HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use JEMPERLI safely and effectively. See full prescribing information for JEMPERLI.

JEMPERLI (dostarlimab-gxly) injection, for intravenous use
Initial U.S. Approval: 2021

----------RECENT MAJOR CHANGES----------

Indications and Usage (1.1)	8/2024
Dosage and Administration (2.1, 2.2)	8/2024
Warnings and Precautions, Severe and Fatal Immune-Mediated Adverse Reactions (5.1)	3/2024

---------- INDICATIONS AND USAGE----------

JEMPERLI is a programmed death receptor-1 (PD-1)–blocking antibody indicated:

Endometrial Cancer

- in combination with carboplatin and paclitaxel, followed by JEMPERLI as a single agent, for the treatment of adult patients with primary advanced or recurrent endometrial cancer (EC). (1.1)
- as a single agent for the treatment of adult patients with mismatch repair deficient (dMMR) recurrent or advanced EC, as determined by an FDA-approved test, that has progressed on or following prior treatment with a platinum-containing regimen in any setting and are not candidates for curative surgery or radiation. (1.1, 2.1)

Mismatch Repair Deficient Recurrent or Advanced Solid Tumors

- as a single agent for the treatment of adult patients with dMMR recurrent or advanced solid tumors, as determined by an FDA-approved test, that have progressed on or following prior treatment and who have no satisfactory alternative treatment options.[1] (1.2, 2.1)

[1]This indication is approved under accelerated approval based on tumor response rate and durability of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial(s). (1.2)

----------DOSAGE AND ADMINISTRATION----------

- JEMPERLI, in combination with carboplatin and paclitaxel, for primary advanced or recurrent EC: 500 mg every 3 weeks for 6 cycles followed by 1,000 mg monotherapy every 6 weeks for all cycles thereafter. (2.2)
- JEMPERLI, as a single agent, for dMMR recurrent or advanced EC: 500 mg every 3 weeks for 4 cycles followed by 1,000 mg every 6 weeks for all cycles thereafter. (2.2)
- JEMPERLI, as a single agent, for dMMR recurrent or advanced solid tumors: 500 mg every 3 weeks for 4 cycles followed by 1,000 mg every 6 weeks for all cycles thereafter. (2.2)
- Administer as an intravenous infusion over 30 minutes. (2.2)
- For complete dosing instructions, see full prescribing information.

----------DOSAGE FORMS AND STRENGTHS----------

Injection: 500 mg/10 mL (50 mg/mL) solution in a single-dose vial. (3)

---------- CONTRAINDICATIONS ----------

None. (4)

---------- WARNINGS AND PRECAUTIONS ----------

- Immune-mediated adverse reactions, which may be severe or fatal, can occur in any organ system or tissue, including the following: immune-mediated pneumonitis, immune-mediated colitis, immune-mediated hepatitis, immune-mediated endocrinopathies, immune-mediated nephritis with renal dysfunction, immune-mediated dermatologic adverse reactions, and solid organ transplant rejection. Monitor for signs and symptoms of immune-mediated adverse reactions. Evaluate clinical chemistries, including liver enzymes, creatinine, and thyroid function, at baseline and periodically during treatment. Withhold or permanently discontinue JEMPERLI and administer corticosteroids based on the severity of reaction. (2.3, 5.1)
- Infusion-related reactions: Interrupt, slow the rate of infusion, or permanently discontinue JEMPERLI based on severity of reaction. (2.3, 5.2)
- Complications of allogeneic hematopoietic stem cell transplantation (HSCT): Fatal and other serious complications can occur in patients who receive allogeneic HSCT before or after being treated with a PD-1/PD-L1–blocking antibody. (5.3)
- Embryo-fetal toxicity: Can cause fetal harm. Advise females of reproductive potential of the potential risk to a fetus and to use effective contraception. (5.4, 8.1, 8.3)

---------- ADVERSE REACTIONS ----------

- Most common adverse reactions (≥20%), including laboratory abnormalities, with JEMPERLI in combination with carboplatin and paclitaxel in patients with EC are decreased hemoglobin, increased creatinine, peripheral neuropathy, decreased white blood cell count, fatigue, nausea, alopecia, decreased platelets, increased glucose, decreased lymphocytes, decreased magnesium, decreased neutrophils, increased aspartate aminotransferase (AST), arthralgia, rash, constipation, diarrhea, increased alanine aminotransferase (ALT), decreased potassium, decreased albumin, decreased sodium, increased alkaline phosphatase, abdominal pain, dyspnea, decreased appetite, increased amylase, decreased phosphate, urinary tract infection, and vomiting. (6.1)
- Most common adverse reactions (≥20%) with JEMPERLI as a single agent in patients with dMMR solid tumors are fatigue/asthenia, anemia, diarrhea, and nausea. Most common Grade 3 or 4 laboratory abnormalities (≥2%) are decreased lymphocytes, decreased sodium, increased alkaline phosphatase, and decreased albumin. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact GlaxoSmithKline at 1-888-825-5249 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

---------- USE IN SPECIFIC POPULATIONS ----------

Lactation: Advise not to breastfeed. (8.2)

See 17 for PATIENT COUNSELING INFORMATION and Medication Guide.

Revised: 8/2024

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FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

1.1 Endometrial Cancer

JEMPERLI, in combination with carboplatin and paclitaxel, followed by JEMPERLI as a single agent, is indicated for the treatment of adult patients with primary advanced or recurrent endometrial cancer (EC).

JEMPERLI, as a single agent, is indicated for the treatment of adult patients with mismatch repair deficient (dMMR) recurrent or advanced EC, as determined by an FDA-approved test, that has progressed on or following prior treatment with a platinum-containing regimen in any setting and are not candidates for curative surgery or radiation *[see Dosage and Administration (2.1)]*.

1.2 Mismatch Repair Deficient Recurrent or Advanced Solid Tumors

JEMPERLI, as a single agent, is indicated for the treatment of adult patients with dMMR recurrent or advanced solid tumors, as determined by an FDA-approved test, that have progressed on or following prior treatment and who have no satisfactory alternative treatment options *[see Dosage and Administration (2.1)]*. This indication is approved under accelerated approval based on tumor response rate and durability of response *[see Clinical Studies (14.2)]*. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial(s).

2 DOSAGE AND ADMINISTRATION

2.1 Patient Selection

Single Agent

Select patients for treatment with JEMPERLI as a single agent based on the presence of dMMR in tumor specimens in:

- recurrent or advanced EC *[see Clinical Studies (14.1)]*.
- recurrent or advanced solid tumors *[see Clinical Studies (14.2)]*.

Information on FDA-approved tests for the detection of dMMR status is available at https://www.fda.gov/companiondiagnostics.

Because the effect of prior chemotherapy on test results for dMMR in patients with high-grade gliomas is unclear, it is recommended to test for this marker in the primary tumor specimen obtained prior to initiation of temozolomide chemotherapy in patients with high-grade gliomas.

2.2 Recommended Dosage

The recommended dosage for JEMPERLI is presented in Table 1.

Table 1. Recommended Dosage of JEMPERLI

Indication	Recommended Dosage	Duration/Timing of Treatment
Combination Therapy		
Adults with primary advanced or recurrent EC	500 mg[a] JEMPERLI every 3 weeks for 6 cycles in combination with carboplatin and paclitaxel[b] followed by 1,000 mg JEMPERLI as monotherapy every 6 weeks for all cycles thereafter. Administer JEMPERLI prior to carboplatin and paclitaxel when given on the same day.	Until disease progression, unacceptable toxicity, or up to 3 years.
Monotherapy		
Adults with dMMR recurrent or advanced EC and dMMR recurrent or advanced solid tumors	500 mg[a] JEMPERLI every 3 weeks for 4 cycles followed by 1,000 mg[a] JEMPERLI every 6 weeks for all cycles thereafter.	Until disease progression or unacceptable toxicity.

dMMR = Mismatch Repair Deficient; EC = endometrial cancer.

[a] 30-minute intravenous infusion.

[b] Refer to the Prescribing Information for the agents administered in combination with JEMPERLI, as appropriate.

2.3 Dosage Modifications for Adverse Reactions

No dose reductions of JEMPERLI are recommended. In general, withhold JEMPERLI for severe (Grade 3) immune-mediated adverse reactions. Permanently discontinue JEMPERLI for life-threatening (Grade 4) immune-mediated adverse reactions, recurrent severe (Grade 3) immune-mediated reactions that require systemic immunosuppressive treatment, or an inability to reduce corticosteroid dose to 10 mg or less of prednisone equivalent per day within 12 weeks of initiating steroids.

Dosage modifications for JEMPERLI for adverse reactions that require management different from these general guidelines are summarized in Table 2.

Table 2. Recommended Dosage Modifications for Adverse Reactions

Adverse Reaction	Severity[a]	Dosage Modification
Immune-Mediated Adverse Reactions *[see Warnings and Precautions (5.1)]*		
Pneumonitis	Grade 2	Withhold[b]
	Grade 3 or 4 or recurrent Grade 2	Permanently discontinue
Colitis	Grade 2 or 3	Withhold[b]
	Grade 4	Permanently discontinue
Hepatitis with no tumor involvement of the liver	AST or ALT increases to more than 3 and up to 8 times ULN or Total bilirubin increases to more than 1.5 and up to 3 times ULN	Withhold[b]
	AST or ALT increases to more than 8 times ULN or Total bilirubin increases to more than 3 times ULN	Permanently discontinue
Hepatitis with tumor involvement of the liver[c]	Baseline AST or ALT is more than 1 and up to 3 times ULN and increases to more than 5 and up to 10 times ULN or Baseline AST or ALT is more than 3 and up to 5 times ULN and increases to more than 8 and up to 10 times ULN	Withhold[b]
	AST or ALT increases to more than 10 times ULN or Total bilirubin increases to more than 3 times ULN	Permanently discontinue
Endocrinopathies	Grade 2, 3, or 4	Withhold until clinically stable or permanently discontinue, depending on severity[b]

Nephritis with renal dysfunction	Grade 2 or 3 increased blood creatinine	Withhold[b]
	Grade 4 increased blood creatinine	Permanently discontinue
Exfoliative dermatologic conditions	Suspected SJS, TEN, or DRESS	Withhold[b]
	Confirmed SJS, TEN, or DRESS	Permanently discontinue
Myocarditis	Grade 2, 3, or 4	Permanently discontinue
Neurological toxicities	Grade 2	Withhold[b]
	Grade 3 or 4	Permanently discontinue
Other Adverse Reactions		
Infusion-related reactions *[see Warnings and Precautions (5.2)]*	Grade 1 or 2	Interrupt or slow the rate of infusion
	Grade 3 or 4	Permanently discontinue

ALT = alanine aminotransferase; AST = aspartate aminotransferase; DRESS = drug rash with eosinophilia and systemic symptoms; SJS = Stevens-Johnson syndrome; TEN = toxic epidermal necrolysis; ULN = upper limit of normal.

