JEMPERLI Dosing and Administration Guide

Jemperli (dostarlimab-gxly) Injection 500 mg

Indications

- 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, or
  - 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. 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).

IMPORTANT SAFETY INFORMATION

Severe and Fatal Immune-Mediated Adverse Reactions

- Immune-mediated adverse reactions, which can be severe or fatal, can occur in any organ system or tissue and can occur at any time during or after treatment with a PD-1/PD-L1–blocking antibody, including JEMPERLI.
- Monitor closely for signs and symptoms of immune-mediated adverse reactions. Evaluate liver enzymes, creatinine, and thyroid function tests at baseline and periodically during treatment. For suspected immune-mediated adverse reactions, initiate appropriate workup to exclude alternative etiologies, including infection. Institute medical management promptly, including specialty consultation as appropriate.

Please see additional Important Safety Information on the next pages and full Prescribing Information including Medication Guide.

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 endometrial cancer.
- recurrent or advanced solid tumors.

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.

Dosage

The recommended dosage for JEMPERLI is presented in the table below.

Indication	Recommended Dosage	Duration/Timing of Treatment
Combination therapy		
Adults with primary advanced or recurrent EC	500 mg* JEMPERLI every 3 weeks for 6 cycles in combination with carboplatin and paclitaxel† followed by 1000 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* JEMPERLI every 3 weeks for 4 cycles followed by 1000 mg* JEMPERLI every 6 weeks for all cycles thereafter.	Until disease progression or unacceptable toxicity.

Preparation and Administration

1. **Preparation for intravenous (IV) infusion:**
   Visually inspect the solution for particulate matter and discoloration. The solution is clear to slightly opalescent, colorless to yellow.‡
2. **Do not shake.**
3. **Prepare the required dose. Each vial contains 500 mg/10 mL (50 mg/mL) solution for intravenous infusion after dilution.**
4. **Mix diluted solution by gentle inversion. Do not shake.**
5. **Discard any unused portion left in the vial.**

For the 500 mg Dose	For the 1000 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)§	Withdraw 10 mL of JEMPERLI from each of 2 vials (withdraw 20 mL total) using a disposable sterile syringe made of polypropylene 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)§

*30-minute intravenous infusion. †Refer to the Prescribing Information for the agents administered in combination with JEMPERLI, as appropriate.
‡Discard the vial if visible particles are observed. Please contact GSK at 1-888-825-5249 to report the issue.
§JEMPERLI is compatible with an infusion bag made of polyolefin, ethylene vinyl acetate, or polyvinyl chloride with di(2-ethylhexyl) phthalate (DEHP).
PD-1 = programmed death protein 1; PD-L1 = programmed death-ligand 1; USP = United States Pharmacopeia.

Storage

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 (36°F to 46°F) 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.

Dosage Modifications

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 below.

Recommended Dosage Modifications for Adverse Reactions

Adverse Reaction	Severity*	Dosage Modification
Immune-Mediated Adverse Reactions		
Pneumonitis	Grade 2	Withhold†
	Grade 3 or 4 or recurrent Grade 2	Permanently discontinue
Colitis	Grade 2 or 3	Withhold†
	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†
	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‡	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†
	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†
Nephritis with renal dysfunction	Grade 2 or 3 increased blood creatinine	Withhold†
	Grade 4 increased blood creatinine	Permanently discontinue
Exfoliative dermatologic conditions	Suspected SJS, TEN, or DRESS	Withhold†
	Confirmed SJS, TEN, or DRESS	Permanently discontinue
Myocarditis	Grade 2, 3, or 4	Permanently discontinue
Neurological toxicities	Grade 2	Withhold†
	Grade 3 or 4	Permanently discontinue
Other Adverse Reactions		
Infusion-related reactions	Grade 1 or 2	Interrupt or slow the rate of infusion
	Grade 3 or 4	Permanently discontinue

*Based on National Cancer Institute Common Terminology Criteria for Adverse Events, Version 5.0.

†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.

‡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.

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.

IMPORTANT SAFETY INFORMATION (CONT'D)

Severe and Fatal Immune-Mediated Adverse Reactions (cont'd)

- Based on the severity of the adverse reaction, withhold or permanently discontinue JEMPERLI. 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. Upon improvement to ≤Grade 1, 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.

Monitoring

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.

IMPORTANT SAFETY INFORMATION (CONT'D)

Immune-Mediated Pneumonitis

- 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. Pneumonitis occurred in 2.3% (14/605) of patients, including Grade 2 (1.3%), Grade 3 (0.8%), and Grade 4 (0.2%) pneumonitis.

