Regimen Monograph

A - Regimen Name

CISPPACL(IP) Regimen

PACLitaxel-CISplatin (intraperitoneal)

Disease Site	Gynecologic - Ovary
Intent	Adjuvant
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	Post-operative regimen for patients with stage III optimally debulked (≤1 cm residual disease) epithelial ovarian cancer, primary peritoneal, or fallopian tube carcinoma, who did not receive neoadjuvant chemotherapy

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B - Drug Regimen

PACLitaxel	135 mg /m²	IV	Day 1
CISplatin	75 to 100 mg /m²	Intraperitoneal	Day 1
PACLitaxel	60 mg /m²	Intraperitoneal	Day 8

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C - Cycle Frequency

REPEAT EVERY 21 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: High (D1)
Low (D8)

Febrile Neutropenia Risk: Low

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 before Paclitaxel OR 20 mg IV 30 minutes before Paclitaxel
- DIPHENHYDRAMINE 50mg IV 30 minutes before Paclitaxel
- RANITIDINE 50mg IV 30 minutes before Paclitaxel
- Oral hydration is strongly encouraged; poorly hydrated patients may need more IV hydration

Also refer to CCO Antiemetic Recommendations.

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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 may be considered.

Dosage with toxicity

Hematologic Toxicities

Refer to Appendix 6 for general recommendations.

Neurotoxicity Grade 3 or 4*: **REDUCE** Paclitaxel to **80%** dose

* Dose of Cisplatin was reduced with grade 2 peripheral neuropathy in the pivotal trial. (Armstrong et al. NEJM 354:34-43, 2006)

Hepatic Impairment

Bilirubin	Dose
1. If Bilirubin 2-4 x ULN	Give **MAXIMUM DOSE** of Paclitaxel of **135mg/m^2**
2. If Bilirubin > 4 x ULN	**OMIT** Paclitaxel dose or Give **MAXIMUM DOSE** of Paclitaxel **50mg/m^2**

Renal Impairment

Creatinine Clearance or Serum Creatinine	Dose
1. If CrCl = 0.5-1.0mL/sec or Serum Creatinine=136-185µmol/L	**REDUCE** Cisplatin* to **50%** dose
2. If CrCl < 0.5mL/sec or Serum Creatinine>185µmol/L	**OMIT** Cisplatin* dose

*Upon the discretion of the prescriber, less dose reduction may be suggested. See Cisplatin drug monograph

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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, vomiting • Alopecia • Neuropathy (may be severe) • Musculoskeletal pain • Nephrotoxicity (may be severe) • Hearing impaired • Myelosuppression +/- infection, bleeding • Diarrhea • Increased LFTs • Mucositis • Fatigue • Abnormal electrolytes	• ECG changes • Hypersensitivity • Arterial thromboembolism • Venous thromboembolism • GI obstruction/perforation • Hemolytic uremic syndrome • Pancreatitis • Pnuemonitis • Vasculitis • Cystoid macular edema

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G - Interactions

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

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H - Drug Administration and Special Precautions

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

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I - Recommended Clinical Monitoring

Recommended Clinical Monitoring

- Clinical toxicity (including local toxicity, neurotoxicity, ototoxicity, abdominal pain) assessment; at each visit
- CBC; baseline and before each cycle. Interim counts should be done in first cycle and repeated if dose modifications necessary.
- Baseline and regular liver and renal function (including electrolytes and magnesium) tests.

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

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J - Administrative Information

Approximate Patient Visit	7 to 8 hours
Pharmacy Workload (average time per visit)	44.749 minutes
Nursing Workload (average time per visit)	106.5 minutes

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K - References

Armstrong DK, Bundy B, Wenzel L, et al: Intraperitoneal cisplatin and paclitaxel in ovarian cancer. N Engl J Med 354:34-43, 2006

Cisplatin and paclitaxel drug monographs, Cancer Care Ontario.

Markham M, Walker J. Intraperitoneal Chemotherapy of Ovarian Cancer: A Review, With a Focus on Practical Aspects of Treatment. JCO 24(6): February 20th, 2006 (Early Publication).

Markman M, Bundy BN, Alberts DS, et al: Phase III trial of standard-dose intravenous cisplatinplus paclitaxel versus moderately high-dose carboplatin followed by intravenous paclitaxel and intraperitoneal cisplatin in small-volume stage III ovarian carcinoma: An intergroup study of the Gynecologic Oncology Group, Southwestern Oncology Group, and Eastern Cooperative Oncology Group. J Clin Oncol 19:1001-1007, 2001

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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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