[a] Based on National Cancer Institute Common Terminology Criteria for Adverse Events, Version 5.0.

[b] Resume in patients with complete or partial resolution (Grade 0 to 1) after corticosteroid taper. Permanently discontinue if no complete or partial resolution within 12 weeks of initiating steroids or inability to reduce prednisone to less than 10 mg/day (or equivalent) within 12 weeks of initiating steroids.

[c] If AST and ALT are less than or equal to ULN at baseline in patients with liver involvement, withhold or permanently discontinue JEMPERLI based on recommendations for hepatitis with no liver involvement.

2.4 Preparation and Administration

Preparation for Intravenous Infusion

- Visually inspect the solution for particulate matter and discoloration. The solution is clear to slightly opalescent, colorless to yellow. Discard the vial if visible particles are observed.
- Do not shake.
- JEMPERLI is compatible with an infusion bag made of polyolefin, ethylene vinyl acetate, or polyvinyl chloride with di(2-ethylhexyl) phthalate (DEHP).
- For the 500-mg dose, withdraw 10 mL of JEMPERLI from a vial using a disposable sterile syringe made of polypropylene and dilute into an intravenous infusion bag containing 0.9%

Sodium Chloride Injection, USP or 5% Dextrose Injection, USP to a final concentration between 2 to 10 mg/mL (maximum 250 mL).

- For the 1,000-mg dose, withdraw 10 mL from each of 2 vials (withdraw 20 mL total) and dilute into an intravenous bag containing 0.9% Sodium Chloride Injection, USP or 5% Dextrose Injection, USP to a final concentration between 4 to 10 mg/mL (maximum 250 mL).
- Mix diluted solution by gentle inversion. Do not shake.
- Discard any unused portion left in the vial.

Storage of Infusion Solution

Store in the original carton until time of preparation in order to protect from light. The prepared dose may be stored either:

- At room temperature for no more than 6 hours from the time of preparation until the end of infusion.
- Under refrigeration at 2°C to 8°C (36ºF to 46ºF) for no more than 24 hours from time of preparation until end of infusion. If refrigerated, allow the diluted solution to come to room temperature prior to administration.

Discard after 6 hours at room temperature or after 24 hours under refrigeration.

Do not freeze.

Administration

Administer infusion solution intravenously over 30 minutes through an intravenous line using tubing made of polyvinyl chloride or platinum cured silicon; fittings made of polyvinyl chloride or polycarbonate; and a sterile, non-pyrogenic, low-protein binding, 0.2-micron, in-line or add-on filter.

JEMPERLI must not be administered as an intravenous push or bolus injection. Do not co-administer other drugs through the same infusion line.

3 DOSAGE FORMS AND STRENGTHS

Injection: 500 mg/10 mL (50 mg/mL) clear to slightly opalescent, colorless to yellow solution in a single-dose vial for intravenous infusion after dilution.

4 CONTRAINDICATIONS

None.

5 WARNINGS AND PRECAUTIONS

5.1 Severe and Fatal Immune-Mediated Adverse Reactions

JEMPERLI is a monoclonal antibody that belongs to a class of drugs that bind to either the programmed death receptor-1 (PD-1) or PD-ligand 1 (PD-L1), blocking the PD-1/PD-L1 pathway, thereby removing inhibition of the immune response, potentially breaking peripheral tolerance, and inducing immune-mediated adverse reactions. Important immune-mediated adverse reactions listed in WARNINGS AND PRECAUTIONS may not include all possible severe and fatal immune-mediated reactions.

Immune-mediated adverse reactions, which can be severe or fatal, can occur in any organ system or tissue. Immune-mediated adverse reactions can occur at any time after starting a PD-1/PD-L1–blocking antibody. While immune-mediated adverse reactions usually manifest during treatment with PD-1/PD-L1–blocking antibodies, they can also manifest after discontinuation of PD-1/PD-L1–blocking antibodies.

Early identification and management of immune-mediated adverse reactions are essential to ensure safe use of PD-1/PD-L1–blocking antibodies. Monitor closely for symptoms and signs that may be clinical manifestations of underlying immune-mediated adverse reactions. Evaluate liver enzymes, creatinine, and thyroid function tests at baseline and periodically during treatment. In cases of suspected immune-mediated adverse reactions, initiate appropriate workup to exclude alternative etiologies, including infection. Institute medical management promptly, including specialty consultation as appropriate.

Withhold or permanently discontinue JEMPERLI depending on severity *[see Dosage and Administration (2.3)]*. In general, if JEMPERLI requires interruption or discontinuation, administer systemic corticosteroids (1 to 2 mg/kg/day prednisone or equivalent) until improvement to Grade 1 or less. Upon improvement to Grade 1 or less, initiate corticosteroid taper and continue to taper over at least 1 month. Consider administration of other systemic immunosuppressants in patients whose immune-mediated adverse reaction is not controlled with corticosteroids.

Toxicity management guidelines for adverse reactions that do not necessarily require systemic steroids (e.g., endocrinopathies, dermatologic reactions) are discussed below.

<u>Immune-Mediated Pneumonitis</u>

JEMPERLI can cause immune-mediated pneumonitis, which can be fatal. In patients treated with other PD-1/PD-L1–blocking antibodies, the incidence of pneumonitis is higher in patients who have received prior thoracic radiation.

Immune-mediated pneumonitis occurred in 2.3% (14/605) of patients receiving JEMPERLI, including Grade 2 (1.3%), Grade 3 (0.8%) and Grade 4 (0.2%) pneumonitis. Pneumonitis led to discontinuation of JEMPERLI in 1.3% of patients.

Systemic corticosteroids were required in 79% (11/14) of patients with pneumonitis. Pneumonitis resolved in 11 of the 14 patients. JEMPERLI was withheld for 9 patients. Five patients reinitiated JEMPERLI after symptom improvement; of these, 2 patients had recurrence of pneumonitis.

Immune-Mediated Colitis

JEMPERLI can cause immune-mediated colitis. Cytomegalovirus infection/reactivation have occurred in patients with corticosteroid-refractory immune-mediated colitis treated with PD-1/PD-L1–blocking antibodies. In cases of corticosteroid-refractory colitis, consider repeating infectious workup to exclude alternative etiologies.

Immune-mediated colitis occurred in 1.3% (8/605) of patients receiving JEMPERLI, including Grade 2 (0.7%) and Grade 3 (0.7%) adverse reactions. Colitis led to discontinuation of JEMPERLI in 1 (0.2%) patient.

Systemic corticosteroids were required in 75% (6/8) of patients with colitis. Colitis resolved in 5 of the 8 patients. Of the 4 patients in whom JEMPERLI was withheld for colitis, all reinitiated treatment with JEMPERLI; of these, 1 patient had recurrence of colitis.

Immune-Mediated Hepatitis

JEMPERLI can cause immune-mediated hepatitis, which can be fatal.

Immune-mediated hepatitis occurred in 0.5% (3/605) of patients receiving JEMPERLI, all were Grade 3. Hepatitis led to discontinuation of JEMPERLI in 1 (0.2%) patient. Systemic corticosteroids were required in 2 patients with hepatitis and the events resolved in 2 of the 3 patients.

Immune-Mediated Endocrinopathies

Adrenal Insufficiency: JEMPERLI can cause primary or secondary adrenal insufficiency. For Grade 2 or higher adrenal insufficiency, initiate symptomatic treatment per institutional guidelines, including hormone replacement as clinically indicated. Withhold or permanently discontinue JEMPERLI depending on severity *[see Dosage and Administration (2.3)]*.

Adrenal insufficiency occurred in 1.2% (7/605) patients receiving JEMPERLI, including Grade 2 (0.5%) and Grade 3 (0.7%). Adrenal insufficiency resulted in discontinuation in 1 (0.2%) patient and resolved in 4 of the 7 patients. Of the 4 patients in whom JEMPERLI was withheld for adrenal insufficiency, all reinitiated treatment with JEMPERLI. Systemic corticosteroids were required in 5 of the 7 patients with adrenal insufficiency.

Hypophysitis: JEMPERLI can cause immune-mediated hypophysitis. Hypophysitis can present with acute symptoms associated with mass effect such as headache, photophobia, or visual field cuts. Hypophysitis can cause hypopituitarism. Initiate hormone replacement as clinically indicated. Withhold or permanently discontinue JEMPERLI depending on severity *[see Dosage and Administration (2.3)]*.

JEMPERLI in Combination with Carboplatin and Paclitaxel: Hypophysitis (Grade 3) occurred in 0.4% (1/241) of patients receiving JEMPERLI in combination with carboplatin and paclitaxel. Systemic corticosteroids were required, and the event resolved. JEMPERLI was withheld and the patient reinitiated treatment.

JEMPERLI as a Single Agent: Hypophysitis (Grade 2) occurred in 0.2% (1/605) of patients receiving JEMPERLI as a single agent. Systemic corticosteroids were required, and the event did not resolve. JEMPERLI was withheld and the patient reinitiated treatment.

Thyroid Disorders: JEMPERLI can cause immune-mediated thyroid disorders. Thyroiditis can present with or without endocrinopathy. Hypothyroidism can follow hyperthyroidism. Initiate thyroid hormone replacement or medical management of hyperthyroidism as clinically indicated. Withhold or permanently discontinue JEMPERLI depending on severity *[see Dosage and Administration (2.3)]*.

Thyroiditis: Thyroiditis occurred in 0.5% (3/605) of patients receiving JEMPERLI; all were Grade 2. Systemic corticosteroids were required in 1 of 3 patients and anti-thyroid therapy was required for 2 of 3 patients with thyroiditis. JEMPERLI was withheld for 1 patient and the patient reinitiated treatment. None of the events of thyroiditis resolved; there were no discontinuations of JEMPERLI due to thyroiditis.

Hypothyroidism: JEMPERLI in Combination with Carboplatin and Paclitaxel: Hypothyroidism occurred in 12% (30/241) of patients receiving JEMPERLI in combination with carboplatin and paclitaxel, all of which were Grade 2. Hypothyroidism led to discontinuation of JEMPERLI in 1 patient and resolved in 23% (7/30) of patients. JEMPERLI was withheld for 5 patients and all reinitiated treatment with JEMPERLI. Thyroid hormone replacement was required for 27 of the 30 patients with hypothyroidism.

JEMPERLI as a Single Agent: Hypothyroidism occurred in 8% (46/605) of patients receiving JEMPERLI as a single agent, all of which were Grade 2. Hypothyroidism did not lead to discontinuation of JEMPERLI and resolved in 37% (17/46) of patients. JEMPERLI was withheld for 2 patients and both reinitiated treatment. Thyroid hormone replacement therapy was required for 45 of the 46 patients with hypothyroidism.

