Drug Monograph

A - Drug Name

dostarlimab

COMMON TRADE NAME(S): Jemperli

back to top

B - Mechanism of Action and Pharmacokinetics

Dostarlimab is a humanized IgG4 monoclonal antibody which inhibits programmed cell death protein-1 (PD-1) activity by binding to the PD-1 receptor on T-cells and blocking its interaction with PD-1 ligands, PD-L1 and PD-L2. This prevents PD-1 pathway-mediated inhibition of tumour immune response and restores T-cell proliferation, cytokine production and cytotoxic T-cell activity.

Dostarlimab exhibits linear pharmacokinetics in the dose range of 1 to 10 mg/kg.

Absorption	T max	0.96 h (after a single 500mg dose)
Metabolism	Expected to be degraded into small peptides and amino acids via catabolic non-specific pathways.	
Elimination	Half-life	23.2 days (terminal)

back to top

C - Indications and Status

Health Canada Approvals:

- Endometrial cancer

Refer to the product monograph for a full list and details of approved indications

back to top

D - Adverse Effects

Emetogenic Potential: Minimal

The following adverse events were reported in ≥ 1% of patients with recurrent or advanced dMMR/MSI-H endometrial cancer who received dostarlimab monotherapy (following prior treatment with platinum-containing therapy). Severe or life-threatening adverse events may also be included from other sources or post-marketing.

ORGAN SITE	SIDE EFFECT* (%)	ONSET**
Dermatological	Rash, pruritus (19%) (1% severe)	E D
Gastrointestinal	Diarrhea (29%) (rarely enterocolitis)	E
	Nausea, vomiting (33%) (<1% severe)	I E
General	Fever, chills (14%)	I E
Hematological	Anemia (33%) (17% severe)	E
	Hemolytic anemia (autoimmune) (rare)	E
Hepatobiliary	Hepatitis (rare)	E
	↑ LFTs (9%)	E D
	Pancreatitis (rare)	E
Hypersensitivity	Infusion related reaction (1%)	I E
Metabolic / Endocrine	Adrenal insufficiency (1%)	E D
	Hyperthyroidism (5%)	E D
	Hypophysitis (rare)	E D
	Hypothyroidism (12%)	E D

Musculoskeletal	Musculoskeletal pain (22%) (rarely myositis)	E
Nervous System	Encephalitis (rare)	E
Ophthalmic	Eye disorders (rare) (uveitis, iridocyclitis)	E
Renal	Nephritis (rare)	E
Respiratory	Pneumonitis (4%) (1% severe)	E D

* "*Incidence*" may refer to an absolute value or the higher value from a reported range.
"*Rare*" may refer to events with < 1% incidence, reported in post-marketing, phase 1 studies, isolated data or anecdotal reports.

** I = *immediate* (onset in hours to days) E = *early* (days to weeks)
D = *delayed* (weeks to months) L = *late* (months to years)

The most common side effects for dostarlimab include anemia, nausea, vomiting, diarrhea, musculoskeletal pain, rash, pruritus, fever, chills and hypothyroidism.

Refer to CCO's Immune Checkpoint Inhibitor Toxicity Management Guideline for detailed descriptions of Immune-related toxicities and their management.

Presentation of immune-mediated reactions may be different compared to other anti-cancer agents and early diagnosis and appropriate management is critical

Immune-related reactions may occur in any organ or tissue and may affect more than one body system simultaneously. Immune-related reactions including **pneumonitis, colitis, hepatitis, pancreatitis, nephritis, endocrinopathies, and neuropathies** have been reported and may be severe or fatal. Onset may vary from days to many months and may occur after treatment has ended.

Immune-related rash (e.g. maculo-papular rash, pemphigoid, drug eruption, skin toxicity) occurred in 5% of patients with an onset time of 57 days (median) but ranged from 2 days to 1485 days. Severe skin rashes, including Stevens-Johnson Syndrome (SJS) and Toxic Epidermal Necrolysis (TEN) have been reported, including fatal cases, in patients treated with PD-1 inhibitors.

