Drug Monograph

A - Drug Name

cemiplimab

COMMON TRADE NAME(S): Libtayo™

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B - Mechanism of Action and Pharmacokinetics

Cemiplimab is a recombinant human immunoglobulin G4 (IgG4) monoclonal antibody that binds to the PD-1 receptor on T-cells, blocking interaction with PD-L1 and PD-L2 and countering PD-1 mediated immune response inhibition.

Distribution	Cemiplimab exhibits linear and dose proportional pharmacokinetics in the dose range of 1 to 10 mg/kg q2 weekly and 350 mg q3 weekly. Steady state exposure is reached after approximately 4 months of treatment.	
Metabolism	Cemiplimab is metabolized by proteolysis without formation of active metabolites.	
Elimination	Half-life	22 days (at steady state)

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C - Indications and Status

Health Canada Approvals:

- Cutaneous squamous cell carcinoma (CSCC)
- Basal cell carcinoma
- Non-small cell lung cancer (NSCLC)
- Cervical cancer

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

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D - Adverse Effects

Emetogenic Potential: Minimal

Extravasation Potential: None

The following adverse effects include those reported in ≥ 5 patients from the pivotal phase II study in metastatic CSCC. It also includes severe or life-threatening adverse effects from other sources or post-marketing.

ORGAN SITE	SIDE EFFECT* (%)	ONSET**
Cardiovascular	Myocarditis (<1%)	E D
Dermatological	Rash, pruritus (15%) (including SJS, TEN; may be severe)	E
Gastrointestinal	Anorexia, weight loss (14%)	E
	Constipation (15%)	E
	Diarrhea (27%) (including colitis; may be severe)	E
	Mucositis (may be severe)	E
	Nausea, vomiting (17%)	E
General	Fatigue (24%)	E
Hematological	Immune thrombocytopenic purpura (rare)	E D
	Myelosuppression (9%) (including anemia; 2% severe)	E
Hepatobiliary	↑ LFTs (9%) (including hepatitis; may be severe)	E D
Hypersensitivity	Infusion related reaction (3%)	I
Immune	Hemophagocytic lymphohistiocytosis (rare)	E D

	Immune-mediated reactions - solid organ transplant rejection (rare)	D L
	Other - Sjogren's syndrome (rare)	E D
Metabolic / Endocrine	Adrenal insufficiency (<1%)	E D
	Diabetes mellitus (<1%) (new onset)	E D
	Hyperthyroidism (2%) (< 1% severe)	E D
	Hypophysitis (<1%)	E D
	Hypothyroidism (9%)	E D
Nervous System	Headache (14%)	E
	Meningitis (<1%)	E
	Myasthenia (rare)	E D
	Myositis (rare)	E D
	Neurotoxicity (<1%)	E D
Ophthalmic	Uveitis (rare)	E D
Renal	Nephritis (<1%)	E D
Respiratory	Cough (14%)	E
	Pneumonitis (9%) (3% severe)	E D
Vascular	Vasculitis (rare)	E

* "*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 cemiplimab include diarrhea, fatigue, nausea, vomiting, constipation, rash, pruritus, anorexia, weight loss, cough, and headache.

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-mediated reactions, including **pneumonitis, hepatitis, colitis, endocrinopathies, nephritis, neuropathies and rash**, have been reported and may be severe or fatal.

Immune-related **pneumonitis,** including fatal cases, has been reported. The median time to onset was 2 months and the median duration of pneumonitis was 1 month.

Immune-related **diarrhea** or **colitis** has been observed. The median time to onset was 4 months and the median duration was 2 months.

Severe or fatal cases of immune-related **hepatitis** have been observed in patients treated with cemiplimab. Two percent of patients experienced ≥ Grade 3 immune-related hepatitis. The median time to onset was 3 months and the median duration of hepatitis was 2 months.

Immune-related **endocrinopathies**, including **thyroid disorders, hypophysitis, adrenal insufficiency** and **type 1 diabetes mellitus**, have occurred. Thyroid disorders can occur at any time during the treatment. For hypothyroidism, the median time to onset and duration were 4 months and 8 months, respectively. For hyperthyroidism, the median time to onset and duration were 2 months and 2 months, respectively. The median time to onset and duration for adrenal insufficiency were 12 months and 5 months, respectively.