Hyperthyroidism: JEMPERLI in Combination with Carboplatin and Paclitaxel: Hyperthyroidism occurred in 3.3% (8/241) of patients receiving JEMPERLI in combination with carboplatin and paclitaxel, including Grade 2 (2.9%) and Grade 3 (0.4%). Hyperthyroidism did not lead to discontinuation of JEMPERLI and resolved in 75% (6/8) of patients. JEMPERLI was withheld for 1 patient and the patient reinitiated treatment. Anti-thyroid therapy was required for 2 of the 8 patients while systemic corticosteroids were required for 1 of the 8 patients with hyperthyroidism.

JEMPERLI as a Single Agent: Hyperthyroidism occurred in 2.3% (14/605) of patients receiving JEMPERLI as a single agent, including Grade 2 (2.1%) and Grade 3 (0.2%).

Hyperthyroidism did not lead to discontinuation of JEMPERLI and resolved in 71% (10/14) of the 14 patients. JEMPERLI was withheld for 2 patients and both reinitiated treatment. Anti-thyroid therapy was required for 10 of the 14 patients with hyperthyroidism.

Type 1 Diabetes Mellitus, Which Can Present with Diabetic Ketoacidosis: JEMPERLI can cause type 1 diabetes mellitus, which can present with diabetic ketoacidosis. Monitor patients for hyperglycemia or other signs and symptoms of diabetes. Initiate treatment with insulin as clinically indicated. Withhold or permanently discontinue JEMPERLI depending on severity *[see Dosage and Administration (2.3)]*.

JEMPERLI in Combination with Carboplatin and Paclitaxel: Type 1 diabetes mellitus (Grade 3) occurred in 0.4% (1/241) of patients receiving JEMPERLI in combination with carboplatin and paclitaxel. Type 1 diabetes mellitus led to withholding JEMPERLI; the patient reinitiated treatment and required long-term insulin therapy.

JEMPERLI as a Single Agent: Type 1 diabetes mellitus occurred in 0.2% (1/605) of patients receiving JEMPERLI as a single agent, which was Grade 3. Type 1 diabetes mellitus did not result in treatment discontinuation and did not resolve.

Immune-Mediated Nephritis with Renal Dysfunction

JEMPERLI can cause immune-mediated nephritis, which can be fatal. Nephritis, including tubulointerstitial nephritis, occurred in 0.5% (3/605) of patients receiving JEMPERLI; all were Grade 2. Nephritis led to discontinuation of JEMPERLI in 1 (0.2%) patient and resolved in all patients. JEMPERLI was withheld for 1 patient and the patient reinitiated treatment. Systemic corticosteroids were required in 2 of the 3 patients experiencing nephritis.

Immune-Mediated Dermatologic Adverse Reactions

JEMPERLI can cause immune-mediated rash or dermatitis. Bullous and exfoliative dermatitis, including Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN), and drug rash with eosinophilia and systemic symptoms (DRESS), have occurred with PD-1/PD-L1–blocking antibodies. Topical emollients and/or topical corticosteroids may be adequate to treat mild to moderate non-bullous/exfoliative rashes. Withhold or permanently discontinue JEMPERLI depending on severity *[see Dosage and Administration (2.3)]*.

Other Immune-Mediated Adverse Reactions

The following clinically significant immune-mediated adverse reactions occurred in <1% of the 605 patients treated with JEMPERLI or were reported with the use of other PD-1/PD-L1–blocking antibodies. Severe or fatal cases have been reported for some of these adverse reactions.

Nervous System: Meningitis, encephalitis, myelitis and demyelination, myasthenic syndrome/myasthenia gravis, Guillain-Barré syndrome, nerve paresis, autoimmune neuropathy.

Cardiac/Vascular: Myocarditis, pericarditis, vasculitis.

Ocular: Uveitis, iritis, other ocular inflammatory toxicities. Some cases can be associated with retinal detachment. Various grades of visual impairment to include blindness can occur. If uveitis occurs in combination with other immune-mediated adverse reactions, consider a Vogt-Koyanagi-Harada–like syndrome, as this may require treatment with systemic steroids to reduce the risk of permanent vision loss.

Gastrointestinal: Pancreatitis, including increases in serum amylase and lipase levels, gastritis, duodenitis.

Musculoskeletal and Connective Tissue: Myositis/polymyositis, rhabdomyolysis and associated sequelae including renal failure, arthritis, polymyalgia rheumatica.

Endocrine: Hypoparathyroidism.

Other (Hematologic/Immune): Autoimmune hemolytic anemia, aplastic anemia, hemophagocytic lymphohistiocytosis, systemic inflammatory response syndrome, histiocytic necrotizing lymphadenitis (Kikuchi lymphadenitis), sarcoidosis, immune thrombocytopenia, solid organ transplant rejection, other transplant (including corneal graft) rejection.

5.2 Infusion-Related Reactions

Severe or life-threatening infusion-related reactions have been reported with PD-1/PD-L1–blocking antibodies. Severe infusion-related reactions (Grade 3) occurred in 0.2% (1/605) of patients receiving JEMPERLI. All patients recovered from the infusion-related reactions.

Monitor patients for signs and symptoms of infusion-related reactions. Interrupt or slow the rate of infusion or permanently discontinue JEMPERLI based on severity of reaction *[see Dosage and Administration (2.3)]*.

5.3 Complications of Allogeneic HSCT

Fatal and other serious complications can occur in patients who receive allogeneic hematopoietic stem cell transplantation (HSCT) before or after being treated with a PD-1/PD-L1–blocking antibody. Transplant-related complications include hyperacute graft-versus-host disease (GVHD), acute GVHD, chronic GVHD, hepatic veno-occlusive disease after reduced intensity conditioning, and steroid-requiring febrile syndrome (without an identified infectious cause). These complications may occur despite intervening therapy between PD-1/PD-L1 blockade and allogeneic HSCT.

Follow patients closely for evidence of transplant-related complications and intervene promptly. Consider the benefit versus risks of treatment with a PD-1/PD-L1–blocking antibody prior to or after an allogeneic HSCT.

5.4 Embryo-Fetal Toxicity

Based on its mechanism of action, JEMPERLI can cause fetal harm when administered to a pregnant woman. Animal studies have demonstrated that inhibition of the PD-1/PD-L1 pathway can lead to increased risk of immune-mediated rejection of the developing fetus, resulting in fetal

death. Advise pregnant women of the potential risk to a fetus. Advise females of reproductive potential to use effective contraception during treatment with JEMPERLI and for 4 months after the last dose *[see Use in Specific Populations (8.1, 8.3)]*.

6 ADVERSE REACTIONS

The following clinically significant adverse reactions are described elsewhere in the labeling:

- Severe and fatal immune-mediated adverse reactions *[see Warnings and Precautions (5.1)]*
- Infusion-related reactions *[see Warnings and Precautions (5.2)]*

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared with rates in the clinical trials of another drug and may not reflect the rates observed in practice.

The safety population described in the *Warnings and Precautions* for use of JEMPERLI in combination with carboplatin and paclitaxel was evaluated in 241 patients with primary advanced or recurrent EC in the randomized, double-blind, active-controlled RUBY trial.

Additionally, the pooled safety population described in *Warnings and Precautions* reflects exposure to JEMPERLI as a single agent in 605 patients with advanced or recurrent solid tumors in the non-randomized, open-label, multicohort GARNET trial that enrolled 314 patients with EC and 291 patients with other solid tumors. JEMPERLI was administered intravenously at doses of 500 mg every 3 weeks for 4 cycles followed by 1,000 mg every 6 weeks until disease progression or unacceptable toxicity. Among the 605 patients, 32% were exposed for >1 year and 19% were exposed for >2 years.

<u>Primary Advanced or Recurrent Endometrial Cancer: JEMPERLI in Combination with Carboplatin and Paclitaxel</u>

The safety of JEMPERLI in patients with primary advanced or recurrent EC was evaluated in RUBY *[see Clinical Studies (14.1)]*. Patients received JEMPERLI 500 mg (n = 241) or placebo (n = 246) in combination with carboplatin and paclitaxel every 3 weeks for 6 cycles followed by JEMPERLI 1,000 mg or placebo every 6 weeks until disease progression or unacceptable toxicity. Among the 241 patients, 38.6% were exposed for >1 year and 24.1% were exposed for >2 years.

Serious adverse reactions occurred in 39% of patients receiving JEMPERLI in combination with carboplatin and paclitaxel; the most common serious adverse reactions were sepsis, including urosepsis (3.7%), and pulmonary embolism (3.3%). Fatal adverse reactions occurred in 1.2% of patients receiving JEMPERLI including septic shock (0.8%) and myelosuppression (0.4%).

In patients receiving JEMPERLI in combination with carboplatin and paclitaxel, JEMPERLI was permanently discontinued due to adverse reactions in 46 patients (19%). Adverse reactions that

required permanent discontinuation in ≥2 patients included 3 cases (1.2%) of rash maculo-papular, and 2 cases (0.8%) each of increased alanine aminotransferase (ALT), increased aspartate aminotransferase (AST), diarrhea, pancreatitis, fatigue, pneumonitis, and arthralgia.

Dosage interruptions due to an adverse reaction occurred in 37% of patients who received JEMPERLI in combination with carboplatin and paclitaxel. Adverse reactions that required dosage interruption in ≥5% of patients who received JEMPERLI in combination with carboplatin and paclitaxel were anemia, thrombocytopenia, and peripheral neuropathy.

The most common adverse reactions, including laboratory abnormalities (≥20%), were decreased hemoglobin, increased creatinine, peripheral neuropathy, decreased white blood cell count, fatigue, nausea, alopecia, decreased platelets, increased glucose, decreased lymphocytes, decreased magnesium, decreased neutrophils, increased AST, arthralgia, rash, constipation, diarrhea, increased ALT, decreased potassium, decreased albumin, decreased sodium, increased alkaline phosphatase, abdominal pain, dyspnea, decreased appetite, increased amylase, decreased phosphate, urinary tract infection, and vomiting.

Table 3 summarizes the adverse reactions that occurred in ≥20% of patients with primary advanced or recurrent EC receiving JEMPERLI in combination with carboplatin and paclitaxel in RUBY.

Table 3. Adverse Reactions (≥20%) in Patients with Endometrial Cancer Who Received JEMPERLI with Carboplatin and Paclitaxel in RUBY

Adverse Reaction	JEMPERLI with Carboplatin and Paclitaxel N = 241		Placebo with Carboplatin and Paclitaxel N = 246	
	All Grades %	Grade 3 or 4 %	All Grades %	Grade 3 or 4 %
Nervous System Disorders				
Peripheral neuropathy[a]	64	4.1	61	2.0
General				
Fatigue[b]	56	3.3	63	5
Gastrointestinal Disorders				
Nausea	54	2.9	46	1.6
Constipation	35	0.4	36	0
Diarrhea	32	1.7	29	0.8
Abdominal pain[c]	24	2.5	29	2
Vomiting	20	1.7	20	1.6
Skin and Subcutaneous Tissue				
Alopecia	54	0	50	1.2
Rash[d]	37	7	18	1.2
Musculoskeletal and Connective Tissue				
Arthralgia	37	1.2	35	0.4
Respiratory, Thoracic and Mediastinal Disorders				
Dyspnea[e]	23	1.7	26	0.8
Metabolism and Nutrition Disorders				
Decreased appetite	22	2.1	18	0.4
Infections and Infestations				
Urinary tract infection[f]	21	3.3	18	1.6

Graded per National Cancer Institute Common Terminology Criteria for Adverse Events Version 4.03.

