Regimen Monograph

A - Regimen Name

CISPGEMC Regimen

Gemcitabine-CISplatin

Disease Site	Lung - Non-Small Cell
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	Treatment of locally advanced or metastatic non-small cell lung cancer

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B - Drug Regimen

gemcitabine*	1000-1250 mg /m²	IV	Day 1 and Day 8
CISplatin*	75 mg /m²	IV	Day 1

*Gemcitabine 1000 mg/m^2 on days 1, 8, and 15 and Cisplatin 80 to 100 mg/m^2 on day 1, q28days, can also be used

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C - Cycle Frequency

REPEAT EVERY 21 DAYS

For a usual total of 4 to 6 cycles in responding patients, unless disease progression or unacceptable toxicity occurs

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D - Premedication and Supportive Measures

Antiemetic Regimen: High (D1)
Low (D8)

Other Supportive Care:

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. 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%
Worst Toxicity in Previous Cycle				
Non-hematologic (related organ)		**Hematologic**	**Gemcitabine % Full dose**	**Cisplatin % Full dose**
Day 8 holds in > 1 cycle			75%	100%
• 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 restart until ANC ≥1500x 10^6/L, platelets ≥100,000 x 10^6/L and non-hematologic toxicity ≤ grade 2.

Dose on Day 8 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		50,000-	Consider Omit,

			or	100,000	or ↓ to 75%
Grade 3 or 4	or	< 500	or	< 50,000	Omit, ↓ to 75% at restart (if applicable) for non-hematologic toxicity
Pneumonitis, HUS, SJS, TEN, CLS, PRES		-		-	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

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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) • Reproductive risk	• Hemolytic uremic syndrome, vasculitis • Hemolysis • Pneumonitis, ARDS • Capillary leak syndrome • Arrhythmia • Cardiotoxicity • Arterial thromboembolism • Secondary leukemia • Posterior reversible encephalopathy syndrome • 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

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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.

Schiller JH, Harrington D, Belani CP, Langer C, Sandler A, Krook J, et al. Comparison of four chemotherapy regimens for advanced non-small-cell lung cancer. New Engl J Med 2002;346:92-8.

Cardenal F, Lopez-Cabrerizo MP, Anton A, Alberola V, Massuti B, Carrato A, et al. Randomized phase III study of gemcitabine-cisplatin versus etoposide-cisplatin in the treatment of locally advanced or metastatic non-small-cell lung cancer. J Clin Oncol 1999;17:12-8.

PEBC Advice Documents or Guidelines

- Systemic Treatment for Patients with Advanced Non-Small Cell Lung Cancer

August 2021 Modified Rationale and Uses section

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L - Other Notes

There is no convincing evidence that any new agent (gemcitabine, vinorelbine, docetaxel, paclitaxel, irinotecan, pemetrexed) in combination with platinum is superior to any other platinum plus new agent combination.

For patients receiving platinum-based doublet therapy, a recommendation in favour of cisplatin over carboplatin is made based on a probable modest improvement in survival and an improvement in response. Cisplatin regimens result in more frequent nausea/vomiting and nephropathy, while thrombocytopenia is worse with carboplatin. Given the poor prognosis in this population, the relative toxicities and QOL differences should be given strong consideration.

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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.

The information set out in the drug monographs, regimen monographs, appendices and symptom management information (for health professionals) contained in the Drug Formulary (the "Formulary") is intended for healthcare providers and is to be used for informational purposes only. The information is not intended to cover all possible uses, directions, precautions, drug interactions or adverse effects of a particular drug, nor should it be construed to indicate that use of a particular drug is safe, appropriate or effective for a given condition. The information in the Formulary is not intended to constitute or be a substitute for medical advice and should not be relied upon in any such regard. All uses of the Formulary are subject to clinical judgment and actual prescribing patterns may not follow the information provided in the Formulary.

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Some Formulary documents, such as the medication information sheets, regimen information sheets and symptom management information (for patients), are intended for patients. Patients should always consult with their healthcare provider if they have questions regarding any information set out in the Formulary documents.

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