Drug Monograph

A - Drug Name

durvalumab

COMMON TRADE NAME(S): Imfinzi®

back to top

B - Mechanism of Action and Pharmacokinetics

Durvalumab is a fully human, high-affinity, immunoglobulin G1 kappa ($IgG1_K$) monoclonal antibody that selectively blocks the PD-L1 interaction with PD-1 and CD-80 (B7.1) while leaving the PD-1/PD-L2 interaction intact. This selective blockade enhances anti-tumour immune responses that may be related to increased T-cell activation. Durvalumab does not induce antibody dependent cell-mediated cytotoxicity (ADCC).

Absorption	Time to reach steady state	approx. 16 weeks
Metabolism	Monoclonal antibodies are catabolized into peptides and amino acids.	
Elimination	Half-life	18 days (terminal)

back to top

C - Indications and Status

Health Canada Approvals:

- Urothelial carcinoma
- Non-small cell lung cancer (NSCLC)
- Small cell lung cancer (SCLC)
- Biliary tract cancer

(Includes conditional approvals)
Refer to the product monograph for a full list and details of approved indications.

back to top

D - Adverse Effects

Emetogenic Potential: Minimal

Extravasation Potential: None

The following table lists adverse effects considered drug-related that occurred in ≥ 5% of patients in the durvalumab phase III NSCLC trial comparing durvalumab to placebo. Serious adverse events from other studies and post-marketing may also be included. Adverse effects marked with "†" were based on a pooled data set across multiple monotherapy studies in various tumour types.

ORGAN SITE	SIDE EFFECT* (%)	ONSET**
Cardiovascular	Hypertension (6%)	E
	Myocarditis (rare)	D
Dermatological	Rash, pruritus (22%) (may be severe)	E D
	Stevens-Johnson syndrome (rare)	E
	Toxic epidermal necrolysis (rare)	E
Gastrointestinal	Abdominal pain (10%)	E
	Anorexia (14%)	E
	Constipation (12%)	E
	Diarrhea (18%) (may be severe - 2% colitis†)	E D
	Nausea, vomiting (14%)	E

General	Edema (8%)	E
	Fatigue (24%)	E
Hematological	Immune thrombocytopenic purpura (immune-mediated; rare)	E D
Hepatobiliary	↑ LFTs (6%) (may be severe - 2% hepatitis†)	E D
	Pancreatitis (rare)	E
Hypersensitivity	Infusion related reaction (2%) †	I
Infection	Infection (26%) (may be severe)	E
Metabolic / Endocrine	Adrenal insufficiency (rare)	E D L
	Diabetes mellitus (type 1; rare)	E D
	Hyperthyroidism (8%)	E D
	Hypophysitis (rare)	E D
	Hypothyroidism (12%)	E D
	Thyroiditis (2%)	E D
Musculoskeletal	Musculoskeletal pain (12%)	E
	Rhabdomyolysis (rare)	E
Nervous System	Encephalitis (rare)	E
	Guillain-Barre syndrome (rare)	E
	Headache (11%)	E
	Insomnia (10%)	E
	Meningitis (aseptic; rare)	E
	Myasthenia gravis (rare)	E
	Myositis (rare)	E D
Ophthalmic	Uveitis (rare)	E
Renal	Creatinine increased (5%) (may be severe - nephritis (rare))	E D
Respiratory	Cough, dyspnea (40%) (1% severe)	E
	Dysphonia (4%)	E
	Pneumonitis (3%) † (NSCLC: 34 % (3% severe), including radiation pneumonitis and interstitial lung disease)	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 durvalumab include infection, fatigue, rash, pruritus, diarrhea, anorexia, nausea/vomiting, constipation, hypothyroidism, musculoskeletal pain, and cough/dyspnea.

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.

