Immune-Mediated Adverse Reactions with JEMPERLI

Jemperli (dostarlimab-gxly) Injection 500 mg

This material is for healthcare professionals to provide information about immune-mediated adverse reactions for patients who have been prescribed JEMPERLI. This resource includes JEMPERLI-related information regarding potential immune-mediated adverse reactions, counseling points, monitoring reminders, and recommended dosage modifications.

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.

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.

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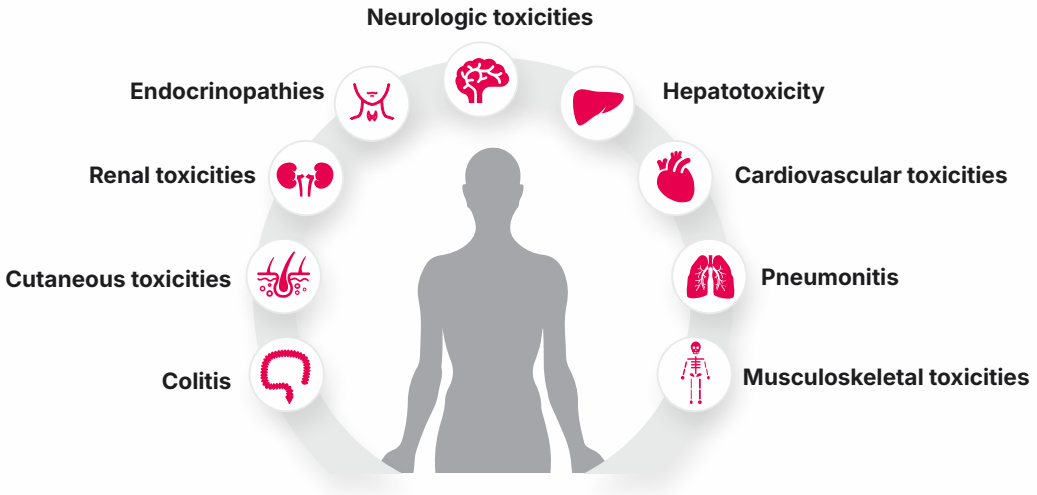
Please see Important Safety Information throughout and on pages 6-8 and full Prescribing Information, including Medication Guide.

Potential 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.[1]

- 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.

Examples of immune-mediated adverse reactions*



* Based on immune-mediated adverse reactions from patients receiving an immune checkpoint inhibitor monotherapy that have been reported in the literature.[2]

Counseling Patients on the Risk of Immune-Mediated Adverse Reactions[1]

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

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

These immune-mediated reactions may include:

- **Pneumonitis:** Advise patients to contact their healthcare provider immediately for new or worsening cough, chest pain, or shortness of breath

- **Colitis:** Advise patients to contact their healthcare provider immediately for diarrhea or severe abdominal pain

- **Hepatitis:** Advise patients to contact their healthcare provider immediately for jaundice, severe nausea or vomiting, or easy bruising or bleeding

- **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

- **Nephritis:** Advise patients to contact their healthcare provider immediately for signs or symptoms of nephritis

- **Severe skin reactions:** Advise patients to contact their healthcare provider immediately for any signs or symptoms of severe skin reactions, SJS, TEN, or DRESS

- **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
  - 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

Please refer to Section 17 of the Prescribing Information for additional patient counseling information regarding other potential adverse reactions such as infusion-related reactions, complications of allogeneic hematopoietic stem cell transplantation, embryo-fetal toxicity, and lactation.

DRESS, drug rash with eosinophilia and systemic symptoms; **SJS**, Stevens-Johnson syndrome; **TEN**, toxic epidermal necrolysis.

Please see Important Safety Information throughout and on pages 6-8 and full Prescribing Information, including Medication Guide.

Monitoring for Immune-Mediated Adverse Reactions[1]

- 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

General Management of Immune-Mediated Adverse Reactions[1]

Withhold or permanently discontinue JEMPERLI depending on severity (see next page for more details). 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.

Dosage Modifications for Adverse Reactions[1]

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 >3× and up to 8× ULN or total bilirubin increases to >1.5× and up to 3× ULN	Withhold†
	AST or ALT increases to >8× ULN or total bilirubin increases to >3× ULN	Permanently discontinue
Hepatitis with tumor involvement of the liver‡	Baseline AST or ALT is >1× and up to 3× ULN and increases to >5× and up to 10× ULN or baseline AST or ALT is >3× and up to 5× ULN and increases to >8× and up to 10× ULN	Withhold†
	AST or ALT increases to >10× ULN or total bilirubin increases to >3× 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 ≤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; **ULN,** upper limit of normal.

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

- 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.
- 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.

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

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.

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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.

Please see the full Prescribing Information, including the Medication Guide.

References: 1. JEMPERLI. Prescribing Information. GSK; 2024. **2.** Schneider BJ, et al. *J Clin Oncol*. 2021;39.4073-4126.

For more information, visit www.JEMPERLIHCP.com

File name: Adverse Reactions Guide