[a] Includes neuropathy peripheral and peripheral sensory neuropathy.

[b] Includes fatigue and asthenia.

[c] Includes abdominal pain, abdominal pain upper, abdominal pain lower, gastrointestinal pain, abdominal discomfort, epigastric discomfort, and abdominal tenderness.

[d] Includes rash, rash maculo-papular, palmar-plantar erythrodysesthesia syndrome, rash pustular, skin exfoliation, and vulvovaginal rash.

[e] Includes dyspnea and dyspnea exertional.

[f] Includes urinary tract infection, urinary tract infection bacterial, cystitis, and pyelonephritis.

Clinically relevant adverse reactions in <20% of patients with primary advanced or recurrent EC who received JEMPERLI in combination with carboplatin and paclitaxel included:

Endocrine Disorders: Hypothyroidism, hyperthyroidism, thyroiditis, adrenal insufficiency.

Eye Disorders: Keratitis, uveitis.

Gastrointestinal Disorders: Colitis, pancreatitis.

Metabolism and Nutrition Disorders: Type 1 diabetes mellitus.

Musculoskeletal and Connective Tissue Disorders: Immune-mediated arthritis.

Respiratory, Thoracic, and Mediastinal Disorders: Pneumonitis.

Cardiac Disorders: Myocarditis.

Nervous System Disorders: Encephalopathy.

Vascular Disorders: Hypertension, hemorrhage.

Table 4 summarizes the laboratory abnormalities in patients with primary advanced or recurrent EC receiving JEMPERLI in combination with carboplatin and paclitaxel in RUBY.

Table 4. Select Laboratory Abnormalities that Worsened from Baseline Occurring in ≥20% of Patients with Endometrial Cancer Receiving JEMPERLI with Carboplatin and Paclitaxel in RUBY

	JEMPERLI with Carboplatin and Paclitaxel N = 241		Placebo with Carboplatin and Paclitaxel N = 246	
Laboratory Test	**All Grades[a] %**	**Grade 3 or 4[a] %**	**All Grades[a] %**	**Grade 3 or 4[a] %**
Hematology				
Decreased hemoglobin	79	14	83	16
Decreased white blood cell count	62	13	58	11
Decreased platelet count	48	4.1	48	7
Decreased lymphocytes	44	14	39	13
Decreased neutrophils	42	14	52	18
Chemistry				
Increased creatinine	75	1.7	82	0.4
Increased glucose	47	10	44	10
Increased AST	38	3.3	23	1.6
Increased ALT	30	2.5	19	0.8
Decreased albumin	29	0.8	21	0
Increased alkaline phosphatase	28	1.7	22	0.4
Increased amylase	21	5	11	1.6
Electrolytes				
Decreased magnesium	44	2.1	47	2
Decreased potassium	30	6	29	4.1
Decreased sodium	29	6	22	3.7
Decreased phosphate	21	1.2	18	3.7

ALT = alanine aminotransferase; AST = aspartate aminotransferase.

[a] Consists of new onset of laboratory abnormality or worsening of baseline laboratory abnormality.

Mismatch Repair Deficient Recurrent or Advanced Endometrial Cancer: JEMPERLI as a Single Agent

The safety of JEMPERLI was evaluated in GARNET in 150 patients with advanced or recurrent dMMR EC who received at least 1 dose of JEMPERLI *[see Clinical Studies (14.1)]*. Patients received JEMPERLI 500 mg every 3 weeks for 4 cycles followed by 1,000 mg every 6 weeks as an intravenous infusion until disease progression or unacceptable toxicity. Patients with

autoimmune disease that required systemic therapy within 2 years of treatment or a medical condition that required immunosuppression were ineligible. Among patients receiving JEMPERLI, 41% were exposed for >1 year and 23% were exposed for >2 years.

A fatal adverse reaction occurred in one patient (0.7%) who received JEMPERLI, due to concurrent immune-mediated encephalitis and urinary tract infection.

Serious adverse reactions occurred in 38% of patients receiving JEMPERLI. Serious adverse reactions in >2% of patients included urinary tract infection (4%), sepsis (3.3%), acute kidney injury (2.7%), and abdominal pain (2.7%).

JEMPERLI was permanently discontinued due to adverse reactions in 15 (10%) patients, including increased transaminases, sepsis, bronchitis, pneumonitis, rash, pruritus, pancreatitis, encephalitis, and nephritis. Dosage interruptions due to an adverse reaction occurred in 28% of patients who received JEMPERLI. Adverse reactions that required dosage interruption in >1% of patients who received JEMPERLI were anemia, diarrhea, asthenia, colitis, sepsis, and pneumonitis.

The most common adverse reactions (≥20%) were fatigue/asthenia, anemia, nausea, diarrhea, constipation, vomiting, and rash.

Table 5 summarizes the adverse reactions that occurred in ≥10% of patients with dMMR EC on JEMPERLI in GARNET.

Table 5. Adverse Reactions (≥10%) in Patients with dMMR Endometrial Cancer Who Received JEMPERLI in GARNET

	JEMPERLI N = 150	
Adverse Reaction	**All Grades %**	**Grade 3 or 4 %**
General and administration site		
Fatigue[a]	49	3.3
Pyrexia	13	0
Blood and lymphatic system		
Anemia[b]	35	18
Gastrointestinal		
Nausea	32	0.7
Diarrhea	29	2.7
Constipation	23	0.7
Vomiting	23	0.7

Skin and subcutaneous tissue		
Rash[c]	21	0
Pruritus	19	1.3
Infections		
Urinary tract infection	19	4
Metabolism and nutrition		
Decreased appetite	15	0
Respiratory, thoracic, and mediastinal		
Cough	15	0
Musculoskeletal and connective tissue		
Myalgia	10	0
Investigations		
Increased transaminases[d]	13	4
Endocrine Disorders		
Hypothyroidism	11	0

dMMR = Mismatch Repair Deficient.
Toxicity was graded per National Cancer Institute Common Terminology Criteria for Adverse Events Version 4.03.
[a] Includes fatigue and asthenia.
[b] Includes anemia, decreased hemoglobin, iron deficiency, and iron deficiency anemia.
[c] Includes rash, rash maculo-papular, rash pruritic, erythema, and pemphigoid.
[d] Includes increased alanine aminotransferase, increased aspartate aminotransferase, increased transaminases, and hypertransaminasemia.

Clinically relevant adverse reactions in <10% of patients who received JEMPERLI included:

Endocrine Disorders: Hyperthyroidism, adrenal insufficiency, hypophysitis.

Eye Disorders: Iridocyclitis, uveitis.

Gastrointestinal Disorders: Colitis, pancreatitis, enterocolitis, gastritis.

General Disorders and Administration Site Conditions: Chills.

Musculoskeletal and Connective Tissue Disorders: Immune-mediated myositis, immune-mediated arthritis.

Nervous System Disorders: Encephalitis.

Renal and Urinary Disorders: Nephritis.

Respiratory, Thoracic, and Mediastinal Disorders: Pneumonitis, interstitial lung disease.

Table 6 summarizes laboratory abnormalities worsening from baseline to Grade 3 or 4 in ≥1% of patients with dMMR EC on JEMPERLI in GARNET.

Table 6. Laboratory Abnormalities that Worsened from Baseline to Grade 3 or 4 Occurring in ≥1% of Patients with dMMR Endometrial Cancer Receiving JEMPERLI in GARNET

	JEMPERLI N = 150	
Laboratory Test	**All Grades[a] %**	**Grade 3 or 4[a] %**
Hematology		
Decreased lymphocytes	46	15
Decreased leukocytes	21	2
Decreased neutrophils	17	2.7
Chemistry		
Decreased albumin	36	2.7
Increased creatinine	33	3.4
Increased alkaline phosphatase	31	2.7
Increased aspartate aminotransferase	31	2
Increased alanine aminotransferase	25	4.7
Electrolytes		
Decreased sodium	29	5
Decreased magnesium	28	2
Decreased potassium	22	2
Increased calcium	8	2

dMMR = Mismatch Repair Deficient.

[a] Consists of new onset of laboratory abnormality or worsening of baseline laboratory abnormality.

Mismatch Repair Deficient Recurrent or Advanced Solid Tumors

The safety of JEMPERLI was investigated in 267 patients with recurrent or advanced dMMR solid tumors enrolled in GARNET *[see Clinical Studies (14.2)]*. Patients received JEMPERLI 500 mg every 3 weeks for 4 cycles followed by 1,000 mg every 6 weeks as an intravenous infusion until disease progression or unacceptable toxicity. Patients with autoimmune disease that required systemic therapy within 2 years of treatment or a medical condition that required immunosuppression were ineligible. The median duration of exposure to JEMPERLI was 25 weeks (range: 1 to 139 weeks).

Serious adverse reactions occurred in 34% of patients receiving JEMPERLI. Serious adverse reactions in >2% of patients included abdominal pain (3.7%), sepsis (2.6%), and acute kidney injury (2.2%). Fatal adverse reaction occurred in 1 patient who received JEMPERLI due to respiratory failure.

JEMPERLI was permanently discontinued due to adverse reactions in 9% patients; the most common adverse reaction (≥1%) leading to discontinuation was increased alanine aminotransferase (1.1%).

Dosage interruptions due to an adverse reaction occurred in 23% of patients who received JEMPERLI. Adverse reactions that required dosage interruption in ≥1% of patients who received JEMPERLI were anemia, pneumonitis, diarrhea, adrenal insufficiency, increased alanine aminotransferase, and increased aspartate aminotransferase.

The most common adverse reactions (≥20%) were fatigue/asthenia, anemia, diarrhea, and nausea.

Table 7 summarizes the adverse reactions that occurred in ≥10% of patients with dMMR recurrent or advanced solid tumors in GARNET.

Table 7. Adverse Reactions (≥10%) in Patients with dMMR Recurrent or Advanced Solid Tumors in GARNET

	JEMPERLI N = 267	
Adverse Reaction	**All Grades %**	**Grade 3 or 4 %**
General and administration site		
Fatigue[a]	42	3.4
Pyrexia	12	0
Blood and lymphatic system		
Anemia[b]	30	11
Gastrointestinal		
Diarrhea	25	1.5
Nausea	22	0.4
Vomiting	17	1.5
Constipation	16	0.4
Skin and subcutaneous tissue		
Pruritus	15	0.4
Rash[c]	14	0.4
Respiratory, thoracic, and mediastinal		
Cough	13	0
Metabolism and nutrition		
Decreased appetite	12	0.4
Investigations		
Increased transaminases[d]	12	3

dMMR = Mismatch Repair Deficient.