Rare cases of other significant immune-related toxicities have been reported with durvalumab or other PD-L1 inhibitors: Stevens-Johnson Syndrome, toxic epidermal necrolysis, rhabdomyolysis, encephalitis, demyelinating polyneuropathy, autoimmune hemolytic anemia, Guillain-Barré syndrome, and aplastic anemia.

Both immune-mediated and radiation pneumonitis occurred more frequently in patients with locally advanced unresectable NSCLC who were treated with durvalumab within 6 weeks of chemoradiation compared to those who received placebo. The median time to onset was 55 days (range: 1-406 days).

Severe **infections** occurred in patients receiving durvalumab (some fatal). The most common grade 3 or 4 infections were urinary tract infections (urothelial carcinoma study) and pneumonia (NSCLC study). The overall incidence of infections was higher in a NSCLC study, compared to patients in other studies in whom radiation therapy was typically not administered immediately prior to durvalumab.

back to top

E - Dosing

Refer to protocol by which the 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.

Avoid the use of corticosteroids or immunosuppressants before starting treatment.

Consider pre-medication in patients with prior infusion related reactions.

Adults:

Monotherapy:

Durvalumab 10 mg/kg IV every 2 weeks

OR

Durvalumab 1500 mg IV every 4 weeks

Patients with weight ≤ 30 kg must receive 10mg/kg every 2 weeks weight-based dosing, until weight increases to > 30 kg.

(For dosing in durvalumab maintenance, refer to the DURV(MNT) regimen monographs.)

Combination therapy:

Dosing schedules depend on the indication. Refer to the product monograph or related regimen monograph(s) for details.

Dosage with Toxicity:

- Healthcare professionals should also consult the most recent durvalumab product monograph for additional information.
- Dose reductions are not recommended for durvalumab . Doses may be delayed or discontinued based on toxicity.
- Hold durvalumab for severe infections; manage symptoms and treat with anti-infectives.

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 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.**

Non-immune-related toxicity

Severity	Action
Grade 2 or 3	Hold until ≤ Grade 1 or baseline
Grade 4	Discontinue*

*Decision to discontinue for lab abnormalities should be based on signs/ symptoms and clinical judgement.

Management of Infusion related Reactions

Severity	Action
Grade 1 or 2	Interrupt or slow the rate of infusion by 50%. Consider pre-medications prior to subsequent infusions.
Grade 3 or 4	Discontinue

Dosage with Hepatic Impairment:

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

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

Dosage with Renal Impairment:

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

Creatinine Clearance (mL/min)	Durvalumab Dose
≥ 30	No dosage adjustment is required
< 30	No data

Dosage in the elderly:

No dosage adjustment is required for patients aged 65 and older. No overall differences in safety or efficacy were reported between patients ≥ 65 years of age and younger patients.

Children:

Safety and efficacy have not been established in pediatric patients.

back to top

F - Administration Guidelines

- Administer by IV infusion over 60 minutes using a sterile, low-protein binding 0.2-0.22 micron in-line filter.
- Give durvalumab prior to chemotherapy when both are given on the same day.
- Durvalumab 1500 mg IV was given over 60 minutes for the first infusion, then over 30 minutes subsequently, in an advanced biliary tract cancer clinical trial that studied durvalumab with gemcitabine-based chemotherapy. No difference in infusion-related safety between the 30- and 60-minute infusion was observed. (Oh et al, 2024**)**
- Durvalumab is supplied as a single-use, preservative-free vial.
- Visually inspect the vial for particulates and discolouration prior to dilution. Undiluted solution should be clear to opalescent and colorless to slightly yellow.
- Using aseptic technique, withdraw the required drug volume and transfer to an IV bag of NS or D5W to a final concentration of 1 to 15 mg/mL.
- Mix by gentle inversion; do not shake.
- Do not co-administer with other drugs; flush line after each dose.
- Store unopened drug vials under refrigeration (2-8^{o}C) in the original package.
- Protect from light and do not freeze.

back to top

G - Special Precautions

Contraindications:

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

Other Warnings/Precautions:

- 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.
- Some clinical trials excluded patients with a history of immunodeficiency; medical conditions that required systemic immunosuppression; history of severe immune-mediated adverse reactions; history of allogeneic organ transplantation; untreated CNS metastases; HIV; active tuberculosis, hepatitis B or C infection, or patients who received live attenuated vaccine(s) within 30 days before or after starting durvalumab.
- Use caution when driving or operating machinery, as patients may experience adverse effects affecting their ability to concentrate or react.

