatin (PC) followed by single agent dostarlimab ○ As a single agent for mismatch repair deficient (dMMR) EC with progression on a platinum-containing regimen in any setting and are not candidates for curative surgery or radiation • dMMR recurrent or advanced solid tumors, as a single agent with progressive disease on prior treatment and have no satisfactory treatment options (accelerated approval based on response rate and durability) • off-label evidence in dMMR locally advanced rectal cancer
	Dosage Regimen	EC combo therapy: Dostarlimab 500mg IV every 3 weeks for 6 cycles, then 1000mg every 6 weeks EC single agent: Dostarlimab 500mg IV every 3 weeks for 4 cycles, then 1000mg every 6 weeks Solid tumors: Dostarlimab 500mg IV every 3 weeks for 4 cycles, then 1000mg every 6 weeks Neoadjuvant therapy in rectal cancer: Dostarlimab 500mg IV every 3 weeks x 6 cycles
	Dosage Forms Under Review	500mg/10ml [50mg/mL] solution in SDV

EFFICACY CONSIDERATIONS	Trial Design	GARNET (NCT02715284) Non-randomized, multicenter, multicohort, open label																				
	Population	N=327; patients with dMMR recurrent or advanced solid tumors who progressed following systemic therapy and had no satisfactory alternative treatment options N=141 (43%) endometrial cancer N=105 (32%) colorectal cancer N=81 (25%) other solid tumors																				
	Demographic	mAge 63 yrs; 72% female; 63% White; 2% Asian; 2% Black																				
	Intervention	Dostarlimab 500mg IV every 3 weeks for 4 doses followed by 1,000mg IV every 6 weeks																				
	Results	Efficacy Results of dMMR Recurrent or Advanced Solid Tumors in GARNET																				
		<table border="1" style="width: 100%; border-collapse: collapse;"> <thead> <tr> <th style="width: 50%;">Endpoint</th> <th style="width: 50%;">Dostarlimab N=209</th> </tr> </thead> <tbody> <tr> <td>Overall response rate^a</td> <td></td> </tr> <tr> <td> ORR (95% CI)</td> <td style="text-align: center;">44% (38, 49.6)</td> </tr> <tr> <td> Complete response rate</td> <td style="text-align: center;">9.1%</td> </tr> <tr> <td> Partial response rate</td> <td style="text-align: center;">32.5%</td> </tr> <tr> <td>Duration of response^b</td> <td></td> </tr> <tr> <td> Median in months (range)</td> <td style="text-align: center;">NR 2.6, 35.8 +</td> </tr> <tr> <td> Patients with duration ≥ 6 months</td> <td style="text-align: center;">95.4%</td> </tr> <tr> <td>mPFS</td> <td style="text-align: center;">6.9 mos (95% CI, 4.2-13.6)</td> </tr> <tr> <td>24-mos PFS</td> <td style="text-align: center;">40.6% (95% CI, 35-46)</td> </tr> </tbody> </table>	Endpoint	Dostarlimab N=209	Overall response rate ^a		ORR (95% CI)	44% (38, 49.6)	Complete response rate	9.1%	Partial response rate	32.5%	Duration of response ^b		Median in months (range)	NR 2.6, 35.8 +	Patients with duration ≥ 6 months	95.4%	mPFS	6.9 mos (95% CI, 4.2-13.6)	24-mos PFS	40.6% (95% CI, 35-46)
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	dMMR = Mismatch Repair Deficient; + = ongoing at last assessment.																					
	^a Based on confirmed response by blinded independent central review																					
	^b Median follow-up for duration of response was 17.5 months measured from time of first response.																					
Trial Design	RUBY (NCT03981796) Phase 3, global, double-blind, randomized, placebo-controlled																					
Population	N=494; patients with primary advanced stage III or IV or first recurrent endometrial cancer																					

