Regimen Monograph

A - Regimen Name

CISPGEMC Regimen

Gemcitabine-CISplatin

Disease Site Head and Neck (Nasopharynx)

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.

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B - Drug Regimen

gemcitabine	1000 mg /m²	IV	Days 1 and 8
CISplatin	70 mg /m²	IV	Day 1

REPEAT EVERY 21 DAYS

Alternative Schedule:

gemcitabine	1000 mg /m²	IV	Days 1, 8 and 15
CISplatin	70 mg /m²	IV	Day 1

REPEAT EVERY 28 DAYS

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C - Cycle Frequency

Up to 6 cycles unless disease progression or unacceptable toxicity

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D - Premedication and Supportive Measures

Antiemetic Regimen: High (D1)
Low (D8)

Other Supportive Care:

Also refer to CCO Antiemetic Recommendations.

Standard regimens for Cisplatin premedication and hydration should be followed. Refer to Cisplatin monograph

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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 could be considered.

Dosage with toxicity

Dose on Day 1 of Cycle:

Worst Toxicity in Previous Cycle	Gemcitabine	Cisplatin

Non-Hematologic (related organ)		**Hematologic**	**% Full Dose***	**% Full Dose***
Grade 3	or	Febrile neutropenia, thrombocytopenic bleeding	75%	75%
Grade 4			Consider discontinuing, or ↓ to 75%	Consider discontinuing, or ↓ to 75%
Day 8 holds in > 1 cycle			75%	100%
Non-Hematologic (related organ)		**Hematologic**	**Gemcitabine % Full Dose***	**Cisplatin % Full Dose***
• Pneumonitis • Hemolytic Uremic Syndrome (HUS) • Stevens-Johnson syndrome (SJS) • Toxic epidermal necrolysis (TEN) • Capillary Leak Syndrome (CLS)			Discontinue	Discontinue

*Do not restart until ANC ≥1500x 10^6/L, platelets ≥100,000 x 10^6/L and non-hematologic toxicity ≤ grade 2.

Dose on Day 8 (or 15) of Cycle:

Toxicity on Day 8 of cycle					
Non-hematologic (related organ)		**Hematologic**			**Gemcitabine (% Full Dose)**
		AGC (x 10^6/L)		**Platelets (x 10^6/L)**	
≤ grade 2	and	> 1000	and	> 100,000	100%
≤ grade 2	and	500-1000	or	50,000-100,000	Consider Omit, or ↓ to 75%
Grade 3 or 4	or	< 500	or	< 50,000	Omit; ↓ to 75% at restart (if applicable) for non-hematolgic toxicity

Pneumonitis HUS SJS TEN CLS		-		-	Discontinue

Hepatic Impairment

Bilirubin		AST/ALT	Gemcitabine (% previous dose)	Cisplatin (% previous dose)
1-2 x ULN	and/ or	<2 x ULN	100%	100%
2-4 x ULN		2-5 x ULN	Caution	100%
> 4 x ULN		> 5 x ULN	Caution, consider ↓	Caution, consider ↓

Renal Impairment

Creatinine Clearance (mL/min)	Gemcitabine (% previous dose)	Cisplatin (% previous dose)
> 60	100%	100%
>45-60	Caution	75%
30-45	Caution	50%
< 30	Consider discontinuing or ↓	Discontinue

Dosage in the Elderly

gemcitabine: Clearance is lower in the elderly but no dose adjustment necessary.

CISplatin: Geriatric patients may be at higher risk of developing nephrotoxicity, ototoxicity/neurotoxicity or hematologic adverse effects.

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F - Adverse Effects

Refer to gemcitabine, 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
• Myelosuppression ± infection, bleeding (may be severe) • Fatigue, flu-like symptoms, musculoskeletal pain • Edema • Nausea and vomiting • Diarrhea, anorexia • Elevated LFTs (may be severe) • Neurotoxicity and ototoxicity (may be severe) • Nephrotoxicity (may be severe), proteinuria • Electrolyte abnormalities • Rash (may be severe)	• Hemolytic uremic syndrome, vasculitis • Hemolysis • Pneumonitis, ARDS • Capillary leak syndrome • Arrhythmia • Cardiotoxicity • Arterial thromboembolism • Venous thromboembolism • Secondary malignancy • Seizures • Hypersensitivity

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G - Interactions

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

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H - Drug Administration and Special Precautions

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

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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 at each visit
- Electrolytes, including magnesium, sodium, potassium, phosphate and calcium; baseline and regular
- Liver function tests; baseline and regular
- Renal function tests; baseline and regular
- Audiogram; as clinically indicated
- Clinical toxicity assessment (infection, bleeding, flu-like symptoms, lethargy, dyspnea, rash, nausea/vomiting and other GI effects, neurotoxicity, ototoxicity); at each visit

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

Suggested Clinical Monitoring

Audiogram; Periodic
Liver function tests; Baseline and regular
INR for patient receiving warfarin; Baseline and regular
Urinalysis; Baseline and regular

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J - Administrative Information

Approximate Patient Visit	Day 1: 4 to 5 hours; Gemcitabine only day: 0.75 hour
Pharmacy Workload (average time per visit)	31.387 minutes
Nursing Workload (average time per visit)	40.000 minutes

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K - References

Cisplatin and gemcitabine drug monographs, Cancer Care Ontario.

Foo K-F, Tan E-H, Leong S-S, et al. Gemcitabine in metastatic nasopharyngeal carcinoma of the undifferentiated type. Ann Oncol 2002; 13: 150-156.

Ma BY, Tannock IF, Pond G, Edmonds MR, Siu LL. Chemotherapy with gemcitabine-containing regimens for locally recurrent or metastatic nasopharyngeal carcinoma. Cancer, 2002; 95: 2516-2523.

Ngan RKC, Yiu HHY, Lau WH, et al. Combination gemcitabine and cisplatin chemotherapy for metastatic or recurrent nasopharyngeal carcinoma: report of a phase II study. Ann Oncol, 2002; 13: 1252-1258.

Zhang L, Huang Y, Hong S, et al. Gemcitabine plus cisplatin versus fluorouracil plus cisplatin in recurrent or metastatic nasopharyngeal carcinoma: a multicentre, randomised, open-label, phase 3 trial. Lancet 2016;388(10054):1883-92.

PEBC Advice Documents or Guidelines

- The Management of Head and Neck Cancer in Ontario

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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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