Drug Monograph

A - Drug Name

atezolizumab (subcut)

COMMON TRADE NAME(S): Tecentriq® SC

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B - Mechanism of Action and Pharmacokinetics

Atezolizumab is a humanized immunoglobulin G1 (IgG1) monoclonal antibody that binds to programmed cell death-ligand 1 (PD-L1) and blocks interactions with the PD-1 and B7.1 receptors on activated T cells. It releases PD-L1/PD-1 pathway-mediated inhibition of the immune response, leading to activation of an anti-tumour immune response.

Absorption	Bioavailability	72%
	T max	4.5 days (at Cycle 1); 3.8 days (at steady state)
	Time to reach steady state	6 to 9 weeks (2 to 3 cycles)
Metabolism	Antibodies are primarily cleared by catabolism.	
Elimination	Half-life	27 days

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C - Indications and Status

Health Canada Approvals:

- Non-Small Cell Lung Cancer (NSCLC)
- Small Cell Lung Cancer (SCLC)
- Breast Cancer
- Hepatocellular Carcinoma (HCC)

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

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D - Adverse Effects

Emetogenic Potential: Low

Extravasation Potential: None

Adverse reactions listed below are based on a phase III study in first-line NSCLC patients receiving atezolizumab IV monotherapy, mainly with incidences ≥ 10%. Severe adverse effects from other studies are also included.

Adverse effects marked with "†" are based on a pooled data set across multiple monotherapy studies.

Adverse effects from studies that used subcutaneous formulation are denoted with "^".

ORGAN SITE	SIDE EFFECT* (%)	ONSET**
Cardiovascular	Arrhythmia (1%)	E
	Arterial thromboembolism (<1%)	E
	Hypotension (5%)	E
	Myocarditis (rare), pericarditis	E D
	Venous thromboembolism (4%)	E
Dermatological	Rash, pruritus , dry skin (15%) (may be severe)	E D
	Stevens-Johnson syndrome (rare)	E
	Toxic epidermal necrolysis (rare)	E

Gastrointestinal	Anorexia (15%)	E
	Constipation (12%)	E
	Diarrhea (11%) (may be severe; colitis - 1%)†	E D
	Nausea, vomiting (14%)	I E
General	Fatigue (26%)	E D
	Sarcoidosis (rare)	E
Hematological	Aplastic anemia (rare)	E
	Hemolytic anemia (autoimmune - rare)	E
	Myelosuppression (15%) (including anemia)	E
Hepatobiliary	Hepatitis (immune-related) (rare)	E
	↑ LFTs (5%) (2% immune related hepatitis†)	E D
	Pancreatitis (rare)†	E D
Hypersensitivity	Hypersensitivity (<1%)	I
Immune	Hemophagocytic lymphohistiocytosis (rare)	E
Infection	Infection (43%) (11% severe)	E
Injection site	Injection site reaction (5%) ^	I
Metabolic / Endocrine	Abnormal electrolyte(s) (6%) (↓Na, Mg, K, Ca; ↑K, Ca)	E
	Adrenal insufficiency (rare)†	E D
	Hyperglycemia (4%) (including Type 1 Diabetes - rare†)	E D
	Hyperthyroidism (5%)	E D
	Hypophysitis (rare)†	E D
	Hypothyroidism (9%) (may be severe)	E D
Musculoskeletal	Musculoskeletal pain (15%)	E
	Rhabdomyolysis (rare)	E D
Nervous System	Encephalitis (Meningo-encephalitis) (rare)	E D
	Guillain-Barre syndrome (rare)†	E D
	Headache (9%)	E
	Myasthenia (rare - myasthenia gravis or myasthenic syndrome†)	E D
	Myelitis (rare)	E
	Myositis (rare)†	E D
	Peripheral neuropathy (7%)	E
Ophthalmic	Uveitis (and other ocular inflammatory toxicity) (rare)†	E D

Renal	Creatinine increased (1%)	E
	Nephritis (rare)†	D
Respiratory	Cough, dyspnea (14%)	E
	Pneumonitis (3%) †	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 atezolizumab include infection, fatigue, anorexia, musculoskeletal pain, myelosuppression, rash/pruritus, cough/dyspnea, nausea/vomiting, constipation, and diarrhea.