Toxicity was graded per National Cancer Institute Common Terminology Criteria for Adverse Events Version 4.03.

[a] Includes fatigue and asthenia.

[b] Includes anemia, decreased hemoglobin, iron deficiency, and iron deficiency anemia.

[c] Includes rash, rash maculopapular, rash macular, rash erythematous, rash papular, erythema, toxic skin eruption, and pemphigoid.

[d] Includes increased alanine aminotransferase, increased aspartate aminotransferase, increased transaminases, and hypertransaminasemia.

Clinically relevant adverse reactions in <10% of patients who received JEMPERLI included:

Endocrine Disorders: Hypothyroidism, hyperthyroidism, adrenal insufficiency, hypophysitis, autoimmune thyroiditis.

Eye Disorders: Uveitis.

Gastrointestinal Disorders: Colitis, enterocolitis, enterocolitis hemorrhage, pancreatitis, acute pancreatitis.

General Disorders and Administration Site Conditions: Chills.

Injury, Poisoning, and Procedural Complications: Infusion related reaction.

Hepatobiliary Disorders: Hepatocellular injury.

Musculoskeletal and Connective Tissue Disorders: Myalgia.

Renal and Urinary Disorders: Nephritis, tubulointerstitial nephritis.

Respiratory, Thoracic, and Mediastinal Disorders: Pneumonitis, interstitial lung disease.

Table 8 summarizes laboratory abnormalities worsening from baseline to Grade 3 or 4 in ≥1% of patients with dMMR recurrent or advanced solid tumors in GARNET.

Table 8. Laboratory Abnormalities that Worsened from Baseline to Grade 3 or 4 Occurring in ≥1% of Patients with dMMR Recurrent or Advanced Solid Tumors in GARNET

Laboratory Test	JEMPERLI N = 267	
	All Grades[a] %	Grade 3 or 4[a] %
Hematology		
Decreased lymphocytes	33	7
Decreased leukocytes	18	1.1
Decreased neutrophils	12	1.5
Chemistry		
Decreased albumin	26	2.2
Increased alkaline phosphatase	26	3.4
Increased aspartate aminotransferase	26	1.5
Increased alanine aminotransferase	22	1.9
Increased creatinine	21	1.1
Increased total bilirubin	7	1.5
Electrolytes		
Decreased sodium	21	4.9
Decreased magnesium	16	1.1
Decreased potassium	14	1.1
Increased potassium	14	1.1
Increased calcium	6	1.1
Increased magnesium	4.1	1.5
Decreased calcium	2.6	1.5

dMMR = Mismatch Repair Deficient.

[a] Consists of new onset of laboratory abnormality or worsening of baseline laboratory abnormality.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

Based on its mechanism of action, JEMPERLI can cause fetal harm when administered to a pregnant woman *[see Clinical Pharmacology (12.1)]*. There are no available data on the use of JEMPERLI in pregnant women. Animal studies have demonstrated that inhibition of the PD-1/PD-L1 pathway can lead to increased risk of immune-mediated rejection of the developing fetus resulting in fetal death *(see Data)*. Human IgG4 immunoglobulins (IgG4) are known to

cross the placental barrier; therefore, dostarlimab-gxly has the potential to be transmitted from the mother to the developing fetus. Advise women of the potential risk to a fetus.

In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively.

Data

Animal Data: Animal reproduction studies have not been conducted with JEMPERLI to evaluate its effect on reproduction and fetal development. A central function of the PD-1/PD-L1 pathway is to preserve pregnancy by maintaining maternal immune tolerance to the fetus. In murine models of pregnancy, blockade of PD-L1 signaling has been shown to disrupt tolerance to the fetus and to result in an increase in fetal loss; therefore, potential risks of administering JEMPERLI during pregnancy include increased rates of abortion or stillbirth. As reported in the literature, there were no malformations related to the blockade of PD-1/PD-L1 signaling in the offspring of these animals; however, immune-mediated disorders occurred in PD-1 and PD-L1 knockout mice. Based on its mechanism of action, fetal exposure to dostarlimab-gxly may increase the risk of developing immune-mediated disorders or altering the normal immune response.

8.2 Lactation

Risk Summary

There is no information regarding the presence of dostarlimab-gxly in human milk or its effects on the breastfed child or on milk production. Maternal IgG is known to be present in human milk. The effects of local gastrointestinal exposure and limited systemic exposure in the breastfed child to JEMPERLI are unknown. Because of the potential for serious adverse reactions in a breastfed child, advise women not to breastfeed during treatment and for 4 months after the last dose of JEMPERLI.

8.3 Females and Males of Reproductive Potential

JEMPERLI can cause fetal harm when administered to a pregnant woman *[see Use in Specific Populations (8.1)]*.

Pregnancy Testing

Verify pregnancy status in females of reproductive potential prior to initiating JEMPERLI *[see Use in Specific Populations (8.1)]*.

Contraception

Females: Advise females of reproductive potential to use effective contraception during treatment with JEMPERLI and for 4 months after the last dose.

8.4 Pediatric Use

The safety and efficacy of JEMPERLI have not been established in pediatric patients.

8.5 Geriatric Use

In Combination with Carboplatin and Paclitaxel

Of the 241 patients treated with JEMPERLI in RUBY, 52.3% were younger than 65 years, 36.5% were aged 65 through 74 years, and 11.2% were 75 years or older. No overall differences in safety or effectiveness were observed between these patients and younger patients.

As a Single Agent

Of the 605 patients treated with JEMPERLI in GARNET, 51.6% were younger than 65 years, 36.9% were aged 65 through 74 years, and 11.5% were 75 years or older. No overall differences in safety or effectiveness were observed between these patients and younger patients.

11 DESCRIPTION

Dostarlimab-gxly is a programmed death receptor-1 (PD-1)–blocking IgG_4 humanized monoclonal antibody. Dostarlimab-gxly is produced in Chinese hamster ovary cells and has a calculated molecular weight of about 144 kDa.

JEMPERLI (dostarlimab-gxly) injection is a sterile, clear to slightly opalescent, colorless to yellow solution essentially free from visible particles. It is supplied as single-dose vials.

Each vial contains 500 mg of JEMPERLI in 10 mL of solution with a pH of 6. Each mL of solution contains 50 mg of dostarlimab-gxly, citric acid monohydrate (0.48 mg), L-arginine hydrochloride (21.07 mg), polysorbate 80 (0.2 mg), sodium chloride (1.81 mg), trisodium citrate dihydrate (6.68 mg), and Water for Injection, USP.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Binding of the PD-1 ligands, PD-L1 and PD-L2, to the PD-1 receptor found on T cells inhibits T-cell proliferation and cytokine production. Upregulation of PD-1 ligands occurs in some tumors, and signaling through this pathway can contribute to inhibition of active T-cell immune surveillance of tumors. Dostarlimab-gxly is a humanized monoclonal antibody of the IgG4 isotype that binds to the PD-1 receptor and blocks its interaction with PD-L1 and PD-L2, releasing PD-1 pathway-mediated inhibition of the immune response, including the anti-tumor immune response. In syngeneic mouse tumor models, blocking PD-1 activity resulted in decreased tumor growth.

12.2 Pharmacodynamics

The exposure-response relationship and time course of pharmacodynamic response for safety and effectiveness of dostarlimab-gxly have not been fully characterized.

Dostarlimab-gxly provides sustained target engagement as measured by direct PD-1 binding and stimulation of IL-2 production throughout the dosing interval at the recommended dosage.

12.3 Pharmacokinetics

The pharmacokinetics of dostarlimab-gxly as a single agent and in combination with carboplatin and paclitaxel were evaluated in patients with various solid tumors, including patients with EC. Mean C_{max}, $AUC_{0\text{-}inf}$, and $AUC_{0\text{-}tau}$ increased proportionally over the dose range of 1 to 10 mg/kg. The Cycle 1 mean (coefficient of variation [%CV]) C_{max} and $AUC_{0\text{-}tau}$ of dostarlimab-gxly as a single agent were 171 mcg/mL (20%) and 35,730 mcg*h/mL (20%), respectively at the dosage of 500 mg once every 3 weeks and 309 mcg/mL (31%) and 95,820 mcg*h/mL (29%), respectively at the dosage of 1,000 mg every 6 weeks.

Distribution

The mean (%CV) volume of distribution of dostarlimab-gxly at steady state is approximately 5.8 L (15%).

Elimination

The mean terminal elimination half-life of dostarlimab-gxly at steady state is 23.5 days and its mean (%CV) clearance at steady state is 0.007 L/h (30%).

Metabolism: Dostarlimab-gxly is expected to be metabolized into small peptides and amino acids by catabolic pathways.

Specific Populations

No clinically significant differences in the pharmacokinetics of dostarlimab-gxly were observed based on age (24 to 86 years), sex, race/ethnicity (75% White, 2% Asian, and 5% African American), tumor type, and renal impairment based on the estimated creatinine clearance (eGFR ≥15 mL/min/1.73 m^2), and mild to moderate hepatic impairment [total bilirubin (TB) >ULN to 3 times ULN or AST>ULN to any AST].

Drug Interaction Studies

Dostarlimab exposure when administered in combination with carboplatin and paclitaxel was comparable to single agent exposure and there was no evidence to suggest a clinically relevant change of dostarlimab-gxly clearance over time in patients with recurrent or advanced EC.

12.6 Immunogenicity

The observed incidence of anti-drug antibodies is highly dependent on the sensitivity and specificity of the assay. Differences in assay methods preclude meaningful comparisons of the incidence of anti-drug antibodies in the studies described below with the incidence of anti-drug antibodies in other studies, including those of JEMPERLI or of other dostarlimab-gxly products.

The immunogenicity of dostarlimab-gxly was evaluated in RUBY at a dosage of 500 mg every 3 weeks for 6 cycles followed by 1,000 mg every 6 weeks thereafter; there was no formation of anti-drug antibodies and neutralizing antibodies in 225 patients receiving JEMPERLI at the recommended dosage.

The immunogenicity of dostarlimab-gxly was evaluated in GARNET at a dose of 500 mg every 3 weeks for 4 doses followed by 1,000 mg every 6 weeks thereafter. Anti-drug antibodies against dostarlimab-gxly were detected in 2.1% (8/384) of patients who received JEMPERLI at the recommended dosage. Neutralizing antibodies were detected in 1% (4/384) of patients.

Because of the small number of patients who developed anti-drug antibodies, the effect of immunogenicity on the pharmacokinetics, efficacy, and safety of dostarlimab-gxly is inconclusive.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

No studies have been performed to assess the potential of dostarlimab-gxly for carcinogenicity or genotoxicity.

Fertility studies have not been conducted with dostarlimab-gxly. In 1- and 3-month repeat-dose toxicology studies in monkeys, there were no notable effects in the male and female reproductive organs; however, many animals in these studies were not sexually mature.

