Regimen Monograph

A - Regimen Name

CISPPACL Regimen

PACLitaxel-CISplatin

Disease Site

Gynecologic - Ovary

Intent

Adjuvant
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

Alternative to carboplatin-paclitaxel for:

- first-line postoperative treatment for stage II-IV epithelial ovarian cancer, fallopian tube or primary peritoneal cancers
- the treatment of platinum-sensitive recurrent ovarian, fallopian tube or primary peritoneal cancers (with a progression-free interval ≥ 6 months since the last line of platinum-based therapy)

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B - Drug Regimen

PACLitaxel	175 mg /m²	IV over 3 hours (give first)	Day 1
CISplatin	75 mg /m²	IV	Day 1

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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

Febrile Neutropenia Risk: Low

Other Supportive Care:

- 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 Summary

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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

Hematologic Toxicities

Refer to Appendix 6 for general recommendations.

Neurotoxicity

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

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

Cisplatin: 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	Cisplatin (% previous dose)
46-60	75%
30-45	50%
<30	Discontinue

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F - Adverse Effects

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

(Continued on next page)

Most Common Side Effects	Less Common Side Effects, but may be Severe or Life-Threatening
• Nausea and vomiting • Alopecia • Neurotoxicity and ototoxicity • Nephrotoxicity (may be severe) • Myelosuppression +/- infection, bleeding • Fatigue, edema • Hypersensitivity reactions (may be severe) • Musculoskeletal pain • Diarrhea • Increased LFTs	• Arrhythmia • Cardiotoxicity • Arterial thromboembolism • Venous thromboembolism • GI obstruction/perforation • Pancreatitis • Pneumonitis • 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) 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 hours

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K - References

Cisplatin and paclitaxel drug monographs, Cancer Care Ontario.

Kwon JS, Elit L, Finn M et al. A comparison of two prophylactic regimens for hypersensitivity reactions to paclitaxel. Gynecol Oncol 2002 Mar; 84(3): 420-5.

McGuire WP, Hoskins WJ, Brady MF, et al. Cyclophosphamide and cisplatin compared with paclitaxel and cisplatin in patients with stage III and stage IV ovarian cancer. N Engl J Med, 1996; 334: 1-6

Piccart MJ, Bertelsen K, James K , et al. Randomized intergroup trial of cisplatin-paclitaxel versus cisplatin – cyclophosphamide in women with advanced epithelial ovarian cancer: Three year results. J National Cancer Institute, 2000; 92: 699-708.

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L - Other Notes

The definitive study used 24-hour infusions of Paclitaxel. This schedule is often changed to a 3-hour infusion schedule to facilitate ambulatory treatment and to minimize myelosuppression, but at the possible cost of increased neurotoxicity.

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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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