Due to its mechanism of action, dostarlimab may cause other clinically important immune-mediated adverse effects that have been reported in other PD-1inhibitors, such as Guillain Barré syndrome, sarcoidosis or aplastic anemia.

back to top

E - Dosing

Refer to protocol by which patient is being treated.

Screen for hepatitis B virus in all cancer patients starting systemic treatment. Refer to the hepatitis B virus screening and management guideline.

Patients should have MSI-H or dMMR tumour status confirmed by a validated test prior to starting treatment.

Avoid the use of corticosteroids or immunosuppressants before starting treatment.

Premedication (prophylaxis for infusion reactions):

- Routine pre-medication is not recommended.
- May consider antipyretic and H1-receptor antagonist in patients who experienced a grade 2 infusion reaction.

Adults:

Combination with carboplatin and paclitaxel:

IV: 500 mg q 3 weeks x 6 cycles, followed by

1000 mg* q 6 weeks thereafter

*starting 3 weeks after the previous dose

Refer to the CRBPPACL+DOST regimen for carboplatin and paclitaxel dosing.

Monotherapy:

IV: 500 mg q 3 weeks x 4 cycles, followed by

1000 mg* q 6 weeks thereafter

*starting 3 weeks after the previous dose

Dosage with Toxicity:

Dosage with Toxicity:

- Healthcare professionals should also consult the most recent dostarlimab product monograph for additional information.
- Dose reductions are not recommended for dostarlimab. Doses may be delayed or discontinued based on toxicity.

Summary of Principles of Management or immune-related adverse effects (irAEs)

- Immune-related adverse effects (irAEs) are different in their presentation, onset and duration compared to conventional chemotherapy. Patient and provider education is essential.
- Initial irAE presentation can occur months after completion of treatment and affect multiple organs.
- Dose escalation or reduction is not recommended.
- If no other cause can be identified (such as infection), any new symptom should be considered immune-related and prompt treatment initiated.
- Organ-specific system-based toxicity management is recommended.
- **Refer to CCO's Immune Checkpoint Inhibitor Toxicity Management Guideline for detailed descriptions of Immune-related toxicities and their management.**

Management of Infusion-related reactions:

Also refer to the CCO guideline for detailed description of Management of Cancer Medication-Related Infusion Reactions.

Grade	Management	Re-challenge
1	• Continue infusion if appropriate • Manage the symptoms.	• N/A
2	• Stop the infusion • Manage the symptoms. **Restart:** • After symptom resolution, may restart at 50% of the infusion rate (if resolved within 1 hour of stopping) or restart with pre-medications.	• Re-challenge with close monitoring and pre-medications (antipyretic and H1-receptor antagonist). • If Gr. 2 recurs with adequate pre-medication, permanently discontinue (do not re-challenge).
3 or 4	• Stop treatment • Aggressively manage the symptoms.	• Discontinue permanently (do not re-challenge).

Dosage with Hepatic Impairment:

Refer to CCO's Immune Checkpoint Inhibitor Toxicity Management Guideline for detailed descriptions for immune-related hepatic toxicity management.

Severity	Bilirubin		AST	Dostarlimab Dose
Mild	1 to 1.5 x ULN	OR	> ULN	No dose adjustment
Moderate	> 1.5 to 3 x ULN	AND	any	Limited data
Severe	> 3 x ULN	AND	any	No data

Dosage with Renal Impairment:

Refer to CCO's Immune Checkpoint Inhibitor Toxicity Management Guideline for detailed descriptions for immune-related renal toxicity management

Severity	Creatinine Clearance (mL/ min)	Dostarlimab Dose
Mild or Moderate	≥ 30	No dose adjustment
Severe	15 to < 30	Limited data

There is limited data in patients with ESRD undergoing dialysis.

Dosage in the elderly:

No dose adjustment is required in patients ≥ 65 years of age. No differences in safety or efficacy of dostarlimab were observed between patients ≥ 65 years of age and those under 65 years. There is limited data in patients ≥ 75 years of age.