13.2 Animal Toxicology and/or Pharmacology

In animal models, inhibition of PD-L1/PD-1 signaling increased the severity of some infections and enhanced inflammatory responses. *Mycobacterium tuberculosis*-infected PD-1 knockout mice exhibit markedly decreased survival compared with wild-type controls, which correlated with increased bacterial proliferation and inflammatory responses in these animals. PD-1 blockade using a primate anti-PD-1 antibody was also shown to exacerbate *M. tuberculosis* infection in rhesus macaques. PD-L1 and PD-1 knockout mice and mice receiving PD-L1–blocking antibody have also shown decreased survival following infection with lymphocytic choriomeningitis virus.

14 CLINICAL STUDIES

14.1 Endometrial Cancer

<u>In Combination with Carboplatin and Paclitaxel for the Treatment of Primary Advanced or Recurrent Endometrial Cancer</u>

The efficacy of JEMPERLI in combination with carboplatin and paclitaxel, followed by JEMPERLI as a single agent, was evaluated in RUBY (NCT03981796), a randomized, multicenter, double-blind, placebo-controlled trial conducted in 494 patients with primary advanced or recurrent EC.

The trial enrolled patients with primary Stage III or Stage IV disease (per FIGO Staging Classification), including Stage IIIA to IIIC1 patients with evaluable or measurable disease, Stage IIIC1 patients with carcinosarcoma, clear cell, serous, or mixed histology regardless of presence of evaluable or measurable disease, Stage IIIC2 or Stage IV disease regardless of

presence of evaluable or measurable disease. The trial also enrolled patients with first recurrent disease with a low potential for cure by radiation therapy or surgery alone or in combination, including patients who were naïve to systemic anticancer therapy or who had received prior neo-adjuvant/adjuvant systemic anticancer therapy and had a recurrence or disease progression ≥6 months after completing treatment.

Patients were randomized (1:1) to one of the following treatments arms:

- JEMPERLI 500 mg, carboplatin AUC 5 mg/mL/min, paclitaxel 175 mg/m^2 intravenously on Day 1 of each 21-day cycle for 6 cycles followed by JEMPERLI 1,000 mg intravenously every 6 weeks. JEMPERLI was administered prior to chemotherapy on Day 1.
- Placebo, carboplatin AUC 5 mg/mL/min, paclitaxel 175 mg/m^2 intravenously on Day 1 of each 21-day cycle for 6 cycles followed by placebo intravenously every 6 weeks.

Randomization was stratified by mismatch repair (MMR)/microsatellite instability (MSI) status, prior external pelvic radiotherapy, and disease status (recurrent, primary Stage III, or primary Stage IV). Treatment with JEMPERLI continued until disease progression, unacceptable toxicity, or a maximum of 3 years. Administration of JEMPERLI was permitted beyond disease progression (defined by Response Evaluation Criteria in Solid Tumors [RECIST] v1.1) if the patient was clinically stable and considered to be deriving clinical benefit by the investigator.

Assessment of tumor status was performed every 6 weeks through Week 25, every 9 weeks through Week 52 and every 12 weeks thereafter. The major efficacy outcomes were Progression-Free Survival (PFS) using RECIST v1.1 as assessed by investigator in the dMMR/MSI-H and overall populations, and Overall Survival (OS) in the overall population. Additional efficacy outcome measures included Objective Response Rate (ORR) per RECIST v1.1 as assessed by investigator and Duration of Response (DOR).

Among the 494 patients evaluated, the baseline characteristics were: median age 65 years (51% aged 65 years or older); 77% White, 12% Black, 3% Asian, 3% Hispanic or Latino; Eastern Cooperative Oncology Group (ECOG) Performance Status 0 (63%) or 1 (37%); and primary stage III (18%); primary stage IV (34%) and recurrent EC (48%). Overall, 24% were dMMR/MSI-H tumors and 76% were mismatch repair proficient (MMRp)/microsatellite stable (MSS) tumors.

Efficacy results are presented in Table 9 and Figures 1, 2 and 3. Treatment with JEMPERLI in combination with carboplatin and paclitaxel demonstrated statistically significant improvements in OS in the overall population and PFS in both the dMMR/MSI-H and overall population versus placebo in combination with carboplatin and paclitaxel. Pre-specified exploratory analyses of PFS and OS were performed in patients with MMRp/MSS EC.

Table 9. Efficacy Results of Endometrial Cancer Population in RUBY

Endpoint	Overall Population		dMMR/MSI-H Population	
	JEMPERLI with Carboplatin and Paclitaxel N = 245	**Placebo with Carboplatin and Paclitaxel N = 249**	**JEMPERLI with Carboplatin and Paclitaxel N = 60**	**Placebo with Carboplatin and Paclitaxel N = 62**
Overall Survival (OS)				
Number (%) of patients with event	109 (44)	144 (58)	15 (25)	35 (56)
Median in months (95% CI)	44.6 (32.6, NR)	28.2 (22.1, 35.6)	NR (NR, NR)	30.8 (18.7, NR)
Hazard ratio (95% CI)[a]	0.69 (0.54, 0.89)		0.34 (0.18, 0.62)	
P-value[b]	0.002		Not tested	
Progression-Free Survival (PFS)				
Number (%) of patients with event	135 (55)	177 (71)	23 (38)	47 (76)
Median in months (95% CI)	11.8 (9.6, 17.1)	7.9 (7.6, 9.5)	30.3 (11.8, NR)	7.7 (5.6, 9.7)
Hazard ratio (95% CI)[a]	0.64 (0.51, 0.80)		0.29 (0.17, 0.50)	
P-value[b]	<0.0001		<0.0001	
Objective Response Rate (ORR)[c]				
Number of participants with measurable disease at baseline (n)	172	185	42	45
ORR (95% CI)	68% (60, 75)	57% (50, 65)	74% (58, 86)	62% (47, 76)
Complete response rate	20%	12%	26%	11%
Partial response rate	48%	45%	48%	51%
Duration of Response (DOR)[c]				
Median in months (range)	10.8 (1.3+, 28.9+)	6.4 (1.4+, 27.2+)	NR (3.4, 28.3+)	5.4 (2.7, 27.2+)

dMMR = Mismatch Repair Deficient; MSI-H = Microsatellite Instability-High; NR = Not Reached; + = ongoing at last assessment.

[a] Based on stratified Cox regression model.

[b] One-sided *P*-value based on stratified log-rank test.

[c] Confirmed responses.

In patients with MMRp/MSS EC (n = 372), the OS hazard ratio (HR) was 0.82 (95% CI: 0.62, 1.08) with a median OS of 32.5 (95% CI: 28.6, NR) months for JEMPERLI in combination with carboplatin and paclitaxel versus 28.2 (95% CI: 21.9, 36.1) months for placebo in combination with carboplatin and paclitaxel. The PFS HR was 0.78 (95% CI: 0.60, 1.00) with a median PFS of 9.8 (95% CI: 9.0, 12.6) months for JEMPERLI in combination with carboplatin and paclitaxel (n = 185) versus 7.9 (95% CI: 7.6, 9.8) months for placebo in combination with carboplatin and paclitaxel (n = 187).

Figure 1. Kaplan-Meier Curve for Overall Survival in Patients (Overall Population) with Endometrial Cancer in RUBY

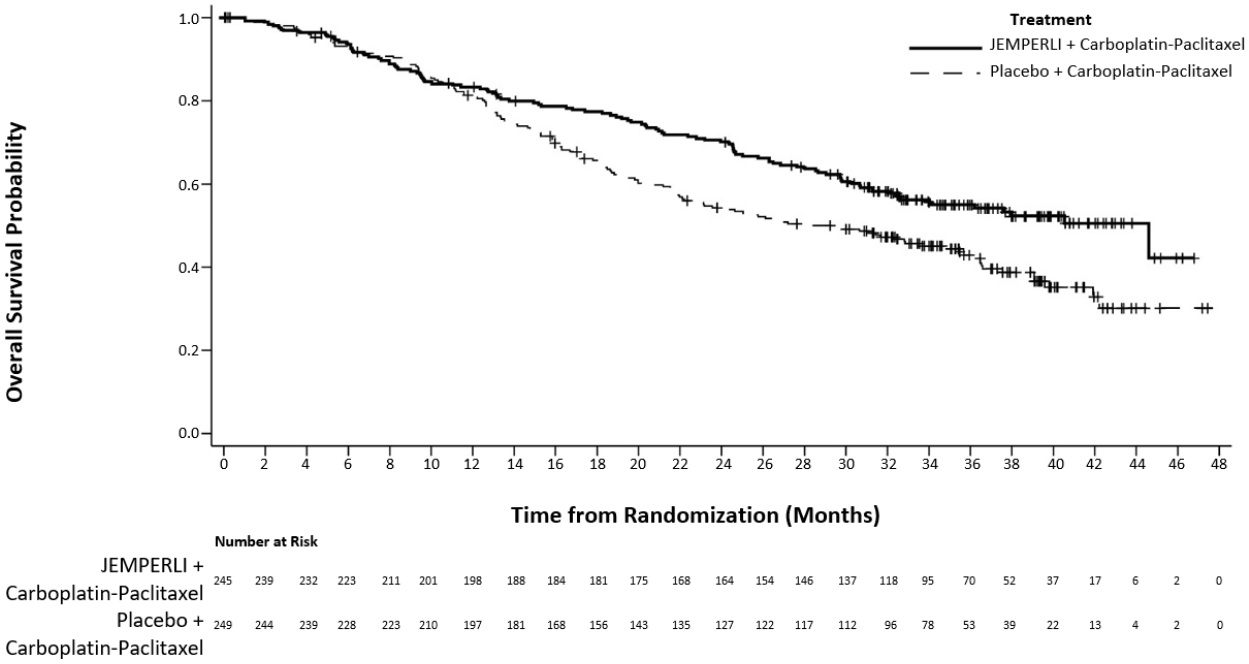


Figure 2. Kaplan-Meier Curve for Progression-Free Survival in Patients (Overall Population) with Endometrial Cancer in RUBY

