Regimen Monograph

Regimen Name | Drug Regimen | Cycle Frequency | Premedication and Supportive Measures | Administrative Information | References | Other Notes | Disclaimer

A - Regimen Name

CRBPPACL(W)+PEMB Regimen

PACLitaxel-CARBOplatin-Pembrolizumab

Disease Site Breast

Intent Neoadjuvant

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.

This **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). 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.

Rationale and Uses

For neoadjuvant treatment of high-risk triple negative breast cancer (TNBC) in patients* without prior systemic therapy for non-metastatic TNBC

*with good performance status and no clinical contraindication for immunotherapy

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]	2 mg /kg	IV (max 200 mg)	Day 1
PACLitaxel	80 mg /m²	IV	Days 1, 8, 15
CARBOplatin	AUC 5*	IV	Day 1
OR			
CARBOplatin	AUC 1.5*	IV	Days 1, 8, 15

[1]Dosing based on NDFP funding criteria. Refer to NDFP form for alternative pembrolizumab dosing schedule (4 mg/kg IV q6 weeks).

[2]Give pembrolizumab before chemotherapy when given on the same day.

*Adjust Carboplatin dose to AUC target (using Calvert formula) as outlined in Other Notes section.

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C - Cycle Frequency

REPEAT EVERY 21 DAYS

For 4 cycles, followed by neoadjuvant AC+PEMB x 4 cycles, unless disease progression or unacceptable toxicity occurs.

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D - Premedication and Supportive Measures

Antiemetic Regimen: Moderate + NK1 antagonist (Carboplatin AUC ≥ 5)
Moderate (Carboplatin AUC < 5)

Febrile Neutropenia Risk: Low

- Also refer to CCO Antiemetic Recommendations.

Premedication for pembrolizumab (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.

Pre-Medications for weekly paclitaxel*: (To be given 30-60 minutes prior to paclitaxel infusion):

- Dexamethasone 10 mg IV, starting in cycle 1
- Diphenhydramine 25-50 mg IV/PO
- Ranitidine 50 mg IV OR Famotidine 20 mg IV

* Consider discontinuing pre-medications for paclitaxel if there was no IR in the first 2 doses.

Pre-medications for carboplatin (prophylaxis for infusion reactions):

- There is insufficient evidence that routine prophylaxis with pre-medications reduce infusion reaction (IR) rates.
- Corticosteroids and H1-receptor antagonists ± H2-receptor antagonists **may** reduce IR rates for some patients (e.g. gynecological patients with a PFI >12 months or a history of drug allergy who are receiving carboplatin starting from the 7th cycle) but no optimal pre-medication regimen has been established.

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

Other Supportive Care:

- Avoid the use of corticosteroids or immunosuppressants before starting treatment.

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J - Administrative Information

Approximate Patient Visit	3 hours
Pharmacy Workload (average time per visit)	24.003 minutes
Nursing Workload (average time per visit)	49.833 minutes

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K - References

Ando M, Yamauchi H, Aogi K et al. Randomized phase II study of weekly paclitaxel with and without carboplatin followed by cyclophosphamide/ epirubicin/5-fluorouracil as neoadjuvant chemotherapy for stage II/IIIA breast cancer without HER2 overexpression. Breast Cancer Res Treat 2014; 145(2): 401–409.

BC Cancer Protocol Summary for NEOAdjuvant Therapy for Triple Negative Breast Cancer Using Carboplatin and Weekly PACLitaxel Followed by DOXOrubicin and Cyclophosphamide. June 14, 2021.

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

Carboplatin, paclitaxel, and pembrolizumab drug monographs, Ontario Health (Cancer Care Ontario).

Loibl S, O'Shaughnessy J, Untch M et al. Addition of the PARP inhibitor veliparib plus carboplatin or carboplatin alone to standard neoadjuvant chemotherapy in triple-negative breast cancer (BrighTNess): a randomised, phase 3 trial. Lancet Oncol. 2018; 19(4): 497–509.

F Poggio, M Bruzzone, M Ceppi, et al. Platinum-based neoadjuvant chemotherapy in triple-negative breast cancer: a systematic review and meta-analysis. Ann Oncol. 2018 Jul 1;29(7):1497-1508. doi: 10.1093/annonc/mdy127

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

Sikov WM, Berry DA, Perou CM et al. Impact of the addition of carboplatin and/or bevacizumab to neoadjuvant once-per-week paclitaxel followed by dose-dense doxorubicin and cyclophosphamide

on pathologic complete response rates in stage II to III triple-negative breast cancer: cALGB 40603 (Alliance). J Clin Oncol 2015; 33(1): 13–21.

September 2023 Updated the "Administrative Information" section with nursing and pharmacy workload.

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L - Other Notes

Calvert Formula

DOSE (mg) = target AUC X (GFR + 25)

- AUC = product of serum concentration (mg/mL) and time (min)
- GFR (glomerular filtration rate) expressed as measured Creatinine Clearance or estimated from Serum Creatinine (by Cockcroft and Gault method or Jelliffe method)

(Calvert AH, Newell DR, Gumbrell LA, et al, Carboplatin dosage: Prospective evaluation of a simple formula based on renal function. J Clin Oncol, 1989; 7: 1748-1756)

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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.

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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 not intended to constitute or be a substitute for medical advice and should not be relied upon in any such regard. All uses of the Formulary are subject to clinical judgment and actual prescribing patterns may not follow the information provided in the Formulary.

The format and content of the drug monographs, regimen monographs, appendices and symptom management information contained in the Formulary will change as they are reviewed and revised on a periodic basis. The date of 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.

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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