Regimen Monograph

A - Regimen Name

CRBPVINO Regimen

Vinorelbine-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-vinorelbine for the treatment of locally advanced or metastatic non-small cell lung cancer

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B - Drug Regimen

vinorelbine	25 mg /m²	IV	Days 1 and 8
CARBOplatin	AUC 5	IV	Day 1

Adjust Carboplatin dose to AUC target (using Calvert formula) as outlined in "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

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D - Premedication and Supportive Measures

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

Febrile Neutropenia Risk: Low

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.

Dosage with toxicity

	Dosage for subsequent cycle	
Worst Toxicity / Counts in the Previous Cycle	**Carboplatin (% previous dose)**	**Vinorelbine (% previous dose)**
Febrile neutropenia, Thrombocytopenic bleeding, ANC < 0.5 x 10^9/L for ≥ 5 to 7 days and/or Grade 4 thrombocytopenia	75%*	75%*
Grade 2 or 3 peripheral neuropathy	n/a	Discontinue
Grade 3 non-hematologic toxicity	75%*	75%*
Grade 4 non-hematologic toxicity	Discontinue	Discontinue

* Do not retreat until non-hematologic/ organ toxicity ≤ grade 2, platelets ≥ 100 x 10^9/L and ANC ≥ 1.5 x 10^9/L

Dose on day 8 of cycle

Toxicity on day 8 of cycle					
Non–hematologic (related organ)		**Hematologic**			**Day 8 Vinorelbine (% day 1 dose)**
		ANC (x 10^9/L)		**Platelets (x 10^9/L)** -	
≤ grade 2	and	≥ 1.5	and	≥ 100	100%
≤ grade 2	and	1-1.49	and/or	75-99	50%
Grade 3 or 4 related organ	or	< 1	or	< 75	Omit

Hepatic Impairment

Total bilirubin	vinorelbine (% usual dose)
2-3 X ULN	50%
>3 X ULN	25%

No dosage adjustment required for carboplatin.

Renal Impairment

As creatinine clearance changes, adjust dosage of Carboplatin using the Calvert Formula . (See "Other Notes" section).

No adjustment needed for vinorelbine.

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F - Adverse Effects

Refer to vinorelbine, 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) • Nausea, vomiting • Fatigue • Constipation • Injection site reaction • Increased LFTs • Nephrotoxicity • Diarrhea • Neuropathy (may be severe) • Anorexia • Mucositis • Hearing impaired • Alopecia • Abnormal electrolytes	• Hypersensitivity • Aterial thromboembolism • Venous thromboembolism • Hemolytic uremic syndrome • Pneumonitis • Radiation recall reaction

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G - Interactions

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

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H - Drug Administration and Special Precautions

Refer to vinorelbine, 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

- CBC; baseline and before each cycle. Interim counts should be done in first cycle and repeated if dose modifications necessary.
- Renal and liver function tests; baseline and before each cycle
- Clinical toxicity asessment (including neuropathy, ototoxicity, local toxicity, infection, bleeding); at each visit
- Grade toxicity using the current NCI-CTCAE (Common Terminology Criteria for Adverse Events) version

Suggested Clinical Monitoring

- INR; Baseline and as clinically indicated

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J - Administrative Information

Approximate Patient Visit	Day 1: 1.5 hours; Day 8: 0.5 hours
Pharmacy Workload (average time per visit)	22.018 minutes
Nursing Workload (average time per visit)	42.917 minutes

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K - References

Carboplatin and vinorelbine drug monographs, Cancer Care Ontario.

Couture F, Vincent M, Sehdev S, et al. Carboplatin and vinorelbine ('CarNavel") : A prospective phase II evaluation of 2 doses of carboplatin in advanced non-small cell lung cancer (S-NSCLC). Proc. ASCO 2003. (Abstract no. 2715)

Tan EH, Szczesna A, Krzakowski M, et al. Randomized study of vinorelbine--gemcitabine versus vinorelbine--carboplatin in patients with advanced non-small cell lung cancer. Lung Cancer. 2005;49:233-40.

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: (area under the curve method)

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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that original references or product monograph be consulted prior to using a chemotherapy regimen for the first time.

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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