**Regimen Monograph**



## A - Regimen Name

# GEMCPACL Regimen

**Gemcitabine-PACLitaxel**

| | |
|---|---|
| **Disease Site** | Genitourinary - Testis |
| **Intent** | Palliative |
| **Regimen Category** | **Evidence-Informed :**<br><br>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 germ cell cancer in patients:<br>• with disease not amenable to cure with either surgery or chemotherapy, or<br>• who failed initial cisplatin combination therapy with curative intent and/or failed one “salvage” regimen<br>• This regimen has also been studied in patients who failed high dose chemotherapy with tandem transplantation |

back to top

## B - Drug Regimen

| | | | |
|---|---|---|---|
| **PACLitaxel** | 100 mg /m² | IV | days 1, 8 and 15 |
| **gemcitabine** | 1000 mg /m² | IV | days 1, 8 and 15 |

back to top

## C - Cycle Frequency

**REPEAT EVERY 28 DAYS**

For a maximum of 6 cycles unless disease progression or unacceptable toxicity occurs

back to top

## D - Premedication and Supportive Measures

**Antiemetic Regimen:** 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 or 20mg IV 30 minutes before paclitaxel
- DIPHENHYDRAMINE 50mg IV 30 minutes before paclitaxel
- RANITIDINE 50mg IV 30 minutes before paclitaxel

Consider the use of filgrastim based on local guidelines.

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**

*Day 1:*

| **Worst Toxicity / Counts (x $10^9$/L) in previous cycle** | | **Worst Toxicity / Counts (x $10^9$/L) in previous cycle** | **PACLitaxel (% previous dose)** | **gemcitabine (% previous dose)** |
|---|---|---|---|---|
| ANC <1.5 | Or | Platelet < 75 | Hold * | |
| Febrile Neutropenia<br>Or<br>ANC < 0.5 for ≥ 5-7 d | Or | Thrombocytopenic bleeding<br>Or<br>Platelets < 25 | Hold *, then 75% | |
| ANC ≥ 1.5 | And | Platelet ≥ 75 | 100% | |
| Grade 3 related organ / non-hematologic, or omitted day 8/15 doses in multiple prior cycles | | | 75% * for suspect drug(s) | |
| Grade 4 related organ / non-hematologic | | | 50%* for suspect drugs or Discontinue | |
| Pneumonitis, Hemolytic Uremic Syndrome (HUS), Stevens-Johnson syndrome (SJS), Toxic epidermal necrolysis (TEN), Capillary Leak Syndrome (CLS) | | | Discontinue | |

*Do not start new cycle until toxicities have recovered to ≤ grade 2, platelets ≥ 75 x $10^9$/L, and ANC ≥ 1.5 x $10^9$/L.

*Days 8 or 15:*

| Toxicity on Day 8 or Day 15 | | Toxicity on Day 8 or Day 15 | PACLitaxel # (% Day 1 dose) | gemcitabine # (% Day 1 dose) |
|---|---|---|---|---|
| ANC ≥ 1.5 | And | Platelet ≥ 75 | 100% | |
| ANC 1 - 1.49 | And/or | Platelets 50 - 74.9 | 75% | |
| ANC 0.5 - 0.99 | And/or | Platelets 25 - 49.9 | 50% | |
| ANC < 0.5 | And/or | Platelets < 25 | OMIT | |
| Grade 3/4 hepatotoxicity | And/or | Grade 4 other organ/non-hematological | OMIT | OMIT (if myalgia alone, 100%) |
| Grade 2 hepatotoxicity | And/or | Grade 3 myalgia or other organ/non-hematological | 50% * | 50% * (if myalgia alone, 100%) |
| Grade 4 nausea/vomiting | And/or | Other grade 2 organ/non-hematological toxicity | 75% * | 75% * |
| Pneumonitis<br>HUS<br>SJS<br>TEN<br>CLS | | | Discontinue | |

*Do not administer until toxicities have recovered to ≤ grade 2.
#Doses of either drug omitted for toxicity or missed were not given at a later time. If day 8 is omitted, continue the cycle with one dose not given. If day 15 is omitted, this is considered the "rest week" and the following week would be considered as day 1 of a new 21-day cycle.