Immune-Mediated Colitis

- Colitis occurred in 1.3% (8/605) of patients, including Grade 2 (0.7%) and Grade 3 (0.7%) adverse reactions. Cytomegalovirus infection/reactivation have occurred in patients with corticosteroid-refractory immune-mediated colitis. In such cases, consider repeating infectious workup to exclude alternative etiologies.

Immune-Mediated Hepatitis

- JEMPERLI can cause immune-mediated hepatitis, which can be fatal. Grade 3 hepatitis occurred in 0.5% (3/605) of patients.

Immune-Mediated Endocrinopathies

- Adrenal Insufficiency
  - Adrenal insufficiency occurred in 1.2% (7/605) of patients, including Grade 2 (0.5%) and Grade 3 (0.7%). 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.
- Hypophysitis
  - JEMPERLI can cause immune-mediated hypophysitis. Grade 3 hypophysitis occurred in 0.4% (1/241) of patients receiving JEMPERLI in combination with carboplatin and paclitaxel. Grade 2 hypophysitis occurred in 0.2% (1/605) of patients receiving JEMPERLI as a single agent. Initiate hormone replacement as clinically indicated. Withhold or permanently discontinue JEMPERLI depending on severity.
- Thyroid Disorders
  - Grade 2 thyroiditis occurred in 0.5% (3/605) of patients. Grade 2 hypothyroidism occurred in 12% (30/241) of patients receiving JEMPERLI in combination with carboplatin and paclitaxel. Grade 2 hypothyroidism occurred in 8% (46/605) of patients receiving JEMPERLI as a single agent. 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 occurred in 2.3% (14/605) of patients receiving JEMPERLI as a single agent, including Grade 2 (2.1%) and Grade 3 (0.2%). Initiate thyroid hormone replacement or medical management of hyperthyroidism as clinically indicated. Withhold or permanently discontinue JEMPERLI depending on severity.
- Type 1 Diabetes Mellitus, Which Can Present with Diabetic Ketoacidosis
  - JEMPERLI can cause type 1 diabetes mellitus, which can present with diabetic ketoacidosis. Grade 3 type 1 diabetes mellitus occurred in 0.4% (1/241) of patients receiving JEMPERLI in combination with carboplatin and paclitaxel. Grade 3 type 1 diabetes mellitus occurred in 0.2% (1/605) of patients receiving JEMPERLI as a single agent. 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.

Immune-Mediated Nephritis with Renal Dysfunction

- JEMPERLI can cause immune-mediated nephritis, which can be fatal. Grade 2 nephritis, including tubulointerstitial nephritis, occurred in 0.5% (3/605) of patients.

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.

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
  - *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

Please see additional Important Safety Information on page 4 and full Prescribing Information including Medication Guide.

IMPORTANT SAFETY INFORMATION (CONT'D)

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. 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.

Complications of Allogeneic HSCT

- Fatal and other serious complications can occur in patients who receive allogeneic hematopoietic stem cell transplantation (HSCT) before or after treatment with a PD-1/PD-L1–blocking antibody, which may occur despite intervening therapy. Monitor patients closely for transplant-related complications and intervene promptly.

Embryo-Fetal Toxicity and Lactation

- Based on its mechanism of action, JEMPERLI can cause fetal harm. 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 their last dose. Because of the potential for serious adverse reactions from JEMPERLI in a breastfed child, advise women not to breastfeed during treatment with JEMPERLI and for 4 months after their last dose.

Common Adverse Reactions

The most common adverse reactions (≥20%), including laboratory abnormalities, in patients with EC who received JEMPERLI in combination with carboplatin and paclitaxel 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.

The most common adverse reactions (≥20%) in patients with dMMR EC who received JEMPERLI as a single agent were fatigue/asthenia, anemia, nausea, diarrhea, constipation, vomiting, and rash. The most common Grade 3 or 4 laboratory abnormalities (>2%) were decreased lymphocytes, decreased sodium, increased alanine aminotransferase, increased creatinine, decreased neutrophils, decreased albumin, and increased alkaline phosphatase.

The most common adverse reactions (≥20%) in patients with dMMR solid tumors who received JEMPERLI as a single agent were fatigue/asthenia, anemia, diarrhea, and nausea. The most common Grade 3 or 4 laboratory abnormalities (≥2%) were decreased lymphocytes, decreased sodium, increased alkaline phosphatase, and decreased albumin.

Please see full Prescribing Information including Medication Guide for patients.

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

dMMR = mismatch repair deficient; EC = endometrial cancer.

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