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

GDP Regimen

Gemcitabine-Dexamethasone-PLATINOL® (CISplatin)

Disease Site	Hematologic - Lymphoma - Hodgkin
Intent	Curative 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	Salvage therapy for refractory Hodgkin's lymphoma.
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
CISplatin	75 mg /m²	IV	Day 1
dexamethasone	40 mg	PO	Days 1 to 4

outpatient prescription in 4mg tablets

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C - Cycle Frequency

REPEAT EVERY 21 DAYS

- If complete or partial response occurs after 2 cycles, may proceed to autologous stem cell transplant (ASCT). May receive a third cycle if patient has not achieved a complete or partial response after 2 cycles.
- Patients with stable disease who were not candidates for stem cell transplant or patients who had any response after 2-3 cycles of GDP may receive up to 6 cycles of treatment.

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D - Premedication and Supportive Measures

Antiemetic Regimen: High (D1)
Low (D8)

Febrile Neutropenia Risk: Moderate

Other Supportive Care:

- The day 1 dexamethasone dose can be given IV before chemotherapy to prevent emesis, with the oral treatment dose reduced accordingly.
- Consider use of filgrastim to maintain dose intensity for patients with febrile neutropenia or prolonged neutropenia.
- Standard regimens for Cisplatin premedication and hydration should be followed. Refer to local guidelines.

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.

Dosage with toxicity

No dose adjustment required for dexamethasone.

Dose for Day 1 of cycle:

Worst Toxicity in Previous Cycle / (Counts x 10^9/L)			**Gemcitabine* (% previous dose)**	**Cisplatin * (% previous dose)**
Febrile Neutropenia	Or	Grade 4 ANC ≥ 7 d	75%	75%
Grade 3 related organ			75%	75%
Grade 4 related organ, Pneumonitis, Hemolytic Uremic Syndrome (HUS), Stevens-Johnson syndrome (SJS), Toxic epidermal necrolysis (TEN), Capillary Leak Syndrome (CLS)			Discontinue	Discontinue

Dose for Day 8 of cycle:

Toxicity / Counts x 10^9/L		**Toxicity / Counts x 10^9/L**	**Gemcitabine (% day 1 dose)**
Febrile Neutropenia	Or	Grade 4 ANC ≥ 7 d	Omit

ANC >1	And	Platelet >100	100%
ANC 0.5 -1	Or	Platelet 50-100	75% (or 100% with G-CSF for isolated low ANC)
ANC < 0.5	Or	Platelet < 50	OMIT; or delay 1 week
Grade 3 related organ			Omit
Grade 4 related organ, Pneumonitis, HUS, SJS, TEN, CLS			Discontinue

* Prior to retreatment, toxicity should have recovered to ≤ grade 2 and ANC to ≥ 1 x 10^9/L and platelets ≥ 100 x 10^9/L.

Hepatic Impairment

Bilirubin		**AST/ALT**	**Cisplatin**	**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 (µmol/L)	**or**	**Creatinine clearance (mL/min)**	**Cisplatin (% previous do**	**Gemcitabine**
140-199	or	10-50	50-75%	Use with caution; no specific recommendation found. Close monitoring for occurrence of hemolytic uremic syndrome is required.
≥ 200	or	< 10	*Discontinue	Discontinue

*See CISPLATIN Drug Monograph.

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F - Adverse Effects

Refer to gemcitabine, CISplatin, dexamethasone 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) • Fatigue and flu-like symptoms • Edema • Nausea and vomiting • ↑ LFTs (may be severe) • Neurotoxicity (including ototoxicity) • Nephrotoxicity (including electrolyte abnormalities, may be severe and include SIADH), proteinuria • Diarrhea, stomatitis • Steroid effect (e.g. weight gain, hyperglycemia, gastric irritation, insomnia, mood changes) • Anorexia • Rash (may be severe) • Electrolyte abnormalities • Alopecia • Musculoskeletal pain	• Hemolytic uremic syndrome • Secondary malignancies • Hemolytic anemia, thrombotic microangiopathy • Pneumonitis, ARDS • Arrhythmia • Cardiotoxicity • Capillary leak syndrome • Vasculitis • Hypersensitivity • Arterial and venous thromboembolism • Seizures • PRES • Optic neuritis • Hyperviscosity • Steroid effects (e.g. cataracts, osteoporosis)