*Paclitaxel - Hypersensitivity:*

- **For mild symptoms** (e.g., mild flushing, rash, pruritus), attempt to complete the infusion under close supervision.
- **For moderate symptoms** (e.g., moderate rash, flushing, mild dyspnea, chest discomfort, mild hypotension),
  - Stop the paclitaxel infusion and give diphenhydramine 25-50 mg IV and methylprednisolone 125 mg IV.
  - Once symptoms have resolved, resume paclitaxel infusion at a rate of 10% of original rate for 15 minutes, then at 25% of original rate for 15 minutes, and if no further symptoms develop, continue at original rate until infusion is complete.
- **For severe symptoms** (e.g., one or more of: respiratory distress requiring treatment,

generalized urticaria, angioedema, hypotension requiring therapy),
- Stop the paclitaxel infusion; give diphenhydramine and methylprednisolone as above. Use epinephrine or bronchodilators if indicated.
- Do not rechallenge with paclitaxel.

**Hepatic Impairment**

| Bilirubin and or AST/ALT | PACLitaxel | Gemcitabine |
|---|---|---|
| 2-4 x ULN | Give Maximum dose of **135mg/m$^2$** | Caution; no specific recommendations found |
| > 4 x ULN | OMIT dose or Give Maximum dose of **50mg/m$^2$** | Consider dose reduction; no specific recommendations found |

**Renal Impairment**

Gemcitabine should be used with caution in patients with renal impairment. Patients with pre-existing renal impairment should be monitored closely for hemolytic uremic syndrome.

Paclitaxel: No dose adjustment required.

back to top

## F - Adverse Effects

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

| Most Common Side Effects | Less Common Side Effects, but may be Severe or Life-Threatening |
|---|---|
| • Myelosuppression ± infection or bleeding (may be severe)<br>• Neuropathy (may be severe)<br>• Diarrhea, mucositis<br>• Edema & proteinuria | • Arrhythmia, cardiotoxicity<br>• Arterial, venous thromboembolism<br>• Pancreatitis, GI perforation, obstruction |

| | |
|---|---|
| • Nausea and vomiting<br>• Hypersensitivity (may be severe)<br>• Musculoskeletal pain<br>• Reproductive risk<br>• Fatigue, flu-like symptoms<br>• Rash (may be severe)<br>• ↑ LFTs (may be severe)<br>• Alopecia | • Secondary malignancies<br>• Pneumonitis/ARDS<br>• Capillary leak syndrome<br>• Hemolytic-uremic syndrome<br>• Vasculitis |

back to top

## G - Interactions

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

back to top

## H - Drug Administration and Special Precautions

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

back to top

## 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; at each visit
- Liver function tests; baseline and regular
- Renal function tests; baseline and regular
- Blood pressure and pulse rate monitoring during paclitaxel infusion, cardiac monitoring with prior arrhythmia
- Clinical assessment of infection, bleeding, flu-like symptoms, fatigue, dyspnea, rash, musculoskeletal, neuropathy, hypersensitivity; at each visit

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

Suggested Clinical Monitoring

INR for patient receiving warfarin; Baseline and regular
Renal function tests (AIDS related Kaposi's sarcoma); Baseline and regular
Urinalysis; Baseline and regular

back to top

## J - Administrative Information

| | |
|---|---|
| Approximate Patient Visit | 3 hours |
| Pharmacy Workload (average time per visit) | 31.018 minutes |
| Nursing Workload (average time per visit) | 44.833 minutes |

back to top

## K - References

Einhorn LH, Brames MJ, Juliar B, et al. Phase II study of paclitaxel plus gemcitabine salvage chemotherapy for germ cell tumors after progression following high-dose chemotherapy with tandem transplant. J Clin Oncol. 2007 Feb 10;25(5):513-6.

Gemcitabine and paclitaxel drug monographs, Cancer Care Ontario.

Hinton S, Catalano P, Einhorn LH, et al. Phase II study of paclitaxel plus gemcitabine in refractory germ cell tumors (E9897): a trial of the Eastern Cooperative Oncology Group. J Clin Oncol 2002;20(7):1859-63.

Mulherin BP, Brames MJ, Einhorn LH, et al. Long-term survival with paclitaxel and gemcitabine for germ cell tumors after progression following high-dose chemotherapy with tandem transplant. Am J Clin Oncol 2015;38(4):373-6.

**January 2018** aligned dosing with QBP

back to top

## M - Disclaimer

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***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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back to top