Regimen Monograph

Regimen Name | Drug Regimen | Cycle Frequency | Premedication and Supportive Measures | Dose Modifications | Adverse Effects | Interactions | Drug Administration and Special Precautions | Recommended Clinical Monitoring | Administrative Information | References | Other Notes | Disclaimer

A - Regimen Name

GDCRBP Regimen

gemcitabine-dexamethasone-CARBOplatin

Disease Site	Hematologic - Lymphoma - Hodgkin Hematologic - Lymphoma - Non-Hodgkin's Intermediate Grade
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 relapsed or refractory non-Hodgkin's or Hodgkin's lymphoma in transplant ineligible patients who are unable to receive or tolerate cisplatin.
Supplementary Public Funding	**dexamethasone** ODB - General Benefit (dexamethasone) (ODB Formulary)

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B - Drug Regimen

gemcitabine	1000 mg /m²	IV	Days 1 and 8
dexamethasone	40 mg	PO	Days 1 to 4
CARBOplatin	AUC 5	IV	Day 1

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C - Cycle Frequency

REPEAT EVERY 21 DAYS

After 2-3 cycles, responding patients may be considered for high-dose chemotherapy and autologous stem cell transplant.

Patients with stable disease who were not candidates for stem cell transplant or patients who had any response after 2-3 cycles of GDCRBP may receive up to 6 cycles of treatment.

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D - Premedication and Supportive Measures

Antiemetic Regimen: Moderate + NK1 antagonist (Carboplatin AUC ≥ 5) (D1)
Low (D8)

Other Supportive Care:

Also refer to CCO Antiemetic Recommendations.

Consider growth factor support and antibiotic prophylaxis for febrile neutropenia, if required.

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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. Patients should have ANC ≥ 1.5 x 10^9/L and platelets ≥ 100 x 10^9/L prior to starting therapy.

Dosage with toxicity

Suggested dose modifications on Day 1 of cycle:

Worst Toxicity in Previous Cycle			Gemcitabine	Carboplatin
Non-hematologic		**Hematologic**	**% Full Dose***	**% Full dose***
Grade 3	or	Febrile neutropenia, thrombocytopenic bleeding	75%	75%
Grade 4 or Day 8 holds on > 1 cycle			Discontinue	Discontinue
• Pneumonitis • Hemolytic Uremic Syndrome (HUS) • Stevens-Johnson syndrome (SJS) • Toxic epidermal necrolysis (TEN) • Capillary Leak Syndrome (CLS) • Posterior reversible encephalopathy syndrome (PRES)			Discontinue	Discontinue

*Do not start new cycle until ANC ≥ 1.5, platelets ≥ 100 and non-hematologic toxicity ≤ grade 2

Suggested dose modifications on Day 8 of cycle:

Non-hematologic		Hematologic			Gemcitabine % Full Dose
		ANC (x 10^9/L)		**Platelets (x 10^9/L)**	
≤ grade 2	and	≥ 1.0	and	≥ 50	100%
≤ grade 2	and	0.5-1.0	or	50-100	↓ to 75%*
grade 3 or 4	or	< 0.5	or	< 50	Omit*

Pneumonitis HUS SJS TEN CLS or PRES		-		-	Discontinue

*Subsequent cycles may proceed at full dose if ANC ≥ 1.0, platelets ≥ 50, non-hematological toxicity ≤ grade 2

Hepatic Impairment

Bilirubin		**AST/ALT**	**Carboplatin**	**Gemcitabine**
2-3 x ULN	or	> 3 x ULN	No dose adjustment required	Use with caution; no specific recommendation found.
> 3 x ULN	or	> 5 x ULN		Discontinue or reduce dose

Renal Impairment

Creatinine Clearance (ml/min)	**Carboplatin**	**Gemcitabine**
20 - 50	Use Calvert or Chatelut formula	Use with caution; no specific recommendation found.
< 20	Discontinue	Discontinue

Dosage in the Elderly

For gemcitabine, clearance is lower in the elderly but no dose adjustment needed. For carboplatin, caution should be exercised and dose reduction considered as elderly patients may have more severe myelosuppression and neuropathy.

