Regimen Monograph

A - Regimen Name

PACL Regimen

PACLitaxel

Disease Site	Gastrointestinal Esophagus Gastric / Stomach
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	Treatment of metastatic or recurrent adenocarcinoma or squamous cell gastroesophageal cancer

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B - Drug Regimen

PACLitaxel	135-175 mg /m²	IV	Day 1

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C - Cycle Frequency

REPEAT EVERY 21 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):

- 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.

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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	Discontinue

grade cystoid macular edema	
*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. • 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.

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.

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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 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 x 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

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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	5 hours
Pharmacy Workload (average time per visit)	18.663 minutes
Nursing Workload (average time per visit)	54.833 minutes

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K - References

Paclitaxel drug monograph, Cancer Care Ontario.

Ajani JA, Ilson DH, Daugherty K, et al. Activity of taxol in patients with squamous cell carcinoma and adenocarcinoma of the esophagus. J Natl Cancer Inst. 1994 Jul 20;86(14):1086-91.

Anderson SE, O'Reilly EM, Kelsen DP, et al. Phase II trial of 96-hour paclitaxel in previously treated patients with advanced esophageal cancer. Cancer Invest 2003;21(4):512-6.

PEBC Advice Documents or Guidelines

- Systemic Therapy for Advanced Gastric and Gastro-Esophageal Carcinoma

November 2022 Added PEBC guideline link

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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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