Regimen Monograph

A - Regimen Name

PACL(W) Regimen

PACLitaxel (weekly)

Disease Site	Sarcoma Soft Tissue
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	Second-line treatment of patients with metastatic or advanced angiosarcoma.

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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

For a usual total of 6 cycles unless disease progression or unacceptable toxicity occurs.

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D - Premedication and Supportive Measures

Antiemetic Regimen: Low

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.

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

Dose levels: 80 mg/m², 70 mg/m², 60 mg/m². Dose re-escalations are not allowed. Discontinue treatment if toxicity recurs after 2 dose reductions.

Worst toxicity in previous cycle	Dose of paclitaxel
Febrile neutropenia Grade 4 ANC ≥ 5-7 days Grade 4 thrombocytopenia	↓ by 1 dose level*
Grade 3 neurotoxicity, mucositis, or other toxicity	↓ by 1 dose level*
Grade 4 neurotoxicity or other toxicity, any grade cystoid macular edema	Discontinue
*Patients should not be retreated with paclitaxel until neutrophils ≥ 1 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-medications ± reduced infusion rate.	• 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.
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.

The following is suggested (adapted from Floyd et al):

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	50%
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 dose 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 (may be severe) • Nausea/vomiting • Myelosuppression +/- infection and bleeding (may be severe) • Hypersensitivity (may be severe)	• Hypotension • ECG changes • Mucositis (may be severe) • 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.

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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 an in-line filter no greater than 0.22 microns).
- Dilute in Normal Saline or 5% Dextrose, in a final concentration of 0.3-1.2 mg/mL.
- 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 ($<1.5 \times 10^9/L$)

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:

- 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: Probable
  Documented in animal studies

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

Casper ES, Waltzman RJ, Schwartz GK, et al. Phase II Trial of Paclitaxel in Patients with Soft-Tissue Sarcoma. Cancer Investigation 1998; 16(7): 442-446.

Fata F, O'Reilly E, Ilson D, et al. Paclitaxel in the Treatment of Patients with Angiosarcoma of the Scalp or Face. Cancer 1999;86:2034–7.

Floyd J, Mirza I, Sachs B, Perry MC. Hepatotoxicity of chemotherapy. Semin Oncol. 2006 Feb;33(1):50-67.

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

Penal N, Bui BN, Bay JO, et al. Phase II Trial of Weekly Paclitaxel for Unresectable Angiosarcoma: The ANGIOTAX Study. J Clin Oncol 2008; 26(32) 5269-74.

Schlemmer M, Riechardt P, Verweij J, et al. Paclitaxel in patients with advanced angiosarcomas of soft tissue: A retrospective study of the EORTC soft tissue and bone sarcoma group. Eur J Cancer 2008; 44: 2433-6.

November 2024 Updated Dose modifications, Adverse effects, 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.

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