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F - Adverse Effects

Refer to gemcitabine, dexamethasone, CARBOplatin 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
• Increased LFTs (may be severe) • Nausea, vomiting • Myelosuppression +/- infection, bleeding (may be severe)	• Fatigue • Flu-like symptoms • Abnormal electrolytes • Proteinuria • Nephrotoxicity (may be severe) • Rash (may be severe)	• Edema • Musculoskeletal pain • Hearing impairment • Alopecia • Diarrhea • Steroid effects (e.g. weight gain, hyperglycemia, GI irritation, mood changes; may be severe)	• Arterial / venous thromboembolism • Arrhythmia • Cardiotoxicity • Hypersensitivity • Peripheral neuropathy • Capillary leak syndrome • Hemolytic uremic syndrome • Pneumonitis • ARDS • PRES • Vasculitis • Secondary malignancy

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G - Interactions

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

- Avoid nephrotoxic and ototoxic drugs (i.e. aminoglycosides) due to additive effects.
- Carboplatin may reduce serum phenytoin level; monitor closely and adjust the phenytoin dose if required
- Both carboplatin and gemcitabine may increase INR and bleeding risk in patients taking warfarin; monitor closely and adjust INR as needed

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H - Drug Administration and Special Precautions

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

Administration

Gemcitabine:

- May dilute reconstituted drug in normal saline for IV infusion, resulting in a minimum final concentration of at least 0.1 mg/mL.
- Infuse over 30 minutes through free-flowing IV. Infusion time beyond 60 minutes has been shown to increase toxicity.

CARBOplatin:

- Mix in 100mL to 250mL bag (5% Dextrose or Normal Saline); infuse IV over 15 to 60 minutes.
- Incompatible with sets, needles or syringes containing aluminum – leads to precipitation and loss of potency.
- Protect from light.

Dexamethasone:

- Oral tablets for self-administration
- Given with food, preferably in the morning
- Store tablets at room temperature

Contraindications

- Patients who have a hypersensitivity to gemcitabine or platinum-containing compounds
- Patients with severe renal impairment, severe myelosuppression or bleeding

Other warnings/precautions

- Patients with impaired hepatic function, including concurrent liver metastases or a previous history of hepatitis, alcoholism or liver cirrhosis
- Patients with abnormal renal function or who are receiving concomitant nephrotoxic drug
- Patients who have received extensive prior treatment, have poor performance status and those over 65 years of age
- Patients receiving concurrent radiation while receiving full dose gemcitabine should be closely monitored for reactions

Pregnancy and lactation

- These drugs are not recommended 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.

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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 dose
- Liver function tests; Baseline and before each cycle
- Renal function tests and electrolytes; Baseline and before each cycle
- Clinical toxicity assessment of flu-like symptoms, hypersensitivity reactions, infection, bleeding, GI, respiratory, cardiovascular and CNS effects; 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
- Urinalysis; Baseline and regular

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J - Administrative Information

Pharmacy Workload (average time per visit)	28.715 minutes
Nursing Workload (average time per visit)	40.417 minutes

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K - References

Carboplatin and gemcitabine drug monographs, Cancer Care Ontario.

Gopal AK, Press OW, Shustov AR, et al. Efficacy and safety of gemcitabine, carboplatin, dexamethasone, and rituximab in patients with relapsed/refractory lymphoma: a prospective multi-center phase II study by the Puget Sound Oncology Consortium. Leuk Lymphoma. 2010 Aug;51(8):1523-9.

June 2019 Updated emetic risk category

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L - Other Notes

Calvert Formula

DOSE (mg) = target AUC X (GFR + 25)

- AUC = product of serum concentration (mg/mL) and time (min)
- GFR (glomerular filtration rate) expressed as measured Creatinine Clearance or estimated from Serum Creatinine (by Cockcroft and Gault method or Jelliffe method)

(Calvert AH, Newell DR, Gumbrell LA, et al, Carboplatin dosage: Prospective evaluation of a simple formula based on renal function. J Clin Oncol, 1989; 7: 1748-1756)

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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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