Severe or fatal immune-related **skin adverse reactions**, including **rash, erythema multiforme, pemphigoid,** and **Stevens-Johnson syndrome (SJS)/toxic epidermal necrolysis (TEN**) have been observed. The median time to onset was 1 month and the median duration was 3 months.

Immune-related **nephritis** has been rarely reported with a median time to onset of 2 months and a median duration of nephritis of 1 month.

Immune-related **nervous system** disorders occurred rarely, including paraneoplastic encephalomyelitis, chronic inflammatory demyelinating polyradiculoneuropathy and central nervous system inflammation.

Cases of severe or fatal immune-related adverse reactions have been reported in patients with prior treatment with idelalisib.

Cases of **solid organ transplant rejection** have been reported during postmarketing surveillance. Cemiplimab may increase the risk of organ rejection; consider the benefit versus the risk of treatment.

Infusion-related reactions occurred in 7% of patients, including 1 patient with Grade 3 infusion-related reaction.

Other immune-related rare adverse effects observed in combination treatment with cemiplimab include vasculitis, Guillain-Barre Syndrome, and CNS inflammation.

Rare cases of other significant immune-related toxicities have been reported with other PD-1/PD-L1 inhibitors, such as graft-versus-host disease (associated with allogeneic hematopoietic stem cell transplant), or aplastic anemia.

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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.

Some treatment indications require a validated test to determine PD-L1 tumour status. Refer to the product monograph for details.

Premedication (prophylaxis for infusion reactions):

- Routine pre-medication is not recommended. No premedication was given for the first dose of cemiplimab during clinical trials.
- May consider premedication in patients who experienced a grade 1-2 infusion reaction (Migden et al). Refer to Management of Infusion-related Reactions table.

Adults:

Intravenous: 350 mg Every 3 weeks

OR

(in patients with a low body weight at the discretion of the treating healthcare professional)

Intravenous: 3 mg/kg Every 2 weeks*

*Dosing based on NDFP funding criteria

Combination therapy

Various dosing and schedules are used depending on the indication. Refer to the product monograph or related regimen monographs for details.

Dosage with Toxicity:

Dose reductions are not recommended for cemiplimab. Doses may be delayed or discontinued based on toxicity.

Healthcare professionals should also consult the most recent cemiplimab product monograph for additional information.

Summary of Principles of Management of 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 irAEs 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:

Grade	Management	Re-challenge*
1	• Stop or slow the infusion rate (e.g. 50%) • Manage the symptoms	Consider premedication (at least 30 min prior to infusion) with: • Diphenhydramine 50mg (or equivalent) and/or acetaminophen 325 mg to 1000 mg
2	• Stop or slow the infusion rate (e.g. 50%) • Manage the symptoms	Consider premedication (at least 30 min prior to infusion) with: • Diphenhydramine 50mg (or equivalent) and/or acetaminophen 325 mg to 1000 mg • Corticosteroids (e.g. hydrocortisone 25 mg or equivalent) as necessary
3 or 4	• Stop treatment • Aggressively manage symptoms	Permanently discontinue (do not re-challenge)

*Based on Migden et al.

Dosage with Hepatic Impairment:

No formal studies in patients with hepatic impairment have been conducted.

Based on population pharmacokinetic analysis:

Hepatic Impairment	Cemiplimab Dose
Mild (bilirubin ≤ ULN and AST > ULN or bilirubin >1 to 1.5 x ULN and any AST) OR Moderate (bilirubin >1.5 to 3 x ULN and any AST)	No dosage adjustment is required
Severe (bilirubin >3 x ULN and any AST)	No data

Refer to CCO's Immune Checkpoint Inhibitor Toxicity Management Guideline for management of immune-related hepatic toxicities.

Dosage with Renal Impairment:

No formal studies in patients with renal impairment have been conducted.

Based on population pharmacokinetic analysis:

Creatinine Clearance (mL/min)	Cemiplimab Dose
≥ 15	No dose adjustment
< 15	No data

Refer to CCO's Immune Checkpoint Inhibitor Toxicity Management Guideline for management of immune-related renal toxicities.

Dosage in the elderly:

No dose adjustment required. No overall differences in efficacy were observed between patients ≥ 65 years of age and younger patients. Trends towards a higher frequency of serious adverse events and discontinuations were observed in patients 65 years and older compared to younger patients.

Children:

Safety and efficacy in children have not been established.