Other Drug Properties:

- Carcinogenicity: Unknown

Pregnancy and Lactation:

- Crosses placental barrier: Yes
- Genotoxicity: Unknown
- Fetotoxicity: Likely
  Durvalumab may cause fetal harm and is not recommended for use in pregnancy. Adequate contraception should be used by patients and their partners during treatment, and for at least **3 months** after the last dose.
- Excretion into breast milk: Likely
  Immunoglobulins are known to be secreted into breast milk; therefore as a human IgG1k antibody, there is potential for infant exposure to durvalumab via breast milk.
  Breastfeeding is not recommended during treatment and for at least **3 months** after the last dose.
- Fertility effects: Unknown

back to top

H - Interactions

No formal pharmacokinetic drug-drug interaction studies have been conducted.

Use of systemic corticosteroids or immunosuppressants should be avoided prior to starting durvalumab because of potential interference with efficacy. They can be used to treat immune-mediated reactions after starting the drug. Corticosteroids may be used as premedication (e.g. antiemetic) when given with chemotherapy.

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
Serum creatinine, urine protein	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 infection, fatigue, infusion reactions, immune-mediated reactions, including GI, skin, ocular, respiratory, neurologic, cardiac, musculoskeletal, and endocrine toxicities	At each visit and as clinically indicated

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)

- Durvalumab - Locally Advanced Unresectable Stage III Non-Small Cell Lung Cancer Following Concurrent Chemoradiation
- Durvalumab - In Combination with Etoposide and Platinum for Extensive-Stage Small Cell Lung Cancer
- Durvalumab - Locally Advanced Unresectable or Metastatic Biliary Tract Cancer
- Durvalumab in combination with Tremelimumab - Previously Untreated Unresectable or Metastatic Hepatocellular Carcinoma (HCC)

back to top

K - References

Antonia SJ, Villegas A, Daniel D, et al. Overall survival with durvalumab after chemoradiotherapy in stage III NSCLC. N Engl J Med. 2018. DOI: 10.1056/NEJMoa1809697

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.

Oh D-Y, He AR, Qin S, et al. Durvalumab plus gemcitabine and cisplatin in advanced biliary cancer. NEJM Evidence. 2022 Jun 1:EVIDoa2200015.

Oh, D-Y, Ikeda M, He AR, et al. Safety of 30 min infusion of durvalumab in combination with gemcitabine-based chemotherapy in first-line treatment of advanced biliary tract cancer: TOURMALINE early results [abstract]. Annals of Oncology 2024;35(Supp 4):S1452-S1453.

Paz-Ares L, Dvorkin M, Chen Y, et al. Durvalumab plus platinum-etoposide versus platinum-etoposide in first-line treatment of extensive-stage small-cell lung cancer (CASPIAN): a randomised, controlled, open-label, phase 3 trial. Lancet . 2019 Nov 23;394(10212):1929-1939. doi: 10.1016/S0140-6736(19)32222-6

Powles T, O'Donnell PH, Massard C, et al. Efficacy and safety of durvalumab in locally advanced or metastatic urothelial carcinoma: Updated results From a phase 1/2 open-label study. JAMA Oncol. 2017 Sep 14;3(9):e172411.

Product monograph: Durvalumab (Imfinzi®). AstraZeneca Canada Inc., December 2023.

May 2025 Modified Administration Guidelines section (info on shorter infusion duration from a clinical trial)

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.

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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.

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back to top