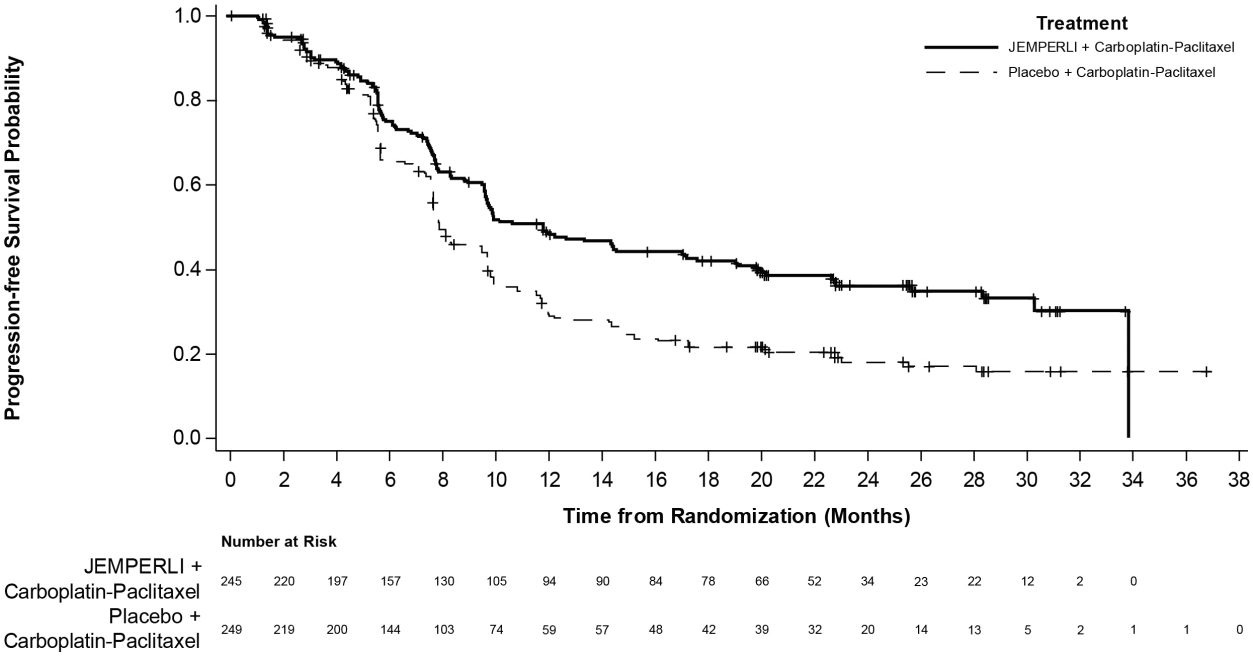
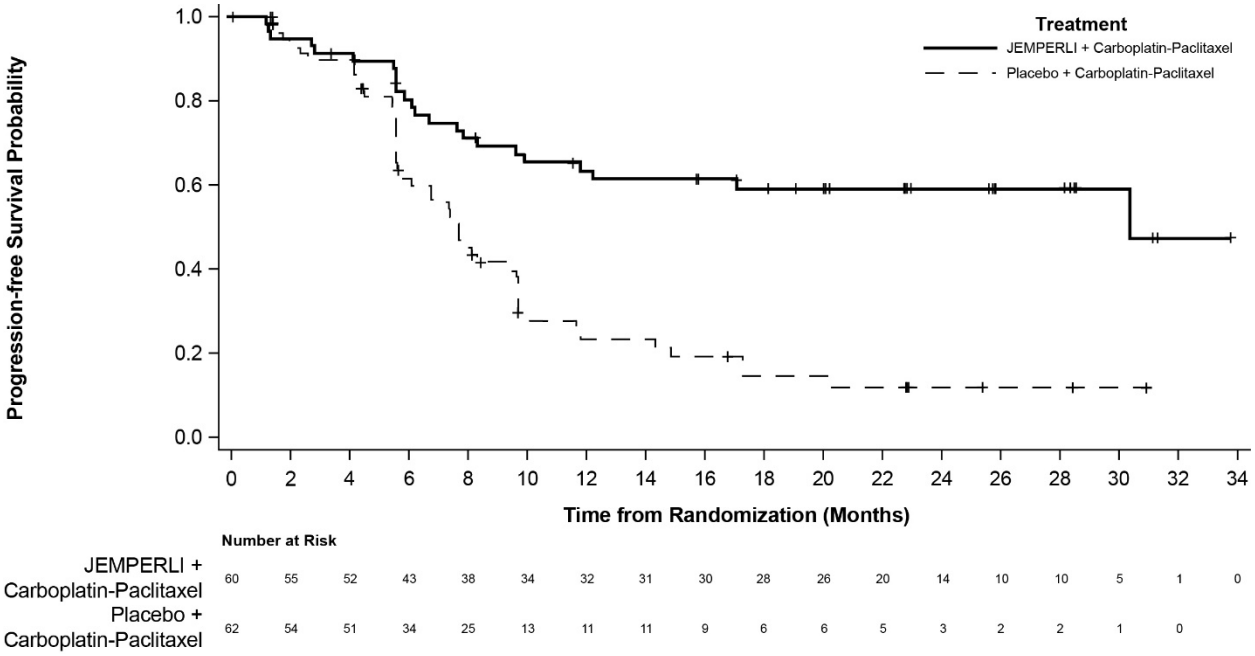


Figure 3. Kaplan-Meier Curve for Progression-Free Survival in Patients with dMMR/MSI-H Endometrial Cancer in RUBY



dMMR = Mismatch Repair Deficient; MSI-H = Microsatellite Instability High.

<u>As a Single Agent for the Treatment of dMMR Recurrent or Advanced Endometrial Cancer</u>

The efficacy of JEMPERLI as a single agent was evaluated in the GARNET trial (NCT02715284), a multicenter, multicohort, open-label trial conducted in patients with advanced solid tumors. The efficacy population consisted of a cohort of 141 patients with dMMR recurrent or advanced EC who had progressed on or after treatment with a platinum-containing regimen. Patients with prior treatment with PD-1/PD-L1–blocking antibodies or other immune checkpoint inhibitor therapy and patients with autoimmune disease that required systemic therapy with immunosuppressant agents within 2 years were excluded from the trial.

Patients received JEMPERLI 500 mg intravenously every 3 weeks for 4 doses followed by 1,000 mg intravenously every 6 weeks. Treatment continued until disease progression or unacceptable toxicity. The major efficacy outcome measures were ORR and DOR as assessed by blinded independent central review (BICR) according to the RECIST v 1.1.

The baseline characteristics were: median age 65 years (53% aged 65 years or older); 77% White, 4% Asian, 3% Black, 4% Hispanic or Latino; and Eastern Cooperative Oncology Group Performance Status 0 (38%) or 1 (62%).

The most common histology seen was endometrioid carcinoma type 1 (65%), Grade 3 endometrioid (15%), followed by serous (5%), mixed (5%) and undifferentiated (2.8%).

All patients with dMMR EC had received prior anticancer treatment, with 89% of patients receiving prior anticancer surgery and 71% receiving prior anticancer radiotherapy. Sixty-three percent of patients had one prior line of anticancer treatment and 37% had two or more prior lines. Forty-eight patients (34%) received treatment only in the neoadjuvant or adjuvant setting before participating in the study.

The dMMR tumor status was retrospectively confirmed using the VENTANA MMR RxDx Panel assay.

Efficacy results are presented in Table 10.

Table 10. Efficacy Results of dMMR Endometrial Cancer Population in GARNET

Endpoint	JEMPERLI N = 141
Overall response rate[a]	
ORR (95% CI)	45.4% (37.0, 54.0)
Complete response rate	15.6%
Partial response rate	29.8%
Duration of response[b]	
Median in months	Not reached
(range)	(1.2+, 52.8+)
Patients with duration ≥12 months	85.9%
Patients with duration >24 months	54.7%

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 27.9 months measured from time of first response.

14.2 Mismatch Repair Deficient Recurrent or Advanced Solid Tumors

The efficacy of JEMPERLI as a single agent was evaluated in GARNET (NCT02715284), a non-randomized, multicenter, open-label, multicohort trial. The efficacy population consisted of a cohort of 209 patients with dMMR recurrent or advanced solid tumors who progressed following systemic therapy and had no satisfactory alternative treatment options. Patients with dMMR EC must have progressed on or after treatment with a platinum-containing regimen. Patients with dMMR colorectal cancer must have progressed after or been intolerant to a fluoropyrimidine, oxaliplatin, and irinotecan.

Patients with prior treatment with PD-1/PD-L1–blocking antibodies or other immune checkpoint inhibitor therapy and patients with autoimmune disease that required systemic therapy with immunosuppressant agents within 2 years were excluded from the trial.

Patients received JEMPERLI 500 mg intravenously every 3 weeks for 4 doses followed by 1,000 mg intravenously every 6 weeks. Treatment continued until disease progression or unacceptable toxicity.

The major efficacy outcome measures were ORR and DOR as determined by a BICR according to RECIST v 1.1.

The baseline characteristics were female (77%); median age 63 years (47% aged 65 years or older); 63% White, 3% Asian, 2% Black; and Eastern Cooperative Oncology Group Performance Status 0 (39%) or 1 (61%).

At time of trial entry, 97.2% of patients (103/106) with non-endometrial dMMR solid tumors had Stage IV disease, and 68.0% (70/103) of patients with dMMR endometrial tumors had FIGO Stage IV disease.

Approximately 43% of patients had received 1 prior line of systemic anticancer treatment, 36% had received 2 prior lines, and 21% had received 3 or more prior lines.

The dMMR tumor status was retrospectively confirmed using the VENTANA MMR RxDx Panel assay.

Efficacy results are presented in Tables 11 and 12.

Table 11. Efficacy Results of dMMR Recurrent or Advanced Solid Tumors in GARNET

Endpoint	JEMPERLI N = 209
Overall response rate[a]	
ORR (95% CI)	41.6% (34.9, 48.6)
Complete response rate	9.1%
Partial response rate	32.5%
Duration of response[b]	
Median in months	34.7
(range)	2.6, 35.8+
Patients with duration ≥6 months	95.4%

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.

Table 12. Efficacy Results of dMMR Tumor Types in GARNET

Tumor Type	Patients N	ORR (per RECIST v 1.1) n (%)	ORR (per RECIST v 1.1) 95% CI[a]	DOR Range (months)
EC	103	46 (44.7)	(34.9, 54.8)	2.6, 35.8+
non-EC	106	41 (38.7)	(29.4, 48.6)	5.6, 30.1+
CRC	69	25 (36.2)	(25.0, 48.7)	5.6, 30.1+
Small intestinal cancer	12	4 (33.3)	(9.9, 65.1)	11.1+, 28.0+
Gastric cancers	8	3 (37.5)	(8.5, 75.5)	8.4+, 17.5
Pancreatic carcinoma	4	0 (0.0)	(0.0, 60.2)	NA
Biliary neoplasm	2	CR, CR	NA	8.4+, 13.5+
Liver cancer	2	PR, PD	NA	13.8+
Ovarian cancer	2	PR, SD	NA	25.1+
Adrenal cortical	1	PR	NA	19.5+
Breast cancer	1	CR	NA	16.8+
Esophageal cancer	1	PD	NA	NA
Genital neoplasm malignant female	1	PR	NA	22.2+
Pleural	1	PR	NA	15.2+
Renal cell carcinoma	1	SD	NA	NA
Unknown origin	1	PR	NA	20.4+

CR = complete response; CRC = colorectal cancer; dMMR = Mismatch Repair Deficient; DOR = Duration of Response; EC = endometrial cancer; ORR = Overall Response Rate; PD = progressive disease; PR = partial response; SD = stable disease; + = ongoing at last assessment.