Children:

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

back to top

F - Administration Guidelines

- Dilute in a 0.9% sodium chloride or D5W IV infusion bag.
- Final drug concentration after dilution should be between 2 mg/mL and 10 mg/mL.
- Gently invert infusion bag to mix. Do not shake.
- Infuse IV over 30 minutes, using a 0.2 or 0.22 micron in-line filter.
- Administer dostarlimab prior to the chemotherapy when given on the same day.
- Do not administer as IV push or bolus.
- Do not co-administer with other drugs through the same line.
- Compatible with polyvinyl chloride (PVC), platinum cured silicon or polypropylene (PP) infusion sets, fittings made from PVC or polycarbonate, and polyethersulfone (PES) in-line filters.
- Store unopened vials refrigerated (2°C to 8°C) and protect from light. Do not freeze.

back to top

G - Special Precautions

Contraindications:

- Patients who are hypersensitive to this drug or to any of its components.

Other Warnings/Precautions:

- Dostarlimab may cause serious immune-mediated reactions affecting multiple organ systems, including GI, hepatic, renal, respiratory, endocrine and others. Use with caution and monitor closely in patients with pre-existing conditions such as colitis, hepatic impairment, respiratory or endocrine disorders, such as hypo- or hyperthyroidism or diabetes mellitus.

- Patients with conditions such as serious active infection (HIV, hepatitis B or C), active autoimmune disease, conditions that require systemic immunosuppressive therapy and a history of interstitial lung disease were excluded from clinical studies.

- Caution in patients who have previously experienced severe or life-threatening skin reactions on prior treatment with immune-stimulatory anticancer agents.

- Solid organ transplant rejection has been reported in patients treated with PD-1 inhibitors (post-marketing). Complications in allogenic HSCT patients (including graft-versus-host disease) can also occur before or after treatment with PD-1/PD-L1 inhibitors. Consider the risks and benefits of dostarlimab treatment in these patients.

Other Drug Properties:

- Carcinogenicity: Unknown

Pregnancy and Lactation:

- Pregnancy:
  Dostarlimab is not recommended for use in pregnancy. Adequate contraception should be used by patients and their partners during treatment, and until **4 months** after the last dose.

- Breastfeeding:
  Breastfeeding is not recommended during treatment and for at least **4 months** after the last dose.
  - Excretion into breast milk: Unknown

- Genotoxicity: Unknown
- Fetotoxicity: Unknown
  PD-L1 signalling blockade has been shown to disrupt tolerance to fetus (increase in fetal loss), indicating potential risk of increased rates of abortion or stillbirth. Human IgG4 immunoglobulins (IgG4) are known to cross the placental barrier and therefore can be transmitted to the fetus.

- Fertility effects: Unknown
  No notable effects in animal studies in male or female reproductive organs.

back to top

H - Interactions

Dostarlimab is not expected to affect the pharmacokinetics of other drugs as it is not metabolized through hepatic enzymes and lacks effect on cytokines, CYP450, and active substance transporters. No pharmacokinetic drug interaction studies have been performed.

The use of systemic corticosteroids and other immunosuppressants before starting dostarlimab should be avoided because of their potential interference with its activity; however, they can be used after starting dostarlimab to treat immune-related adverse reactions.

Acetaminophen may affect the response to immune checkpoint inhibitors. Further clinical studies are needed to determine the exact mechanism and the appropriate clinical management (Bessede et al, 2022).

back to top

I - Recommended Clinical Monitoring

Treating physicians may decide to monitor more or less frequently for individual patients but should always consider recommendations from the product monograph.

Refer to the hepatitis B virus screening and management guideline for monitoring during and after treatment.