Demographics	mAge 65 yrs (51% ≥ 65 yrs); white 77%, Black 3%, Asian 3% ECOG PS 0 (63%), 1 (37%) Stage III 18%; stage IV 34%, recurrent EC 48%; dMMR 24%; 10.2% carcinosarcoma; 55% endometrioid; 20% serous adenocarcinoma
Intervention	Dostarlimab 500mg with PC every 3 weeks (six cycles), followed by dostarlimab 1000mg every 6 weeks for up to 3 years
Comparator	Placebo with PC every 3 weeks for 6 cycles, followed by placebo IV every 6 weeks
Results @ first interim analysis	<p>Overall population</p> <p>Dostarlimab, PC n = 245 vs. Placebo, PC n = 249 mPFS 11.8 vs. 7.9 months [HR 0.64; 95% CI 0.51-0.80] p<0.0001 mOS 44.6 vs. 28.2 mos [HR 0.69 (95% CI 0.54-0.89); p=0.002 ORR 68 vs. 57%; CR 20 vs. 12% mDOR 10.8 vs. 6.4 mos</p> <p>dMMR/MSI-H population</p> <p>Dostarlimab, PC n = 60 vs. Placebo, PC n = 62 mPFS 30.3 vs. 7.7 months [HR 0.29; 95% CI 0.17-0.50] p<0.0001 mOS NR vs. 30.8 mos [HR 0.34 (95% CI 0.18-0.62); p<0.0001 ORR 74 vs. 62%; CR 26 vs. 11% mDOR NR vs. 5.4 mos</p>
Results @ 2nd interim analysis	<p>Dostarlimab, PC n = 245 vs. Placebo, PC n = 249</p> <p>Overall, n=484</p> <p>24-month PFS 36 vs. 18% [HR 0.64] 24-month OS 71 vs. 56% [HR 0.64]</p> <p>dMMR/MSI-H population, n=118</p> <p>24-month PFS 61 vs. 16% [HR 0.28] 24-month OS 83 vs. 59% [HR 0.30]</p>
Off-label indication	<p>PD-1 Blockade in dMMR LA Rectal Cancer</p> <p>Prospective Phase 2 neoadjuvant trial Stage II or III rectal adenocarcinoma; N=12 patients Dostarlimab every 3 weeks x 6 months (9 cycles) followed by chemoRT and surgery Patients with clinical CR post dostarlimab could forgo chemoRT and surgery Results: 12 patients (100%) with CCR; at 12 mos follow-up shows no disease progression or recurrence</p>
NCCN Guidelines v2.2026 Endometrial Carcinoma	<p>Primary or adjuvant therapy (Stage I-IV)</p> <p>Preferred</p> <p>PC + dostarlimab for Stage III-IV (category 1) PC + pembrolizumab for Stage III-IV, except carcinosarcoma (category 1) PC + durvalumab for Stage III-IV dMMR tumors only (category 1)</p> <p>Recurrent disease</p> <p>Preferred</p> <p>PC + dostarlimab (category 1) PC + pembrolizumab (except for carcinosarcoma) (category 1) PC + durvalumab for dMMR only (category 1)</p> <p>Second or subsequent line therapy</p> <p>MSI-H/dMMR tumors</p> <p>Dostarlimab (category 2A) Pembrolizumab (category 2A)</p> <p>dMMR/MSI-H rectal cancer</p> <p>Neoadjuvant, preferred</p> <p>Dostarlimab or nivolumab or pembrolizumab for up to 6 months (category 2A)</p>

SAFETY CONSIDERATIONS	<p>VA Uterine Cancer Clinical Pathway Stage III No Residual Disease, Stage III Preop Gross Nodal Disease, Stage IV Carcinosarcoma: PC + dostarlimab, then dostarlimab maintenance for up to 3 years No carcinosarcoma: PC + pembrolizumab, then pembrolizumab maintenance for up to 2 years No carcinosarcoma; dMMR/MSI-H: PC + pembrolizumab, then pembrolizumab maintenance for up to 2 years</p>
	<p>VA Rectal Cancer Clinical Pathway Stage II and III dMMR/MSI-H Dostarlimab x6 months as neoadjuvant therapy</p>

SAFETY CONSIDERATIONS	Boxed Warnings	None
	Contraindications	None
	Other Warnings	Severe and fatal immune-mediated adverse reactions, Infusion-related reactions Complications of allogeneic hematopoietic stem cell transplant Embryo-fetal toxicity
	Top 5 AEs	Endometrial cancer: decreased hgb, increased creatinine, peripheral neuropathy, decreased WBC, fatigue dMMR solid tumors: fatigue/asthenia, anemia, diarrhea, nausea
	Drug Interactions	None noted

