Regimen Monograph

A - Regimen Name

CISPPACL Regimen

PACLitaxel-CISplatin

Disease Site	Gynecological - Cervix
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	For the treatment of patients with advanced (stage IVB), recurrent or persistent cervical cancer.

back to top

B - Drug Regimen

PACLitaxel [1] (Round to nearest 3 mg)	175 mg /m²	IV over 3 hours	Day 1
CISplatin (Round to nearest 1 mg)	50 mg /m²	IV	Day 1 (after paclitaxel)

back to top

C - Cycle Frequency

REPEAT EVERY 21 DAYS

For a usual total of 6 cycles unless disease progression or unacceptable toxicity occurs. (In clinical trials, patients who continued to respond to treatment may continue beyond six cycles.)

back to top

D - Premedication and Supportive Measures

Antiemetic Regimen: Moderate

Other Supportive Care:

- Paclitaxel: Patients should be pretreated with a corticosteroid as well as an antihistamine and a H2 blocker: For example:
- DEXAMETHASONE 20mg PO 12 & 6 hours or 20mg IV 30 minutes before paclitaxel
- DIPHENHYDRAMINE 50mg IV 30 minutes before paclitaxel
- RANITIDINE 50mg IV 30 minutes before paclitaxel

Standard regimens for Cisplatin premedication and hydration should be followed. Refer to Cisplatin monograph

Also refer to CCO Antiemetic Summary

back to top

E - Dose Modifications

Doses should be modified according to the protocol by which the patient is being treated. The following recommendations have been adapted from clinical trials or product monographs and could be considered.

(Continued on next page)

Dosage with toxicity

Dose levels for paclitaxel: 175, 135, 110, 90 mg/m^2
Dose levels for cisplatin: 50, 37.5, 25 mg/m^2

Worst Toxicity / Counts (x 10^9/L) in previous cycle		**Worst Toxicity / Counts (x 10^9/L) in previous cycle**	**Paclitaxel (% previous dose)**	**Cisplatin (% previous dose)**
ANC < 1.5	or	Platelets < 100	Hold*	Hold*
Febrile Neutropenia Or ANC < 0.5 for ≥ 5-7 d		Thrombocytopenic bleeding Or Platelets < 25	↓ 1 dose level and consider GCSF use next cycle	No change
ANC ≥ 1.5	or	Platelets ≥ 100	No change	No change
Grade 2 neurotoxicity/ototoxicity			↓ 2 dose levels	↓ 2 dose levels
Grade 3 or 4 neurotoxicity/ototoxicity			Discontinue	Discontinue
Grade 3 related non-hematological/organ			↓ 1 dose level	↓ 1 dose level
Grade 3 hepatotoxicity			Discontinue	No change
Grade 4 related non-hematological/organ			Discontinue	Discontinue†

* Do not start new cycle until toxicities have recovered to ≤ grade 2, platelets ≥ 100 x 10^9/L, ANC ≥ 1.5 x 10^9/L, and creatinine ≤ grade 1 (if grade 2 consider reducing cisplatin dose by 50%).

† ↓ 1 dose level for grade 4 nausea/vomiting

Hepatic Impairment

Bilirubin		**AST/ALT**	**PACLitaxel (% previous dose)**	**CISplatin (% previous dose)**
1-2 x ULN			no change	no change
>2-3 x ULN	or	2-5 x ULN	↓ 1 dose level	no change

>3 x ULN	or	> 5 x ULN	discontinue	no change or discontinue

Renal Impairment

In general, renal function should have normalized before patients are retreated. If continued treatment is considered to be mandatory, the following dose modifications could be considered at the physician's discretion:

Creatinine Clearance (mL/min)	**PACLitaxel (% previous dose)**	**CISplatin (% previous dose)**
>60	no change	no change
46-60	no change	75%
30-45	no change	50%
<30	no change	Discontinue

back to top

F - Adverse Effects

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

Most Common Side Effects	Less Common Side Effects, but may be Severe or Life Threatening
• Nausea and vomiting • Alopecia • Nephrotoxicity (may be severe) • Electrolyte abnormalities • Neurotoxicity and ototoxicity (may be severe) • Myelosuppression ± infection / bleeding (may be severe) • Hypersensitivity (may be severe) • Diarrhea • Edema • ↑ LFTs (may be severe)	• Arterial thromboembolism • Venous thromboembolism • Arrhythmia • Hemolytic uremic syndrome, vasculitis • Seizures • Hemolysis • Cardiotoxicity • GI perforation/obstruction • Pancreatitis • Pneumonitis

back to top

G - Interactions

Refer to PACLitaxel, CISplatin drug monograph(s) for additional details

back to top

H - Drug Administration and Special Precautions

Refer to PACLitaxel, CISplatin drug monograph(s) for additional details

back to top

I - Recommended Clinical Monitoring

Recommended Clinical Monitoring

- CBC; baseline and before each cycle
- Electrolytes, including magnesium, phosphate and calcium; baseline and regular
- Liver function tests; baseline and regular
- Renal function tests; baseline and regular
- Clinical toxicity assessment (infection, bleeding, musculoskeletal, cardiac, arrhythmia, thromboembolism, hypersensitivity, flu-like symptoms, nausea/vomiting, neurotoxicity, ototoxicity); at each visit
- Grade toxicity using the current NCI-CTCAE (Common Terminology Criteria for Adverse Events) version

Suggested Clinical Monitoring

- Audiogram; baseline and periodic

back to top

J - Administrative Information

Approximate Patient Visit	7-8 hours

back to top

K - References

Cisplatin and paclitaxel drug monographs, Cancer Care Ontario.

Moore DH, Blessing JA, McQuellon RP, et al. Phase III study of cisplatin with or without paclitaxel in stage IVB, recurrent, or persistent squamous cell carcinoma of the cervix: A gynecologic oncology group study. J Clin Oncol 2004;22:3113-9.

Monk BJ, Sill MW, McMeekin DS, et al. Phase III trial of four cisplatin-containing doublet combinations in stage IVB, recurrent, or persistent cervical carcinoma: a gynecologic oncology group study. J Clin Oncol 2009;27:4649-55.

Tewari KS, Sill MW, Long HJ 3rd, et al. Improved survival with bevacizumab in advanced cervical cancer. N Engl J Med. 2014 Feb 20;370(8):734-43.

PEBC Advice Documents or Guidelines

- Chemotherapy for Recurrent, Metastatic, or Persistent Cervical Cancer

April 2016 updated drug regimen

back to top

M - Disclaimer

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