Regimen Monograph

A - Regimen Name

PACL(W) Regimen

PACLitaxel (weekly)

Disease Site	Lung - Non-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.

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B - Drug Regimen

PACLitaxel	80 mg /m²	IV	Days 1, 8, 15

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C - Cycle Frequency

REPEAT EVERY 28 DAYS

Until disease progression or unacceptable toxicity

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D - Premedication and Supportive Measures

Antiemetic Regimen: Low

Other Supportive Care:

Also refer to CCO Antiemetic Recommendations.

Pre-medications* (prophylaxis for infusion reaction):

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.

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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

Worst toxicity in previous cycle	Dose of paclitaxel
Febrile neutropenia Grade 4 ANC ≥ 5-7 days 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, 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. • Manage the symptoms. **Restart:** • After symptom resolution, restart with pre-	• Consider re-challenge with pre-medications and at a reduced infusion rate. • After 2 subsequent IRs, consider replacing with a different taxane. Give intensified pre-medications and reduce the infusion rate. • May consider adding oral montelukast ± oral acetylsalicylic acid.

	medications ± reduced infusion rate.	
3 or 4	• Stop treatment. • Aggressively manage symptoms.	• Re-challenge is discouraged, especially if vital signs have been affected. • Consider desensitization if therapy is necessary. • There is insufficient evidence to recommend substitution with another taxane at re-challenge. • 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 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	<10x ULN	40%
2.6 to 4 x ULN	And	<10x 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.

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

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G - Interactions

Refer to PACLitaxel drug monograph(s) for additional details

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

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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 Normal Saline or 5% Dextrose, in a final concentration of 0.3-1.2 mg/mL and infuse over 3 hours.
- For weekly dosing, may be infused over 1 hour - mix in 250 mL bag as above (not approved by manufacturer).
- 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 x 10^9/L; < 1 x 10^9/L for patients with AIDS-related Kaposi's)

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

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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.

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

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J - Administrative Information

Approximate Patient Visit	2 hours
Pharmacy Workload (average time per visit)	18.663 minutes
Nursing Workload (average time per visit)	39.833 minutes

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K - References

Ceresoli GL, Gregorc V, Cordio S, et al. Phase II study of weekly paclitaxel as second-line therapy in patients with advanced non-small cell lung cancer. Lung Cancer 2004;44(2):231-9.

Fidias P, Supko JG, Martins R, et al. A phase II study of weekly paclitaxel in elderly patients with advanced non-small cell lung cancer. Clin Cancer Res 2001;7:3942-3949.

Juan O, Albert A, Villarroya T, et al. Weekly paclitaxel for advanced non-small cell lung cancer patients not suitable for platinum-based therapy. Neoplasma. 2003;50(3):204-9.

Tandon N, Noronha V, Prabhash K. Metronomic weekly paclitaxel in metastatic or recurrent non-small cell lung cancers. J Clin Oncol 31, 2013 (suppl; abstr e19095).

Yasuda K, Igishi T, Kawasaki Y, et al. Phase II study of weekly paclitaxel in patients with non-small cell lung cancer who have failed previous treatments. Oncology 2004;66(5):347-52.

Paclitaxel drug monograph, Cancer Care Ontario.

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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

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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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