Regimen Monograph

A - Regimen Name

PEMB Regimen

Pembrolizumab

Disease Site	Breast
Intent	Adjuvant
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	Treatment for high-risk triple negative breast cancer in patients who had neoadjuvant chemotherapy and pembrolizumab
Supplementary Public Funding	**pembrolizumab** New Drug Funding Program (Pembrolizumab - Previously Untreated High-Risk Early-Stage Triple Negative Breast Cancer) (NDFP Website)

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B - Drug Regimen

pembrolizumab[1]	2 mg /kg	IV (max 200 mg)	Day 1; Every 3 weeks
OR			
pembrolizumab[1]	4 mg /kg	IV (max 400 mg)	Day 1; Every 6 weeks

[1]Dosing based on NDFP funding criteria.

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C - Cycle Frequency

2 mg/kg dosing: **REPEAT EVERY 3 WEEKS (q21 days)**

4 mg /kg dosing: **REPEAT EVERY 6 WEEKS (q42 days)**

Until disease progression or unacceptable toxicity up to a maximum of 1 year†, whichever occurs first

†17 doses given every 3 weeks, or 9 doses given every 6 weeks, which includes the combination of doses administered in the neoadjuvant and adjuvant settings. (Refer to NDFP form for details.)

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D - Premedication and Supportive Measures

Antiemetic Regimen: Minimal

Other Supportive Care:

- 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.
- 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 1-2 infusion reaction.

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E - Dose Modifications

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

Dosage with toxicity

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

There are no dose reductions for pembrolizumab. Doses are either delayed or discontinued with 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 or 2	• Stop or slow the infusion. • Manage the symptoms. **Restart:** • No specific recommendations can be made at this time.	• Consider re-challenge with close monitoring and pre-medications (antipyretic and H1-receptor antagonist).
3 or 4	• Stop the infusion. • Aggressively manage symptoms.	• Discontinue permanently (do not re-challenge).

Hepatic Impairment

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

Hepatic Impairment	Pembrolizumab Dose
Mild (bilirubin 1 - 1.5 x ULN or AST > ULN)	No dose adjustment necessary
Moderate (bilirubin >1.5 - 3 x ULN and any AST)	No dose adjustment necessary; limited data
Severe (bilirubin > 3 x ULN and any AST)	Caution; no data

Renal Impairment

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

CrCl (mL/min)	Pembrolizumab Dose
≥ 60	No dose adjustment necessary
30 to 59	No dose adjustment necessary
< 30	Caution; no data

Dosage in the Elderly

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

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F - Adverse Effects

Refer to pembrolizumab 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
• Fatigue	• Diarrhea (may be severe) • Rash / pruritus • Nausea / vomiting • Musculoskeletal pain	• Myocarditis, pericarditis • Colitis • Aplastic anemia, hemolytic anemia • Myelosuppression ± infection, bleeding • Hepatitis • Pancreatitis • Exocrine pancreatic insufficiency • Sclerosing cholangitis • Infusion-related reaction • Hemophagocytic lymphohistiocytosis • Sarcoidosis • Graft loss - solid organ transplant recipients • Hyper / hypothyroidism • Hyperglycemia • Hypopituitarism / hypophysitis • Adrenal insufficiency • Encephalitis • Guillain-Barre syndrome • Myelitis • Myositis, myasthenia • Eye disorders • Nephritis / nephrotoxicity • Pneumonitis • Vasculitis • Vogt-Koyanagi-Harada syndrome • Stevens-Johnson syndrome • Toxic epidermal necrolysis • Veno-occlusive disease* • Graft-versus-host disease**

*Reported in patients who undergo allogeneic HSCT after pembrolizumab.
**Reported in patients who undergo allogeneic HSCT before or after pembrolizumab.

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G - Interactions

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

- Pembrolizumab is not expected to have pharmacokinetic drug-drug interactions as it is not metabolized by drug metabolizing enzymes.
- Use of systemic corticosteroids or immunosuppressants should be avoided prior to starting pembrolizumab 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 pembrolizumab drug monograph(s) for additional details.

Administration

- Dilute in 0.9% sodium chloride or D5W to final concentration of 1 to 10 mg/mL; mix by gentle inversion.
- Administer over 30 minutes using sterile, non-pyrogenic, low protein-binding 0.2 to 5 micron in-line or add-on filter.
- Do not co-administer other drugs through the same infusion line.
- If a planned dose is missed, administer as soon as possible. Adjust the schedule to maintain the prescribed dosing interval.
- Vials should be stored under refrigeration (2 to 8^{o}C). Protect from light. Do not freeze.

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.

Warnings/Precautions

- Patients with conditions such as an active infection, autoimmune disease or require systemic immunosuppressive therapy (i.e. transplant patients), a history of pneumonitis, severe immune-mediated adverse reactions with ipilimumab, or severe hypersensitivity to other monoclonal antibodies were excluded from clinical studies.
- Pembrolizumab 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 ECOG performance status ≥ 2 were excluded from clinical trials.
- Use of a PD-1 or PD-L1 blocking antibody with a thalidomide analogue plus dexamethasone is not recommended outside of controlled clinical trials, due to increased mortality reported.

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: Unknown

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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
- Serum creatinine, urine protein; Baseline and Q3-6 weeks, or as clinically indicated
- Electrolytes; Baseline and as clinically indicated
- Blood glucose; Baseline and as clinically indicated
- Thyroid function tests; Baseline and as clinically indicated
- Clinical toxicity assessment for infusion-related and immune-mediated reactions, fatigue, ocular, endocrine, skin, GI, neurologic, musculoskeletal, cardiac and respiratory effects; 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	0.75 hour
Pharmacy Workload (average time per visit)	19.75 minutes
Nursing Workload (average time per visit)	40.75 minutes

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K - References

CADTH Reimbursement recommendation - Pembrolizumab: For the treatment of adult patients with high-risk early-stage triple negative breast cancer. September 2022.

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

Schmid P, Cortes J, Pusztai L, et al. Pembrolizumab for early triple-negative breast cancer. N Engl J Med 2020;382:810-21. DOI: 10.1056/NEJMoa1910549

Schmid P, Cortes J, Dent R, et al. Event-free survival with pembrolizumab in early triple-negative breast cancer. N Engl J Med 2022;386:556-67.
DOI: 10.1056/NEJMoa2112651

September 2025 Updated Dose modifications, Adverse effects, Administration Guidelines, 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.

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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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