DRUG	VANF	CFU	FDA	KEY ENDPOINTS
Dostarlimab	TBD	No	<ul style="list-style-type: none"> Advanced or recurrent EC: in combo with PC dMMR advanced or recurrent EC: as a single agent following prior platinum-containing regimen in any setting dMMR advanced or recurrent solid tumors: as a single agent following prior treatment and no satisfactory alternative treatment options 	<p>RUBY. Dostarlimab + PC vs. Placebo + PC, then dostarlimab for up to 3 years Stage III or IV, primary advanced or recurrent EC; included carcinosarcoma (10%) Overall population 24-mos PFS 36 vs. 18% [HR 0.64] 24-mos OS 71 vs. 56% [HR 0.64]</p> <ul style="list-style-type: none"> PFS and OS were significantly increased among patients. <p>RUBY. dMMR/MSI-H population 24-mos PFS 61 vs. 16% [HR 0.28] 24-mos OS 83 vs. 59% [HR 0.30] pMMR population 24-mos PFS 28 vs. 19% [HR 0.76] 24-mos OS 68 vs. 55% [HR 0.73; 95% CI 0.52-1.02]; NS</p> <ul style="list-style-type: none"> Significant benefit was noted in dMMR/MSI-H subgroup <p>Grade \geq 3 AEs 71 vs. 60%</p> <p>GARNET. dMMR solid tumors & no alternative therapy; 43% endometrial cancer ORR 41.6% (34.9, 48.6); CR 9.1%; PR 32.5% mDoR 34.7 mos</p>
Pembrolizumab	PA-F	Yes	<ul style="list-style-type: none"> Advanced or recurrent EC: in combo with PC dMMR/MSI-H advanced EC: as a single agent following prior systemic therapy in any setting dMMR/MSI-H solid tumors: as a single agent following prior treatment and no satisfactory alternative treatment options 	<p>NRG-GY018. Pembro + PC vs. Placebo + PC, then pembro for up to 2 years; n=816 Newly diagnosed Stage III-IVB or recurrent pMMR cohort: mPFS 13 vs. 8.7 mos [HR 0.54]</p> <p>dMMR cohort: mPFS NR vs. 7.6 mos 12-months PFS 74 vs. 38% [HR 0.30]</p> <p>Grade \geq 3 AEs 57 vs. 46%</p> <p>KEYNOTE-158. Pembro 200mg q3wk x35 cycles; 22.5% dMMR/MSI-H endometrial cancer ORR 30.8% mPFS 3.5 mos; mOS 20.1 mos mDOR 47.5 mos</p>
Durvalumab	PA-F	Yes	<ul style="list-style-type: none"> dMMR advanced or recurrent EC: in combo with PC 	<p>DUO-E. durvalumab + PC vs. placebo + PC, then durva until progression or unacceptable toxicity; n=718 Newly diagnosed advanced or recurrent dMMR EC ITT mPFS 10.2 vs. 9.6 months [HR 0.71]</p> <p>dMMR cohort mPFS NR vs. 7 months [HR 0.42]</p> <p>pMMR cohort mPFS 9.9 vs. 9.7 months [HR 0.77]; NS</p> <p>Grade \geq 3 AEs 54.9 vs. 56.4%</p>

PLACE IN THERAPY

Potential Use in VHA

Dostarlimab, when combined with paclitaxel and carboplatin, has shown improved efficacy in treating advanced or recurrent endometrial cancer compared to chemotherapy alone. Similar benefits have been observed with other immune checkpoint inhibitors (ICIs), including pembrolizumab and durvalumab;

RUBY study population included patients with carcinosarcoma, as did the DUO-E trial with durvalumab; patients with carcinosarcoma were not included in the pembrolizumab trials, although pembrolizumab still remains a viable treatment option

These agents differ in treatment duration:

- dostarlimab for up to three years
- pembrolizumab for up to two years
- durvalumab until disease progression or unacceptable toxicity

However, as expected, the ICI-containing arms of the RUBY and NRG-GY018 trials showed higher rates of Grade 3 or greater adverse events compared to their placebo-containing arms.

For tumor-agnostic indications, both dostarlimab and pembrolizumab are FDA-approved for use in dMMR/MSI-H solid tumors where no satisfactory treatment alternatives exist.

- Study populations varied, with dostarlimab trials including more patients with endometrial cancer, while pembrolizumab trials were predominantly composed of colorectal cancer patients, with only 23% having endometrial cancer.
- Despite differences in tumor types, both drugs demonstrated efficacy in their agnostic solid tumor trials.

Although not FDA-approved, evidence for use of dostarlimab as neoadjuvant therapy in locally advanced dMMR rectal cancer is striking with 100% of patients responding in this small trial. Long-term results are awaited.

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References

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