Regimen Monograph

A - Regimen Name

VINO Regimen

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	First-line treatment of advanced non-small cell lung cancer in patients who cannot tolerate combination therapy, due to elderly age, toxicity, or other considerations

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B - Drug Regimen

vinorelbine	25-30 mg /m²	IV	Days 1, 8 and 15

Alternative schedule:

vinorelbine	25-30 mg /m²	IV	Days 1 and 8

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C - Cycle Frequency

Standard schedule: REPEAT EVERY 28 DAYS

Alternative schedule: 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: Minimal

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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

Worst toxicity in previous cycle	Dose (% previous dose)
Febrile neutropenia Thrombocytopenic bleeding ANC < 0.5 and/or grade 4 thrombocytopenia for ≥ 5 to 7 days	75 %*
Grade 2 peripheral neuropathy	Discontinue
Grade 3 peripheral neuropathy	Discontinue
Grade 3 related organ/ non-hematological toxicity	75 %*
Grade 4 related organ/ non-hematological toxicity, OR delay > 3 weeks	Discontinue
*Do not start new cycle until platelets ≥ 100 x 10^9/L, neutrophils ≥ 1.5 x 10^9/L, hemoglobin > 80 g/L and major toxicity has recovered to ≤ grade 2 (may consider administering if neutrophils 1-1.5 x 10^9/L at 50% of planned dose).	

Dose on Day 8, 15 of cycle

Toxicity on Day 8, 15 of cycle					
Non–hematologic (related organ)		Hematologic			Day 8 (or 15) (% 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	≥ 100	50%
Grade 3 or 4 related organ	or	< 1	or	<100	Omit

Hepatic Impairment

As vinorelbine undergoes hepatobiliary metabolism and excretion, administer with caution in hepatic insufficiency. Consider adjusting doses with hyperbilirubinemia.

Suggested adjustments for increases in total bilirubin:

Total Bilirubin (micromol/L)	% Usual dose
< 1.5 x ULN	100%
1.5 to 2 x ULN	50%
> 2 x ULN	25%

Renal Impairment

No adjustment required

Dosage in the Elderly

No dosage adjustments are required for increased age

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F - Adverse Effects

Refer to vinorelbine drug monograph(s) for additional details of adverse effects

Very common (≥ 50%)	Common (25-49%)	Less common (10-24%)	Uncommon (< 10%), but may be severe or life-threatening
• Nausea, vomiting • Myelosuppression +/- bleeding (may be severe)	• Constipation (may be severe) • Fatigue	• Alopecia • Anorexia • Diarrhea • Mucositis	• Venous thromboembolism • ↑ LFTs • Hypersensitivity

		• Neuropathy (may be severe) • Injection site reaction	• Pneumonitis • SIADH • Radiation recall

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G - Interactions

Refer to vinorelbine drug monograph(s) for additional details

- Use CYP3A4 inhibitors with caution; consider vinorelbine dose adjustment (reduction) when used with azole antifungals.

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H - Drug Administration and Special Precautions

Refer to vinorelbine drug monograph(s) for additional details

Administration

FOR INTRAVENOUS USE ONLY.

Intrathecal administration of other vinca alkaloids has resulted in death. Syringes containing this product should be labeled "WARNING – FOR INTRAVENOUS USE ONLY. FATAL if given intrathecally."

- Mix in 50mL minibag (D5W, NS) to a final concentration 0.5 - 2mg/mL; infuse over 6-10 minutes through free-flowing IV.
- Or may push (at final concentration of 1.5 – 3mg/mL) through sidearm of free-flowing IV (D5W, NS); inject over 6-10 minutes.
- After administration is completed, the manufacturer recommends flushing IV line with at least 75 to 125mL of D5W or NS.
- Flushing the line before and after administration of vinorelbine may reduce injection site reactions and phlebitis risk.
- Discontinue the injection if extravasation occurs and the remaining dose should be given into another vein. Warm compresses applied for 15 to 20 minutes 4 times per day for 1-2 days

and elevation of affected area for 2-3 days may help disperse the drug and minimize discomfort.
- Refrigerate unopened vials (2-8°C); protect from light and do not freeze.

Contraindications

- Patients with known hypersensitivity to vinorelbine
- Patients who have drug-induced severe myelosuppression
- Intrathecal administration is **absolutely contraindicated**

Precautions

- Use with extreme caution in patients with compromised marrow reserve
- May result in radiosensitizing effects with prior or concomitant radiation therapy
- Patients with pre-existing neuropathy or prior treatment with other neurotoxic drugs may have increased potential for neurotoxicity

Pregnancy/Lactation

- Vinorelbine is not recommended for use in pregnancy. Adequate contraception should be used by both sexes during treatment, and for at least 6 months after the last dose.
- Breastfeeding is not recommended.

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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 dose
- Liver function tests; Baseline and before each cycle
- Clinical toxicity assessment for signs of neurotoxicity, local toxicity, bleeding, infection, hypersensitivity, thromboembolism, lung or GI toxicity, radiation recall; At each visit
- Grade toxicity using the current NCI-CTCAE (Common Terminology Criteria for Adverse Events) version

Suggested Clinical Monitoring

- Local site toxicity ratings, if incidence of phlebitis

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J - Administrative Information

Approximate Patient Visit	0.5 hour
Pharmacy Workload (average time per visit)	16.783 minutes
Nursing Workload (average time per visit)	36.667 minutes

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K - References

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.

Gridelli C, Perrone F, Gallo C, et al. Chemotherapy for elderly patients with advanced non-small-cell lung cancer: the Multicenter Italian Lung Cancer in the Elderly Study (MILES) phase III randomized trial. J Natl Cancer Inst. 2003;95:362-72.

Kudoh S, Takeda T, Nakagawa K, et al. Phase III study of docetaxel compared with vinorelbine in elderly patients with advanced non-small-cell lung cancer: results of the West Japan Thoracic Oncology Group Trial (WJTOG 9904). J Clin Oncol. 2006;24:3657-63.

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

Vinorelbine drug monograph, Cancer Care Ontario.

PEBC Advice Documents or Guidelines

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

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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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