Recommended Clinical Monitoring

Monitor Type	Monitor Frequency
CBC	Baseline and Q3-6 weeks, or as clinically indicated
Liver function tests	Baseline and Q3-6 weeks, or as clinically indicated
Renal function tests (SCr, urine protein and electrolytes)	Baseline and Q3-6 weeks, or as clinically indicated
Thyroid function tests	Baseline and as clinically indicated
Blood glucose	Baseline and as clinically indicated
Clinical toxicity assessment for infusion and immune-mediated reactions, diarrhea, rash, endocrine, respiratory, musculoskeletal, neurologic, cardiac and ophthalmic effects	At each visit

Grade toxicity using the current NCI-CTCAE (Common Terminology Criteria for Adverse Events) version

back to top

J - Supplementary Public Funding

New Drug Funding Program (NDFP Website)

- Dostarlimab - Primary Advanced or Recurrent MSI-H or dMMR Endometrial Cancer

back to top

K - References

Bessede A, Marabelle A, Guegan JP, et al. Impact of acetaminophen on the efficacy of immunotherapy in cancer patients. Ann Oncol 2022;33(9):909-15.

Canada's Drug and Health Technology Agency. CADTH Reimbursement Review Dostarlimab (Jemperli). Canadian Journal of Health Technologies. July 2024; 4 (7).

Dostarlimab: Drug information. Waltham, MA: Lexi-Comp Inc., 2024. https://online.lexi.com. Accessed November 13, 2024.

Jemperli dostarlimab for injection Product Monograph. GlaxoSmithKline Inc. Mississauga, Ontario; July 2024.

Jemperli (dostarlimab-gxly) injection Full Prescribing Information. GlaxoSmithKline LLC. Philadelphia, PA, USA; Aug 2024.

Mirza MR, Chase DM, Slomovitz BM, et al. Dostarlimab for Primary Advanced or Recurrent Endometrial Cancer. N Engl J Med. 2023 Jun 8;388(23):2145-58.

NCCN Practice Guidelines in Oncology (NCCN Guidelines) - Antiemesis v.1.2024. NCCN, Dec 2023. Accessed November 20, 2024.

Protocol for: Mirza MR, Chase DM, Slomovitz BM, et al. Dostarlimab for Primary Advanced or Recurrent Endometrial Cancer. N Engl J Med. 2023 Jun 8;388(23):2145-58.

December 2024 New drug monograph

back to top

L - Disclaimer

Refer to the New Drug Funding Program or Ontario Public Drug Programs websites for the most up-to-date public funding information.

The information set out in the drug monographs, regimen monographs, appendices and symptom management information (for health professionals) contained in the Drug Formulary (the "Formulary") is intended for healthcare providers and is to be used for informational purposes only. The information is not intended to cover all possible uses, directions, precautions, drug interactions or adverse effects of a particular drug, nor should it be construed to indicate that use of a particular drug is safe, appropriate or effective for a given condition. The information in the Formulary is not intended to constitute or be a substitute for medical advice and should not be relied upon in any such regard. All uses of the Formulary are subject to clinical judgment and actual prescribing patterns may not follow the information provided in the Formulary.

The format and content of the drug monographs, regimen monographs, appendices and symptom management information contained in the Formulary will change as they are reviewed and revised on a periodic basis. The date of last revision will be visible on each page of the monograph and regimen. Since standards of usage are constantly evolving, it is advised that the Formulary not be used as the sole source of information. It is strongly recommended that original references or product monograph be consulted prior to using a chemotherapy regimen for the first time.

Some Formulary documents, such as the medication information sheets, regimen information sheets and symptom management information (for patients), are intended for patients. Patients should always consult with their healthcare provider if they have questions regarding any information set out in the Formulary documents.

While care has been taken in the preparation of the information contained in the Formulary, such information is provided on an “as-is” basis, without any representation, warranty, or condition, whether express, or implied, statutory or otherwise, as to the information’s quality, accuracy, currency, completeness, or reliability.

CCO and the Formulary’s content providers shall have no liability, whether direct, indirect, consequential, contingent, special, or incidental, related to or arising from the information in the Formulary or its use thereof, whether based on breach of contract or tort (including negligence), and even if advised of the possibility thereof. Anyone using the information in the Formulary does so at his or her own risk, and by using such information, agrees to indemnify CCO and its content providers from any and all liability, loss, damages, costs and expenses (including legal fees and expenses) arising from such person’s use of the information in the Formulary.

back to top