[a] Exact, 2-sided 95% CI for binomial proportion.

16 HOW SUPPLIED/STORAGE AND HANDLING

JEMPERLI (dostarlimab-gxly) injection is a clear to slightly opalescent, colorless to yellow solution supplied in a carton containing one 500 mg/10 mL (50 mg/mL), single-dose vial (NDC 0173-0898-03).

Store vial refrigerated at 2°C to 8°C (36°F to 46°F) in original carton to protect from light. Do not freeze or shake.

17 PATIENT COUNSELING INFORMATION

Advise the patient to read the FDA-approved patient labeling (Medication Guide).

Immune-Mediated Adverse Reactions

Inform patients of the risk of immune-mediated adverse reactions that may be severe or fatal, may occur after discontinuation of treatment, and may require corticosteroid or other treatment and interruption or discontinuation of JEMPERLI. These reactions may include:

- Pneumonitis: Advise patients to contact their healthcare provider immediately for new or worsening cough, chest pain, or shortness of breath *[see Warnings and Precautions (5.1)]*.
- Colitis: Advise patients to contact their healthcare provider immediately for diarrhea or severe abdominal pain *[see Warnings and Precautions (5.1)]*.
- Hepatitis: Advise patients to contact their healthcare provider immediately for jaundice, severe nausea or vomiting, or easy bruising or bleeding *[see Warnings and Precautions (5.1)]*.
- Immune-mediated endocrinopathies: Advise patients to contact their healthcare provider immediately for signs or symptoms of hypothyroidism, hyperthyroidism, thyroiditis, adrenal insufficiency, hypophysitis, or type 1 diabetes mellitus *[see Warnings and Precautions (5.1)]*.
- Nephritis: Advise patients to contact their healthcare provider immediately for signs or symptoms of nephritis *[see Warnings and Precautions (5.1)]*.
- Severe skin reactions: Advise patients to contact their healthcare provider immediately for any signs or symptoms of severe skin reactions, SJS, TEN, or DRESS *[see Warnings and Precautions (5.1)]*.
- Other immune-mediated adverse reactions:
    - Advise patients that immune-mediated adverse reactions can occur and may involve any organ system, and to contact their healthcare provider immediately for any new signs or symptoms *[see Warnings and Precautions (5.1)]*.
    - Advise patients of the risk of solid organ transplant rejection and to contact their healthcare provider immediately for signs or symptoms of organ transplant rejection [*see Warnings and Precautions (5.1)*].

Infusion-Related Reactions

- Advise patients to contact their healthcare provider immediately for signs or symptoms of infusion-related reactions *[see Warnings and Precautions (5.2)]*.

Complications of Allogeneic HSCT

- Advise patients of the risk of post-allogeneic hematopoietic stem cell transplantation complications *[see Warnings and Precautions (5.3)]*.

Embryo-Fetal Toxicity

- Advise females of reproductive potential of the potential risk to a fetus and to inform their healthcare provider of a known or suspected pregnancy *[see Warnings and Precautions (5.4), Use in Specific Populations (8.1, 8.3)]*.
- Advise females of reproductive potential to use effective contraception during treatment with JEMPERLI and for 4 months after the last dose *[see Warnings and Precautions (5.4), Use in Specific Populations (8.1, 8.3)]*.

Lactation

- Advise women not to breastfeed during treatment with JEMPERLI and for 4 months after the last dose *[see Use in Specific Populations (8.2)]*.

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JMP:7PI

PHARMACIST—DETACH HERE AND GIVE LEAFLET TO PATIENT

MEDICATION GUIDE
JEMPERLI (jem-PER-lee)
(dostarlimab-gxly)
injection

What is the most important information I should know about JEMPERLI?

JEMPERLI is a medicine that may treat certain cancers by working with your immune system. JEMPERLI can cause your immune system to attack normal organs and tissues in any area of your body and can affect the way they work. These problems can sometimes become severe or life-threatening and can lead to death. You can have more than one of these problems at the same time. These problems may happen anytime during treatment or even after your treatment has ended.

Call or see your healthcare provider right away if you develop any new or worsening signs or symptoms, including:

Lung problems.

- cough
- shortness of breath
- chest pain

Intestinal problems.

- diarrhea or more bowel movements than usual
- stools that are black, tarry, sticky, or have blood or mucus
- severe stomach-area (abdomen) pain or tenderness

Liver problems.

- yellowing of your skin or the whites of your eyes
- severe nausea or vomiting
- pain on the right side of your stomach-area (abdomen)
- dark urine (tea colored)
- bleeding or bruising more easily than usual

Hormone gland problems.

- headaches that will not go away or unusual headaches
- eye sensitivity to light
- eye problems
- rapid heartbeat
- increased sweating
- extreme tiredness
- weight gain or weight loss
- feeling more hungry or thirsty than usual
- urinating more often than usual
- hair loss
- feeling cold
- constipation
- your voice gets deeper
- dizziness or fainting
- changes in mood or behavior, such as decreased sex drive, irritability, or forgetfulness

Kidney problems.

- change in the amount or color of your urine
- blood in your urine
- swelling in your ankles
- loss of appetite

Skin problems.

- rash
- itching
- skin blistering or peeling
- swollen lymph nodes
- painful sores or ulcers in your mouth or in your nose, throat, or genital area
- fever or flu-like symptoms

Problems can also happen in other organs and tissues. These are not all of the signs and symptoms of immune system problems that can happen with JEMPERLI. Call or see your healthcare provider right away for any new or worse signs or symptoms.

- chest pain, irregular heartbeat, shortness of breath, swelling of ankles
- confusion, sleepiness, memory problems, changes in mood or behavior, stiff neck, balance problems, tingling or numbness of the arms or legs
- double vision, blurry vision, sensitivity to light, eye pain, changes in eyesight
- persistent or severe muscle pain or weakness, muscle cramps
- low red blood cells, bruising

Infusion reactions that can sometimes be severe or life-threatening. Signs and symptoms of infusion reactions may include:

- chills or shaking
- itching or rash
- flushing
- shortness of breath or wheezing
- dizziness
- feel like passing out
- fever
- back or neck pain

Rejection of a transplanted organ. Your healthcare provider should tell you what signs and symptoms you should report and monitor you, depending on the type of organ transplant that you have had.

Complications, including graft-versus-host-disease (GVHD), in people who have received a bone marrow (stem cell) transplant that uses donor stem cells (allogeneic). These complications can be serious and can lead to death. These complications may happen if you underwent transplantation either before or after being treated with JEMPERLI. Your healthcare provider will monitor you for these complications.

Getting medical treatment right away may help keep these problems from becoming more serious.

Your healthcare provider will check you for these problems during treatment with JEMPERLI. Your healthcare provider may treat you with corticosteroid or hormone replacement medicines. Your healthcare provider may also need to delay or completely stop treatment with JEMPERLI, if you have severe side effects.

What is JEMPERLI?

JEMPERLI is a prescription medicine used to treat adults with:

- a kind of uterine cancer called endometrial cancer (EC)
  - JEMPERLI may be used in combination with the chemotherapy medicines carboplatin and paclitaxel, and then after that, JEMPERLI may be used alone:
    - when your cancer has spread outside your uterus (advanced) **or**,
    - your cancer has returned.
  - JEMPERLI may be used alone:
    - when a laboratory test shows that your tumor is mismatch repair deficient (dMMR), **and**
    - your cancer has returned, or it has spread (advanced EC), **and**
    - you have received chemotherapy that contains platinum, and it did not work or is no longer working, **and**
    - your cancer cannot be treated by surgery or radiation.
- a kind of cancer that is shown by laboratory test to be mismatch repair deficient (dMMR) solid tumor. JEMPERLI may be used alone to treat:
  - cancer that has returned or has spread (advanced cancer) **and**,
  - has progressed during treatment or after treatment, and you have no satisfactory treatment options.

It is not known if JEMPERLI is safe and effective in children.

Before receiving JEMPERLI, tell your healthcare provider about all of your medical conditions, including if you:

- have immune system problems, such as Crohn's disease, ulcerative colitis, or lupus.
- have received an organ transplant.
- have received or plan to receive a stem cell transplant that uses donor stem cells (allogeneic).
- have received radiation treatment to your chest area.
- have a condition that affects your nervous system, such as myasthenia gravis or Guillain-Barré syndrome.
- are pregnant or plan to become pregnant. JEMPERLI can harm your unborn baby.

  Females who are able to become pregnant:
  - Your healthcare provider will do a pregnancy test before you start treatment with JEMPERLI.
  - You should use an effective method of birth control during your treatment and for 4 months after your last dose of JEMPERLI. Talk to your healthcare provider about birth control methods that you can use during this time.
  - Tell your healthcare provider right away if you become pregnant or think you may be pregnant during treatment with JEMPERLI.
- are breastfeeding or plan to breastfeed. It is not known if JEMPERLI passes into your breast milk. Do not breastfeed during treatment and for 4 months after your last dose of JEMPERLI.

Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements.

How will I receive JEMPERLI?

- Your healthcare provider will give you JEMPERLI into your vein through an intravenous (IV) line over 30 minutes.
- When JEMPERLI is used in combination with carboplatin and paclitaxel, JEMPERLI is usually given every 3 weeks for the first 6 doses. Beginning 3 weeks later, it is usually given alone every 6 weeks.
- When JEMPERLI is used alone to treat dMMR recurrent or advanced EC and dMMR recurrent or advanced solid tumors, it is usually given every 3 weeks for the first 4 doses. Beginning 3 weeks later, it is usually given every 6 weeks.
- Your healthcare provider will decide how many treatments you need.
- Your healthcare provider will do blood tests to check you for side effects.
- If you miss any appointments, call your healthcare provider as soon as possible to reschedule your appointment.

What are the possible side effects of JEMPERLI?

JEMPERLI can cause serious side effects.

- **See "What is the most important information I should know about JEMPERLI?"**

The most common side effects of JEMPERLI when given with carboplatin and paclitaxel in people with EC include:

- nerve problems in your arms, hands, legs, and feet
- tiredness
- nausea
- hair loss
- joint pain
- rash
- constipation
- diarrhea
- stomach-area (abdomen) pain
- shortness of breath
- decreased appetite
- urinary tract infections
- vomiting

The most common side effects of JEMPERLI in people with dMMR solid tumors (including EC) when used alone include:

- tiredness and weakness
- low red blood cell count (anemia)
- diarrhea
- nausea
- constipation
- vomiting

These are not all of the possible side effects of JEMPERLI.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

General information about the safe and effective use of JEMPERLI.

Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide. If you would like more information about JEMPERLI, talk with your healthcare provider. You can ask your pharmacist or healthcare provider for information about JEMPERLI that is written for healthcare professionals.

What are the ingredients in JEMPERLI?

Active ingredient: dostarlimab-gxly

Inactive ingredients: citric acid monohydrate, L-arginine hydrochloride, polysorbate 80, sodium chloride, trisodium citrate dihydrate, and Water for Injection.

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