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 such as rash, pneumonitis, colitis, hepatitis, pancreatitis, nephritis, endocrinopathies, meningoencephalitis, and neuropathies were reported and may be severe or fatal. Onset may vary from days to many months.

Severe cutaneous adverse reactions (SCARs) (including reports of erythema multiforme, dermatitis bullous, toxic skin eruption, toxic epidermal necrolysis (TEN), exfoliative rash, and dermatitis exfoliative generalized) have occurred in patients who receiving atezolizumab (IV) as monotherapy or in combination with other anti-cancer agents.

Infections, including fatal cases, have been reported with atezolizumab (IV or subcut). Pneumonia was the most common type of grade 3 or higher infection.

Severe **bleeding**, including fatal events, have been reported in NSCLC and HCC patients treated with the atezolizumab (IV)-bevacizumab combination.

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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.

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

Adults:

Atezolizumab IV and subcutaneous formulations are **not interchangeable**. The dosing and concentration of these products are different.

Monotherapy - NSCLC

Subcutaneous: 1875 mg Every 3 weeks

Combination therapy

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

Dosage with Toxicity:

Healthcare professionals should also consult the most recent atezolizumab (subcut) product monograph for additional information.

Summary of Principles of Management

- 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 administration-related reactions:

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

Grade	Management	Re-Challenge
1 or 2	• Stop or slow the administration rate. • Manage the symptoms. **Restart:** • No specific recommendations can be made at this time.	• Re-challenge with close monitoring. Consider pre-medication with antipyretic and H1-receptor antagonists.
3 or 4	• Stop treatment. • Aggressively manage symptoms.	• Permanently discontinue (do not re-challenge).

Dosage with Hepatic Impairment:

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

Hepatic Impairment	Atezolizumab Dose
Mild (bilirubin ≤ ULN and AST > ULN, OR bilirubin > 1 to 1.5 x ULN and any AST)	No change
Moderate (bilirubin > 1.5 to 3 x ULN and any AST)	No change
Severe (bilirubin > 3 × ULN and any AST)	No data

Dosage with Renal Impairment:

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

Creatinine Clearance (mL/min)	Atezolizumab Dose
≥ 30	No change
< 30	No data

Dosage in the elderly:

No dose adjustment is required in patients ≥ 65 years of age. No differences in safety or efficacy were observed between patients ≥ 65 years of age and younger patients observed. Data in patients > 75 years of age are too limited to draw conclusions.

Children:

The safety and efficacy in children and adolescents below 18 years of age have not been established.

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F - Administration Guidelines

Atezolizumab IV and subcutaneous formulations are **not interchangeable**. The dosing and concentration of these products are different.

- Atezolizuma (subcut) does not require reconstitution or dilution.
- Administer by subcutaneous injection, over approximately 7 minutes.
- Allow vials to come to room temperature (15-30°C) before administration.
- Injection site should be alternated between the left and right thigh only.
- Use of a subcutaneous infusion set (e.g., winged / butterfly) is recommended. Refer to the product monograph for preparation instructions.
- **DO NOT** administer the remaining residual volume in the tubing to the patient.
- Atezolizumab subcut should be given prior to IV combination therapy if given on the same day.
- Atezolizumab (subcut) is compatible with polypropylene (PP), polycarbonate (PC), stainless steel (ss), polyvinyl chloride (PVC), and polyurethanes (PU).
- Inject other subcutaneous medications at separate sites.
- Do not shake vials.
- 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:

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

- Caution in patients who have previously experienced a severe or life-threatening adverse skin reaction on previous treatment with other immune stimulatory anticancer drugs.

