Regimen Monograph

A - Regimen Name

ATEZ(MNT) Regimen

Atezolizumab (Maintenance)

Disease Site
Lung
Small Cell

Intent
Palliative

Regimen Category
Evidence-Informed :

Regimen is considered appropriate as part of the standard care of patients; meaningfully improves outcomes (survival, quality of life), tolerability or costs compared to alternatives (recommended by the Disease Site Team and national consensus body e.g. pan-Canadian Oncology Drug Review, pCODR). Recommendation is based on an appropriately conducted phase III clinical trial relevant to the Canadian context OR (where phase III trials are not feasible) an appropriately sized phase II trial. Regimens where one or more drugs are not approved by Health Canada for any indication will be identified under Rationale and Use.

Rationale and Uses
As maintenance treatment after 4 cycles of platinum/etoposide+atezolizumab combination therapy in patients with extensive-stage small cell lung cancer.

Supplementary Public Funding
atezolizumab
New Drug Funding Program (Atezolizumab - In Combination with Etoposide and Platinum for Extensive-Stage Small Cell Lung Cancer) (NDFP Website)

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B - Drug Regimen

atezolizumab	1200 mg	IV	Day 1

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C - Cycle Frequency

As maintenance after completion of 4 cycles of platinum/etoposide+atezolizumab:

REPEAT EVERY 21 DAYS

Until disease progression or unacceptable toxicity

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D - Premedication and Supportive Measures

Antiemetic Regimen: Low

- Also refer to CCO Antiemetic Recommendations.

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

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E - Dose Modifications

Doses should be modified according to the protocol by which the patient is being treated.

Avoid the use of corticosteroids or immunosuppressants before starting treatment.

Dosage with toxicity

- Healthcare professionals should also consult the most recent atezolizumab 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 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 or 2	• Stop or slow the infusion 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).

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 1 to 1.5 x ULN and any AST, OR bilirubin ≤ ULN and AST > ULN)	No change
Moderate (bilirubin >1.5 to 3 x ULN and any AST)	No change
Severe (bilirubin >3 x ULN and any AST)	No data

Renal Impairment

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

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

Dosage in the Elderly

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

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F - Adverse Effects

Refer to atezolizumab drug monograph(s) for additional details of adverse effects.

Common (25-49%)	Less common (10-24%)	Uncommon (< 10%), but may be severe or life-threatening
• Infection (may be severe) • Fatigue	• Rash, pruritus (may be severe) • Anorexia • Musculoskeletal pain • Anemia • Cough, dyspnea • Nausea, vomiting • Constipation • Diarrhea (may be severe)	• Hypo and hyperthyroidism • Type 1 diabetes mellitus • Pneumonitis • Hypersensitivity; infusion reactions • Adrenal insufficiency • Hypophysitis • Meningo-encephalitis • Pancreatitis • Ocular inflammatory disorders • Hepatitis • Neuropathy, myasthenia gravis, Guillain-Barre syndrome • Myelitis • Myositis / rhabdomyolysis • Myocarditis, pericarditis • Venous thromboembolism • Nephritis • Stevens-Johnson syndrome • Toxic epidermal necrolysis • Hemophagocytic lymphohistiocytosis • Autoimmune hemolytic anemia • Vasculitis

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G - Interactions

Refer to atezolizumab drug monograph(s) for additional details.

- Atezolizumab 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 because of potential interference with efficacy. They can be used to treat immune-mediated reactions after starting the drug.

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H - Drug Administration and Special Precautions

Refer to atezolizumab drug monograph(s) for additional details.

Administration

- Withdraw required volume of drug concentrate from vial and dilute in 250mL of 0.9% sodium chloride solution (concentration 3.2 to 16.8 mg/mL). Mix by gentle inversion; do not shake.
- Dilute with 0.9% Sodium Chloride Injection only in a polyvinyl chloride (PVC), polyethylene (PE), polyolefin (PO) or polypropylene (PP) infusion bag.
- Do not mix atezolizumab with other medicinal products.
- Compatible with in-line filter membranes composed of polyethersulfone or polysulfone. Compatible with infusion sets and other infusion aids composed of PVC, PE, polybutadiene or polyetherurethane.
- The initial dose must be administered over 60 minutes. If the first infusion is tolerated all subsequent infusions may be administered over 30 minutes. DO NOT administer as an IV push or bolus.
- Do not co-administer other drugs through the same infusion line.
- If a planned dose is missed, it should be administered as soon as possible; do not wait until the next planned dose. The schedule of administration should be adjusted to maintain the prescribed interval between doses, based on the regimen used.
- Store vials at 2-8°; do not freeze. Protect from light.

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

Contraindications

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

Other Warnings/Precautions

- Atezolizumab may cause serious immune-mediated reactions affecting multiple organ systems, including GI, hepatic, 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.
- Severe infections have been observed in clinical trials.

Pregnancy/Lactation

- This regimen is not recommended for use in pregnancy. Adequate contraception should be used by patients and their partners while on treatment and after the last treatment dose. Recommended methods and duration of contraception may differ depending on the treatment. Refer to the drug monograph(s) for more information.
- Breastfeeding is not recommended during this treatment and after the last treatment dose. Refer to the drug monograph(s) for recommendations after the last treatment dose (if available).
- Fertility effects: Likely, especially in females

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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

- 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, infusion-related and immune-mediated reactions, such as endocrine, skin, GI, cardiac neurologic, musculoskeletal, ocular and respiratory toxicity; At each visit
- Grade toxicity using the current NCI-CTCAE (Common Terminology Criteria for Adverse Events) version

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J - Administrative Information

Approximate Patient Visit	1 hour
Pharmacy Workload (average time per visit)	18.6 minutes
Nursing Workload (average time per visit)	40.75 minutes

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K - References

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

CADTH reimbursement recommendation: Atezolizumab (In combination with carboplatin and etoposide for the first-line treatment of adult patients with extensive-stage small cell lung cancer). September 2022.

Horn L, Mansfield AS, Szczesna A, et al. First-line atezolizumab plus chemotherapy in extensive stage small-cell lung cancer. N Engl J Med 2018;379:2220-9.

PEBC Advice Documents or Guidelines

- Systemic Therapy for Small-Cell Lung Cancer: ASCO-OH(CCO) Guideline

March 2024 Modified Dosage in hepatic impairment, Adverse effects, Drug administration, Pregnancy/lactation and Monitoring sections

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M - Disclaimer

Regimen Abstracts

A Regimen Abstract is an abbreviated version of a Regimen Monograph and contains only top level information on usage, dosing, schedule, cycle length and special notes (if available). It is intended for healthcare providers and is to be used for informational purposes only. It is not intended to constitute or be a substitute for medical advice, and all uses of the Regimen Abstract are subject to clinical judgment. 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, and Cancer Care Ontario disclaims all liability for the use of this information, and for any claims, actions, demands or suits that arise from such use.

Information in regimen abstracts is accurate to the extent of the ST-QBP regimen master listings, and has not undergone the full review process of a regimen monograph. Full regimen monographs will be published for each ST-QBP regimen as they are developed.

Regimen Monographs

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

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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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