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F - Administration Guidelines

- Undiluted solution should be clear to slightly opalescent, colourless to pale yellow; discard if cloudy, discoloured or contains extraneous particulate matter other than trace amounts of translucent-to-white particles.
- Dilute in 0.9% Normal Saline or 5% Dextrose to a final concentration between 1 to 20mg/mL. Mix by gentle inversion; do not shake.
- Infuse over 30 minutes using a sterile, 0.2 to 5 micron in-line or add-on filter.
- Do not co-administer with other drugs through the same infusion line.
- When administered in combination with chemotherapy agents, infuse the chemotherapy first, followed by cemiplimab on the same day. Use separate infusion bags and filters for each infusion.
- Store vials at 2-8 °C; do not freeze. Protect from light.

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G - Special Precautions

Contraindications:

- Patients who have a hypersensitivity to this drug or any of its components

Other Warnings/Precautions:

- Cemiplimab may cause serious immune-related reactions affecting multiple organ systems. Use with caution and monitor closely in patients with pre-existing conditions such as colitis, hepatic or renal impairment, respiratory or endocrine disorders, such as hypo or hyperthyroidism or diabetes mellitus.
- Patients experiencing fatigue should exercise caution when driving or operating machinery.

Other Drug Properties:

- Carcinogenicity: Unknown

Pregnancy and Lactation:

- Fetotoxicity: Probable
- Genotoxicity: Unknown
- Teratogenicity: Unknown
- Pregnancy:
  Cemiplimab is not recommended for use in pregnancy. Adequate contraception should be used by patients and their partners during treatment, and for at least **4 months** after the last dose.
  Animal reproduction studies have not been conducted.
- Breastfeeding:
  Breastfeeding is not recommended during treatment and for at least **4 months** after the last dose.
- Fertility effects: Unknown
  No clinical data on fertility are available; no effects on fertility or in the male and female reproductive organs were observed in animal studies.

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H - Interactions

No drug interaction studies have been conducted.

Use of systemic corticosteroids or immunosuppressants should be avoided prior to starting cemiplimab due to the potential interference with efficacy. They can be used after initiating cemiplimab to treat immune-mediated 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).

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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 as clinically indicated
Liver function tests	Baseline, before each dose and as clinically indicated; frequent with severe toxicity
Renal function tests	Baseline, before each dose and as clinically indicated; frequent with severe toxicity
Blood glucose	Baseline, before each dose and as clinically indicated; frequent with severe toxicity
Thyroid function tests	Baseline, before each dose and as clinically indicated
Clinical toxicity assessment for infusion-related reactions, immune-related reactions, including GI, endocrine, skin, neurologic, cardiac, respiratory, ocular and musculoskeletal effects	At each visit

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

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J - Supplementary Public Funding

New Drug Funding Program (NDFP Website)

- Cemiplimab - Metastatic or Locally Advanced Cutaneous Squamous Cell Carcinoma
- Cemiplimab - In Combination with Chemotherapy for First-Line Treatment of Advanced Non-Small Cell Lung Cancer
- Cemiplimab - Locally Advanced Basal Cell Carcinoma
- Cemiplimab - Previously Untreated Locally Advanced or Metastatic Non-Small Cell Lung Cancer

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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.

Migden MR, Khushalani K, Chang ALS, et al. Cemiplimab in locally advanced cutaneous squamous cell carcinoma: results from an open-label, phase 2, single-arm trial. Lancet Oncol. 2020 Feb;21(2):294-305.

Migden MR, Rischin D, Schmults CD, et al. PD-1 blockade with cemiplimab in advanced cutaneous squamous-cell carcinoma. N Engl J Med 2018;379:341-51.

National Comprehensive Cancer Network. Clinical Practice Guidelines in Oncology: Antiemesis: Version 2.2020, 2020.

Prescribing information: Libtayo (cemiplimab). Regeneron Pharmaceuticals, Inc. June 2020.

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Product monograph: Libtayo (cemiplimab). Sanofi-Aventis Canada Inc. January 30, 2025.

Sezer A, Kilickap S, Gümüş M, et al. Cemiplimab monotherapy for first-line treatment of advanced non-small-cell lung cancer with PD-L1 of at least 50%: a multicentre, open-label, global, phase 3, randomised, controlled trial. Lancet. 2021 Feb 13;397(10274):592-604.

May 2025 Updated Adverse effects section

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L - Disclaimer

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

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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.

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