- Do not replace nab-paclitaxel with paclitaxel in combination with atezolizumab (subcut) in unresectable locally advanced or metastatic triple negative breast cancer outside of controlled clinical trials. An increase in the risk of death was reported in PD-L1 positive patients treated with atezolizumab IV and paclitaxel vs placebo and paclitaxel.

- Consider the bleeding risks of atezolizumab (subcut) and bevacizumab combination in HCC and NSCLC before starting treatment. Patients with HCC should be evaluated for the presence of varices and have varices treated within 6 months before starting therapy with the atezolizumab (subcut)-bevacizumab combination. The following patients were excluded from IV atezolizumab clinical trials: NSCLC patients who had clear tumour infiltration into the thoracic great vessels or clear cavitation of pulmonary lesion (as seen on imaging), or HCC patients with bleeding varices (including recent bleeds), untreated varices or varices at high risk of bleeding.

- Severe infections have been observed in clinical trials.

Other Drug Properties:

- Carcinogenicity: Unknown

Pregnancy and Lactation:

- Genotoxicity: Unknown
- Fetotoxicity: Documented in animals

- Pregnancy:
  Atezolizumab (subcut) is not recommended for use in pregnancy. Adequate contraception should be used by patients and their partners during treatment, and for at least **5 months** after the last dose.

- Breastfeeding:
  Breastfeeding is not recommended during treatment and for at least **5 months** after the last dose.

- Fertility effects: Probable
  Documented in studies, in female animals

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H - Interactions

- Atezolizumab (subcut) is not expected to have pharmacokinetic drug-drug interactions as it is not metabolized by drug metabolizing enzymes. No pharmacokinetic drug interaction studies have been performed.

- Use of systemic corticosteroids or immunosuppressants should be avoided prior to starting atezolizumab (subcut) 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).

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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 Q3-6 weeks, or as clinically indicated
Liver function tests	Baseline and Q3-6 weeks, or as clinically indicated
Renal function tests, 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, administration-related reactions, and immune-mediated reactions, such as endocrine, skin, GI, cardiac, neurologic, musculoskeletal, ocular or respiratory toxicity	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)

- Atezolizumab - Advanced or Metastatic Non-Small Cell Lung Cancer
- Atezolizumab - Adjuvant Treatment for Non-Small Cell Lung Cancer
- Atezolizumab - In Combination with Etoposide and Platinum for Extensive-Stage Small Cell Lung Cancer
- Atezolizumab with Bevacizumab (Biosimilar) - Previously Untreated Unresectable or Metastatic Hepatocellular Carcinoma

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K - References

Atezolizumab drug monograph. Ontario Health (Cancer Care Ontario).

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.

Burotto M, Zvirbule Z, Mochalova A, et al. IMscin001 Part 2: a randomised phase III, open-label, multicentre study examining the pharmacokinetics, efficacy, immunogenicity, and safety of atezolizumab subcutaneous versus intravenous administration in previously treated locally advanced or metastatic non-small-cell lung cancer and pharmacokinetics comparison with other approved indications. Ann Oncol. 2023 Aug;34(8):693-702. Erratum in: Ann Oncol. 2024 May;35(5):482.

Felip E, Burotto M, Zvirbule Z, et al. Results of a Dose-Finding Phase 1b Study of Subcutaneous Atezolizumab in Patients With Locally Advanced or Metastatic Non-Small Cell Lung Cancer. Clin Pharmacol Drug Dev. 2021 Oct;10(10):1142-1155.

Prescribing information: Tecentriq Hybreza™ (atezolizumab and hyaluronidase-tqjs) injection, for subcutaneous use. Genentech, Inc. Sept 2024.

Product monograph: Tecentriq® SC (atezolizumab injection). Hoffmann-La Roche Limited. January 09, 2025.

May 2025 New drug monograph

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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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