Regimen Monograph

A - Regimen Name

CISPVINO Regimen

CISplatin-Vinorelbine

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

CISplatin	75 mg /m²	IV	Day 1
vinorelbine	25 mg /m²	IV	Days 1 and 8

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C - Cycle Frequency

REPEAT EVERY 21 DAYS

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

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D - Premedication and Supportive Measures

Antiemetic Regimen: High (D1)
Minimal (D8)

Other Supportive Care:

Also refer to CCO Antiemetic Summary

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.

Dosage with toxicity

Hematologic Toxicities

See Appendix 6 for general recommendations.

	Dosage for subsequent cycle	
Worst Toxicity / Counts in the Previous Cycle	**Cisplatin (% previous dose)**	**Vinorelbine (% previous dose)**
Febrile neutropenia, Thrombocytopenic bleeding, ANC < 0.5 for ≥ 5 to 7 days and/or Grade 4 thrombocytopenia	75%*	75%*
≥ Grade 2 ototoxicity	Discontinue	No change
Grade 2 peripheral neuropathy	75%	Discontinue
Grade 3 peripheral neuropathy	Discontinue	Discontinue
Grade 3 organ / non-hematologic toxicity	75%*	75%*
Grade 4 organ / 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 (+/- day 15) of Cycle

Toxicity on Day 8 of cycle					
		Hematologic			Day 8 (or 15) Vinorelbine (% day 1 dose)
Non–hematologic (related organ)		**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	Cisplatin (% previous dose)	Vinorelbine (% previous dose)
< 2 x ULN	No change	100%
2-4 x ULN		25-50%
> 4 x ULN		Discontinue
Consider dose reduction of vinorelbine for moderate- severe elevations of transaminases		

Renal Impairment

Creatinine Clearance (mL/min)	Cisplatin (% previous dose)	Vinorelbine (% previous dose)
>60	100%	No change
>40-60	50%	
<40	OMIT	

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F - Adverse Effects

Refer to vinorelbine, 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) • Nausea and vomiting • Nephrotoxicity • Neurotoxicity (including ototoxicity; may be severe) • Fatigue • Electrolyte imbalances • ↑ LFTs • Anorexia • Mucositis • Diarrhea • Fever • Tumour pain • Alopecia	• Hypersensitivity • Hemolytic uremic syndrome • Arterial thromboembolism • Venous thromboembolism • Pneumonitis • SIADH • Secondary malignancy • Radiation recall reaction • Seizure

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G - Interactions

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

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H - Drug Administration and Special Precautions

Refer to vinorelbine, 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 before each cycle. Interim counts should be done in first cycle and repeated if dose modifications necessary.
- Renal function tests (including electrolytes and magnesium) and urinalysis; baseline and before each cycle
- Liver function tests; baseline and before each cycle
- Clinical toxicity (including nausea, neuropathy, ototoxicity, local toxicity); at each visit
- Grade toxicity using the current NCI-CTCAE (Common Terminology Criteria for Adverse Events) version

Suggested Clinical Monitoring

Audiogram; baseline and as clinically indicated

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J - Administrative Information

Approximate Patient Visit	Day 1: 4 hours; Vinorelbine only: 0.5 hours
Pharmacy Workload (average time per visit)	29.576 minutes
Nursing Workload (average time per visit)	41.667 minutes

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K - References

Cisplatin and vinorelbine drug monographs, Cancer Care Ontario.

Comella P, Frasci G, Panza N, et al. Randomized trial comparing cisplatin, gemcitabine, and vinorelbine With either cisplatin and gemcitabine or cisplatin and vinorelbine in advanced non–small-cell lung cancer: interim analysis of a phase III trial of the southern Italy cooperative oncology group. J Clin Oncol 2000; 18: 1451-7.

Comella P, Filippelli G, De Cataldis G, et al. Efficacy of the combination of cisplatin with either gemcitabine and vinorelbine or gemcitabine and paclitaxel in the treatment of locally advanced or metastatic non-small-cell lung cancer: a phase III randomised trial of the Southern Italy Cooperative Oncology Group (SICOG 0101). J Clin Oncol 2007; 18: 324-30.

Depierre A, Chastang Cl, Quoix E, et al. Vinorelbine versus vinorelbine plus cisplatin in advanced non-small cell lung cancer: a randomized trial. Ann Oncol 1994;5:37-42.

Georgoulias V, Ardavanis A, Tsiafaki X, et al. Vinorelbine plus cisplatin Versus docetaxel plus gemcitabine in advanced non–small-cell lung cancer: a phase III randomized trial. J Clin Oncol J Clin Oncol 2005; 23: 2937-45.

Kelly K, Crowley J, Bunn PA, et al. Randomized phase III Trial of paclitaxel plus carboplatin versus vinorelbine plus cisplatin in the treatment of patients with advanced non–small-cell lung cancer: a southwest oncology group trial. J Clin Oncol 2001; 19: 3210-8.

LeChevalier T, Brisgand D, Douillard J-Y, et al, Randomized study of vinorelbine and cisplatin versus vindesine and cisplatin versus vinorelbine alone in advanced non-small cell cancer: Results of a European Multicentre trial including 612 patients. J Clin Oncol, 1994; 12: 360-367

Pujol JL, Breton JL, Gervais R, et al. Gemcitabine–docetaxel versus cisplatin–vinorelbine in advanced or metastatic non-small-cell lung cancer: a phase III study addressing the case for cisplatin. Ann Oncol 2005; 16: 602-10.

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.

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 newer agents (gemcitabine, vinorelbine, docetaxel, paclitaxel, irinotecan, pemetrexed) in combination with platinum is superior, in terms of efficacy in all tumour types, to any other platinum plus new agent combination, although different regimens have different toxicity profiles, cost and convenience.

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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