**Regimen Monograph**



## A - Regimen Name

# PACL Regimen

**PACLitaxel**

| | |
|---|---|
| **Disease Site** | Gynecologic - Ovary |
| **Intent** | Palliative |
| **Regimen Category** | **Evidence-Informed :**<br><br>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 of platinum-sensitive recurrent ovarian cancer, when platinum is contraindicated (e.g. due to toxicity)<br>• Treatment of platinum-resistant recurrent ovarian cancer |

back to top

## B - Drug Regimen

| | | | |
|---|---|---|---|
| **PACLitaxel** | 135-175 mg /m² | IV | Day 1 |

back to top

## C - Cycle Frequency

**REPEAT EVERY 21 DAYS**

Until disease progression or unacceptable toxicity

back to top

## D - Premedication and Supportive Measures

**Antiemetic Regimen:** Low

**Other Supportive Care:**

Also refer to CCO Antiemetic Recommendations.

**Pre-medications* (prophylaxis for infusion reaction):**

Pre-Medications for Q3W paclitaxel:

- Dexamethasone 20 mg PO 12-and 6-hours OR Dexamethasone 20 mg IV 30 minutes pre-infusion†
- Diphenhydramine 25-50 mg IV/PO 30-60 minutes pre-infusion
- Ranitidine 50 mg IV OR Famotidine 20 mg IV 30-60 minutes pre-infusion

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

† Oral and IV dexamethasone are both effective at reducing overall IR rates. Some evidence suggests that oral dexamethasone may be more effective for reducing severe reactions; however, adverse effects and compliance remain a concern.

back to top

## E - Dose Modifications

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

**Dosage with toxicity**

| Worst toxicity in previous cycle | Dose of paclitaxel |
|---|---|
| Febrile neutropenia<br>Grade 4 ANC ≥ 5-7 days<br>Grade 4 thrombocytopenia | ↓ by 20%* |
| Grade 3 neurotoxicity or other toxicity | ↓ by 20%* |
| Grade 4 neurotoxicity or other toxicity, any grade cystoid macular edema | Discontinue |
| *Patients should not be retreated with paclitaxel until neutrophils ≥ 1.5 x $10^9$/L (≥ 1.0 x $10^9$/L in AIDS-related Kaposi's sarcoma) and platelet counts ≥ 100 x $10^9$/L and other toxicity has recovered to ≤ grade 2 | |

**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.<br>• Manage the symptoms.<br><br>**Restart:**<br><br>• After symptom resolution, restart with pre-medications ± reduced infusion rate. | • Consider re-challenge with pre-medications and at a reduced infusion rate.<br>• After 2 subsequent IRs, consider replacing with a different taxane. Give intensified pre-medications and reduce the infusion rate.<br>• May consider adding oral montelukast ± oral acetylsalicylic acid. |
| 3 or 4 | • Stop treatment.<br>• Aggressively manage symptoms. | • Re-challenge is discouraged, especially if vital signs have been affected.<br>• Consider desensitization if therapy is necessary.<br>• There is insufficient evidence to recommend substitution with another taxane at re-challenge.<br>• High cross-reactivity rates have been reported. |

**Hepatic Impairment**

Caution and dose reduction advised in patients with moderate to severe hepatic impairment.

Patients with hepatic impairment may be at risk of toxicity, especially severe myelosuppression.

Suggested dose modifications are:

| Bilirubin | | AST/ALT | Dose (% usual dose) |
|---|---|---|---|
| ≤1.25 x ULN | And | 2-10 x ULN | 75% |
| 1.26 to 2.5 x ULN | And | <10 x ULN | 40% |
| 2.6 to 4 x ULN | And | <10 x ULN | 25% |
| >4 x ULN | And/Or | ≥10 x ULN | Consider risk-benefit or Omit |

**Renal Impairment**

No adjustment required.

**Dosage in the Elderly**

No adjustment required, but elderly patients are more at risk for severe toxicity.

back to top

## F - Adverse Effects

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

| Very common (≥ 50%) | Common (25-49%) | Less common (10-24%) | Uncommon (< 10%), but may be severe or life-threatening |
|---|---|---|---|
| • Alopecia (may be | • Diarrhea | • Hypotension | • Arrhythmia |

| | | | |
|---|---|---|---|
| permanent)<br>• Musculoskeletal pain (may be severe)<br>• Neuropathy (may be severe, includes cranial nerves and autonomic) | • Nausea/vomiting<br>• Myelosuppression +/- infection and bleeding (may be severe)<br>• Hypersensitivity (may be severe) | • ECG changes<br>• Mucositis<br>• Edema<br>• Fatigue<br>• ↑ LFTs (may be severe) | • Arterial thromboembolism<br>• Venous thromboembolism<br>• Cardiotoxicity<br>• Injection site reactions<br>• Rash<br>• GI obstruction<br>• GI perforation<br>• Pancreatitis<br>• Secondary malignancy<br>• Encephalopathy<br>• Seizures<br>• Cystoid macular edema<br>• Pneumonitis<br>• Typhlitis<br>• Radiation recall |

back to top

## G - Interactions

Refer to PACLitaxel drug monograph(s) for additional details

- Caution with concurrent use of CYP2C8/3A4 substrates, inhibitors and inducers

back to top

## H - Drug Administration and Special Precautions

Refer to PACLitaxel drug monograph(s) for additional details

### Administration

- In order to minimize patients' exposure to DEHP leaching from PVC bags or sets, use polyolefin or polypropylene infusion bags and polyethylene-lined administration sets (with a 0.22 micron in-line filter).

