Regimen Monograph

A - Regimen Name

CRBPGEMC Regimen

Gemcitabine-CARBOplatin

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	An alternative to cisplatin-gemcitabine for the 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 8
CARBOplatin	AUC 5	IV	Day 1

Adjust Carboplatin dose to AUC target (using Calvert formula) as outlined in the "Other Notes" section.

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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: Moderate + NK1 antagonist (Carboplatin AUC ≥ 5) (Day 1)
Low (Day 8)

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 are in use at some centres.

Dosage with toxicity

Dose on day 1 of Cycle

Worst Toxicity in Previous Cycle			Gemcitabine	Carboplatin
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%
• 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 retreat until AGC ≥ 1.5 x 10^9/L, platelets ≥ 100 x 10^9/L and toxicity ≤ grade 2. # use Egorin formula if isolated thrombocytopenia				

(Continued on next page)

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	or	50,000-100,000	Consider Omit, or ↓ to 75%
Grade 3 or 4		< 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)**	**Carboplatin (% 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

CrCl (mL/min)	**Gemcitabine (% previous dose)**	**Carboplatin (% previous dose)**
> 60	100%	Use Calvert formula
40-60	100%	
20-40	Caution	
< 20	Consider discontinuing or ↓	Discontinue

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F - Adverse Effects

Refer to gemcitabine, CARBOplatin 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 • Rash (may be severe) • Edema • Nausea or vomiting • Diarrhea • Elevated LFTs (may be severe) • Neurotoxicity (ototoxicity) • Nephrotoxicity, proteinuria • Abnormal electrolytes	• Pneumonitis/ARDS • Hemolytic-uremic syndrome • Secondary malignancies • Capillary leak syndrome • Arterial/venous thromboembolism • Arrhythmia • Cardiotoxicity • Hypersensitivity • Vasculitis

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G - Interactions

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

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H - Drug Administration and Special Precautions

Refer to gemcitabine, CARBOplatin 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

- Clinical toxicity assessment (including flu-like symptoms, fatigue, rash, edema, GI, pulmonary, neurotoxicity, infection, bleeding, ototoxicity); at each visit
- CBC before each cycle and on day 8.
- Baseline and regular liver function tests
- Baseline and regular renal function tests and electrolytes (including magnesium)

- 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: 2 hours; Day 8: 45 minutes
Pharmacy Workload (average time per visit)	28.715 minutes
Nursing Workload (average time per visit)	42.917 minutes

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K - References

Carboplatin, gemcitabine drug monographs, Cancer Care Ontario.

Sederholm C. Gemcitabine versus gemcitabine/carboplatin in advanced non-small cell lung cancer: preliminary findings in a phase III trial of the Swedish Lung Cancer Study Group. Proc ASCO 2002: 21;291a (Abstract 1162)

Mazzani P, Massacesi C, Rocchi M, et al. Randomized, multicenter, phase II study of gemcitabineplus cisplatin versus gemcitabine plus carboplatin in patients with advanced non-small cell lung cancer. Lung Cancer (2003) 41: 81-89.

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.

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.

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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