JEMPERLI (dostarlimab-gxly) injection 500 mg

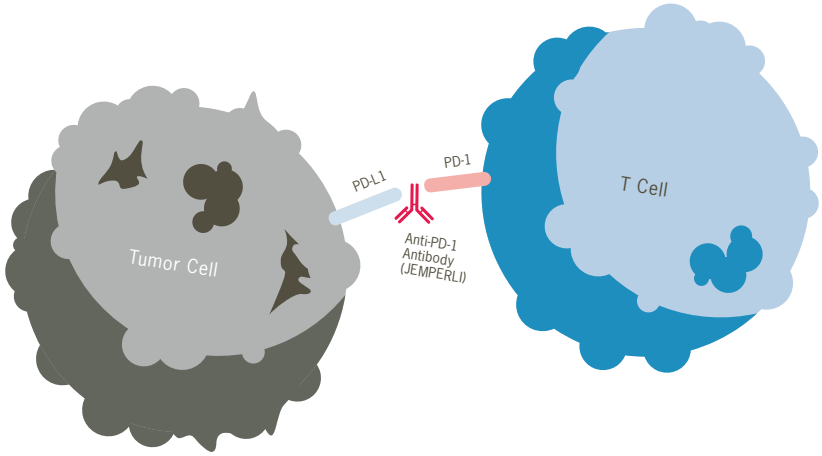
JEMPERLI is indicated for the treatment of adult patients with mismatch repair deficient (dMMR) recurrent or advanced endometrial cancer (EC), as determined by an FDA-approved test, that has progressed on or following prior treatment with a platinum-containing regimen.[i]

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]

Mechanism of Action

JEMPERLI binds with high affinity to the PD-1 receptor, working to block its interaction with programmed death receptor ligands 1 and 2 (PD-L1 and PD-L2).[i]

Signaling through the PD-1 pathway can reduce the immune system's ability to recognize and eliminate cancer cells. JEMPERLI is designed to interfere with this pathway, which may enhance the anti-cancer immune response.



[1] Laken H, Kehry M, Mcneeley P, et al. Identification and characterization of TSR-042, a novel anti-human PD-1 therapeutic antibody. European Journal of Cancer. 2016;69,S102. doi:10.1016/s0959-8049(16)32902-1.

Important Safety Information

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.
- 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.

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Important Safety Information (cont.)

Immune-Mediated Pneumonitis

- JEMPERLI can cause immune-mediated pneumonitis, which can be fatal. The incidence of pneumonitis in patients receiving PD-1/PD-L1 inhibitors, including JEMPERLI, may be increased in patients who have received prior thoracic radiation.

- Immune-mediated pneumonitis occurred in 1.1% (5/444) of patients, including Grade 2 (0.9%) and Grade 3 (0.2%) pneumonitis. Pneumonitis led to discontinuation of JEMPERLI in 0.7% of patients. Systemic corticosteroids were required in all patients with pneumonitis. Pneumonitis resolved in 80% of the 5 patients. Three patients reinitiated JEMPERLI after symptom improvement; of these, 33% 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 1.4% (6/444) of patients, including Grade 3 (0.7%) and Grade 2 (0.7%). Colitis did not lead to discontinuation of JEMPERLI in any patients. Systemic corticosteroids were required in 17% (1/6) of patients with colitis. Colitis resolved in 50% of the 6 patients. Of the 2 patients in whom JEMPERLI was withheld for colitis, both reinitiated JEMPERLI.

Immune-Mediated Hepatitis

- JEMPERLI can cause immune-mediated hepatitis, which can be fatal. Immune-mediated Grade 3 hepatitis occurred in 0.2% (1/444) of patients. Systemic corticosteroids were required, and the event resolved.

Immune-Mediated Endocrinopathies

- Adrenal Insufficiency

o 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 JEMPERLI if not clinically stable. Adrenal insufficiency occurred in 0.9% (4/444) of patients, including Grade 3 (0.5%) and Grade 2 (0.5%). Adrenal insufficiency resulted in discontinuation in 1 (0.2%) patient and resolved in 25% of the 4 patients.

- Hypophysitis

o 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 JEMPERLI if not clinically stable.

- Thyroid Disorders

o JEMPERLI can cause immune-mediated thyroid disorders. Thyroiditis can present with or without endocrinopathy. Hypothyroidism can follow hyperthyroidism. Initiate hormone replacement or medical management of hyperthyroidism as clinically indicated. Withhold JEMPERLI if not clinically stable.

o Thyroiditis occurred in 0.5% (2/444) of patients; both were Grade 2. Neither event of thyroiditis resolved; there were no discontinuations of JEMPERLI due to thyroiditis.

o Hypothyroidism occurred in 5.6% (25/444) of patients, all of which were Grade 2. Hypothyroidism did not lead to discontinuation of JEMPERLI and resolved in 40% of the 25 patients. Systemic corticosteroids were not required for any of the 25 patients with hypothyroidism.

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Important Safety Information (cont.)

o Hyperthyroidism occurred in 1.8% (8/444) of patients, including Grade 2 (1.6%) and Grade 3 (0.2%). Hyperthyroidism did not lead to discontinuation of JEMPERLI and resolved in 63% of the 8 patients. Systemic corticosteroids were not required for any of the 8 patients with hyperthyroidism.

- Type 1 Diabetes Mellitus, Which Can Present with Diabetic Ketoacidosis

o 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.

Immune-Mediated Nephritis with Renal Dysfunction

- JEMPERLI can cause immune-mediated nephritis, which can be fatal. Nephritis occurred in 0.5% (2/444) of patients; both were Grade 2. Nephritis did not lead to discontinuation of JEMPERLI and resolved in both patients. Systemic corticosteroids were required in 1 of the 2 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.

Other Immune-Mediated Adverse Reactions

- The following clinically significant immune-mediated adverse reactions occurred in <1% of the 444 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.

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

o *Cardiac/Vascular:* Myocarditis, pericarditis, vasculitis

o *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.

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

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

o *Endocrine:* Hypoparathyroidism

o *Other (Hematologic/Immune):* Hemolytic anemia, aplastic anemia, hemophagocytic lymphohistiocytosis, systemic inflammatory response syndrome, histiocytic necrotizing lymphadenitis (Kikuchi lymphadenitis), sarcoidosis, immune thrombocytopenia, solid organ transplant 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% (1/444) of patients receiving JEMPERLI. All patients recovered from the infusion-related reactions.

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Important Safety Information (cont.)

- 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 after PD-1/PD-L1–Blocking Antibody:

- 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. 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.

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 (Grades 1-4) in ≥10% of 104 dMMR endometrial cancer patients who received JEMPERLI as monotherapy were fatigue (48%), nausea (30%), diarrhea (26%), anemia (24%), constipation (20%), vomiting (18%), pruritus (14%), cough (14%), decreased appetite (14%), urinary tract infection (13%), and myalgia (12%).

- JEMPERLI was permanently discontinued due to adverse reactions in 5 (4.8%) patients, including transaminases increased, sepsis, bronchitis, and pneumonitis. 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, diarrhea, increased lipase, and pyrexia.

Please see full Prescribing Information.