- Dilute in 500-1000 mL Normal Saline or 5% Dextrose, in a final concentration of 0.3-1.2 mg/mL and infuse over 3 hours.
- Extended infusion of paclitaxel is not recommended as primary prophylaxis to reduce paclitaxel IRs.
- Excessive shaking, agitation, or vibration may induce precipitation and should be avoided.
- Precipitation may rarely occur with infusions longer than 3 hours.

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

**Contraindications:**

- Patients with a history of severe hypersensitivity reactions to paclitaxel or other drugs formulated in Cremophor EL (polyethoxylated castor oil)
- Patients with severe baseline neutropenia ($<1.5 \times 10^9$/L)

**Other Warnings/Precautions:**

- Paclitaxel contains ethanol and is administered with agents such as antihistamines which cause drowsiness. Patients should be cautioned regarding driving and the use of machinery.

**Pregnancy/Lactation:**

- Paclitaxel is not recommended for use in pregnancy.
- Adequate contraception should be used by both sexes during treatment, and for at least **6 months** after the last dose.
- Breastfeeding is not recommended.
- Fertility effects: Yes

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.

Recommended Clinical Monitoring

- CBC; Baseline and before each visit
- Liver function tests; Baseline and before each cycle
- Renal function tests; Baseline and as clinically indicated
- Blood pressure and pulse; Per usual institutional protocol; also during infusion (more frequently during the first hour)
- Ophthalmology if visual impairment; As clinically indicated
- Continuous cardiac monitoring in patients who developed serious conduction abnormalities; During subsequent infusions
- Clinical assessment of bleeding, infection, diarrhea, musculoskeletal, neurologic (sensory), hypersensitivity, respiratory, thromboembolism; At each visit

- Grade toxicity using the current NCI-CTCAE (Common Terminology Criteria for Adverse Events) version

back to top

## J - Administrative Information

| | |
|---|---|
| Approximate Patient Visit | 5 hours |
| Pharmacy Workload (average time per visit) | 18.663 minutes |
| Nursing Workload (average time per visit) | 54.833 minutes |

back to top

## K - References

Buda A. Floriani I. Rossi R, et al. Randomised controlled trial comparing single agent paclitaxel vs epidoxorubicin plus paclitaxel in patients with advanced ovarian cancer in early progression after platinum-based chemotherapy: An Italian Collaborative Study from the 'Mario Negri' Institute, Milan, G.O.N.O. (Gruppo Oncologico Nord Ovest) group and I.O.R. (Istituto Oncologico Romagnolo) group. Br J Cancer 2004;90(11):2112-17.

Cantu MG, Buda A, Parma G, et al. Randomized controlled trial of single-agent paclitaxel versus cyclophosphamide, doxorubicin, and cisplatin in patients with recurrent ovarian cancer who responded to first-line platinum-based regimens. J Clin Oncol 2002;20:1232-7.

Bolis G, Parazzini F Scarfone G, et al. Paclitaxel vs epidoxorubicin plus paclitaxel as second-line therapy for platinum-refractory and –resistant ovarian cancer. Gynecol Oncol 1999 Jan;72(1):60-4.

Kwon JS, Elit L, Finn M et al. A comparison of two prophylactic regimens for hypersensitivity reactions to paclitaxel. Gynecol Oncol 2002 Mar; 84(3): 420-5.

O'Byrne KJ, Bliss P, Graham JD, et al. A phase III study of Doxil/Caelyx versus paclitaxel in platinum-treated, taxane-naive relapsed ovarian cancer [abstract 808]. Proc Soc Clin Oncol. 2002;21:203a.

Paclitaxel drug monograph, Cancer Care Ontario.

Piccart MJ, Green JA, Jimenez Lacave A, et al. Oxaliplatin or paclitaxel in patients with platinum-pretreated advanced ovarian cancer : a randomized phase II study of the European organization for research and treatment of cancer gynecology group. J Clin Oncol 2000;18(6):1193-202.

ten Bokkel Huinink W, Lane SR, Ross GA. Long-term survival in a phase III, randomised study of topotecan versus paclitaxel in advanced epithelial ovarian carcinoma. Ann Oncol 2004;15(1):100-3.

Torri V, Floriani I, Tinazzi A, et al. Randomized trial comparing paclitaxel + doxorubicin versus paclitaxel as second line therapy for advanced ovarian cancer patients in early progression after platinum based chemotherapy. Proc Soc Clin Oncol. 2000(19):A1506.

**PEBC Advice Documents or Guidelines**

- Systemic Therapy for Recurrent Epithelial Ovarian Cancer

**June 2021** removed paclitaxel NDFP funding info

back to top

## 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 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.*

*While care has been taken in the preparation of the information contained in the Formulary, 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.*

*CCO and the Formulary’s content providers shall have no liability, whether direct, indirect, consequential, contingent, special, or incidental, related to or arising from the information in the Formulary or its use thereof, whether based on breach of contract or tort (including negligence), and even if advised of the possibility thereof. Anyone using the information in the Formulary does so at his or her own risk, and by using such information, agrees to indemnify CCO and its content providers from any and all liability, loss, damages, costs and expenses (including legal fees and expenses) arising from such person’s use of the information in the Formulary.*

back to top