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G - Interactions

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

- Avoid nephrotoxic and ototoxic drugs (i.e. aminoglycosides) due to additive effects.
- Concomitant use of renally excreted drugs (i.e. methotrexate) may decrease renal clearance and enhance toxicities of these drugs. Avoid use, if possible. If not possible, modify doses as necessary.
- Cisplatin may decrease phenytoin levels; monitor levels and patient.
- 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, CISplatin, dexamethasone drug monograph(s) for additional details

Administration

Gemcitabine:

- Dilute reconstituted drug in normal saline for IV infusion; to a minimum final concentration of 0.1 mg/mL.
- Infuse over 30 minutes through free-flowing IV.

Cisplatin:

- Ensure good urinary output during chemotherapy visit. Patient should void at least once during chemotherapy visit. Use locally approved hydration regimens.
- Blood pressure should be taken before and after chemotherapy.
- Additional hydration may be ordered for hypovolemic patients.
- Hydration and diuresis for patients with pre-existing renal, cardiac, or diabetic history at discretion of physician.
- Oral hydration with 8 glasses of fluid per day is strongly encouraged on treatment day and for 1-2 days after cisplatin; if nausea and vomiting prevent oral hydration, the patient may need to return for more IV hydration.
- Infuse over 60 minutes through free-flowing IV.
- Cisplatin is physically incompatible with any IV set, needle or syringe containing aluminum.
- Store unopened vials between 15°C to 25°C and protect from light. Do not refrigerate or freeze since precipitation will occur

Contraindications

- Patients with known hypersensitivity to gemcitabine or platinum containing compounds

Other Warnings/Precautions

- All patients should receive appropriate hydration and antiemetic protocols according to local guidelines.
- Gemcitabine use in patients with impaired hepatic function, including concurrent liver metastases or a previous history of hepatitis, alcoholism or liver cirrhosis may lead to exacerbation of the hepatic insufficiency
- Cisplatin and gemcitabine are not recommended for use in pregnancy or breastfeeding.

Appropriate contraception should be used by both sexes during treatment, and for at least 6 months after the last dose

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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
- Renal function tests (including electrolytes and magnesium); Baseline and before each dose
- Liver function tests; Baseline and before each cycle
- Audiogram; as clinically indicated
- Clinical toxicity assessment (including flu-like symptoms, fatigue, dyspnea, rash, infection, bleeding, nausea/vomiting, neurotoxicity, ototoxicity, GI effects); at each visit

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

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J - Administrative Information

Approximate Patient Visit	Day 1: 4-5 hours; Day 8: 0.75 hour
Pharmacy Workload (average time per visit)	35.648 minutes
Nursing Workload (average time per visit)	44.167 minutes

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K - References

Baetz T, Belch A, Couban S et al. Gemcitabine, dexamethasone and cisplatin is an active and non-toxic chemotherapy regimen in relapsed or refractory Hodgkin's disease: a phase II study by the National Cancer Institute of Canada Clinical Trials Group. Annals of Oncology 14: 1762–1767, 2003.

Cisplatin and gemcitabine drug monographs, Cancer Care Ontario.

Kuruvilla J, Nagy T, Pintilie M, et al. Similar Response Rates and Superior Early Progression-Free Survival with Gemcitabine, Dexamethasone, and Cisplatin Salvage Therapy Compared with Carmustine, Etoposide, Cytarabine, and Melphalan Salvage Therapy Prior to Autologous Stem Cell Transplantation for Recurrent or Refractory Hodgkin Lymphoma. Cancer 2006; 106: 353–60.

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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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