

Oral Vinorelbine Monotherapy-7 days

INDICATIONS FOR USE:

INDICATION	ICD10	Regimen Code	Reimbursement Status
Advanced breast cancer	C50	00259a	CDS
Non small cell lung cancer (NSCLC)	C34	00259b	CDS

TREATMENT:

The starting dose of the drugs detailed below may be adjusted downward by the prescribing clinician, using their independent medical judgement, to consider each patients individual clinical circumstances.

Treatment is administered **once every 7 days** until disease progression or unacceptable toxicity develops.

Administration Weeks 1-3

Day	Drug	Dose	Route and Method of Administration
1	Vinorelbine	60mg/m ² (MAX 120mg)	PO Swallow whole with water, without chewing sucking or dissolving capsule. It is recommended to administer the capsule with some food

Administration Week 4 onwards

Day	Drug	Dose	Route and Method of Administration
1	Vinorelbine	*80mg/m ² (MAX 160mg)	PO Swallow whole with water, without chewing sucking or dissolving capsule. It is recommended to administer the capsule with some food
*Dose increase to 80mg/m ² is recommended beyond third administration except in those patients for whom the neutrophil count dropped once below 0.5 x10 ⁹ /L or more than once between 0.5 x10 ⁹ /L and 1 x10 ⁹ /L during the first three administrations at 60mg/m ² .			
If the patient chews or sucks the capsule by error, the liquid is an irritant. Proceed to mouth rinses with water or preferably a normal saline solution. In the event of the capsule being cut or damaged, the liquid content is an irritant, and so may cause damage if in contact with skin, mucosa or eyes. Damaged capsules should not be swallowed and should be returned to the pharmacy or to the doctor in order to be properly destroyed. If any contact occurs, immediate thorough washing with water or preferably with normal saline solution should be undertaken.			
In the case of vomiting within a few hours after drug intake, do not re-administer.			
Vinorelbine is available as 20mg, 30mg and 80mg capsules 30mg/ m ² IV is equivalent to 80mg/m ² PO and 25mg/m ² IV is equivalent to 60mg/ m ² PO.			

Table 1: Summary of treatment days

	DAY						
	1	2	3	4	5	6	7
Week 1	√	x	x	x	x	x	x
Week 2 onwards	√	x	x	x	x	x	x

NCCP Protocol: Oral Vinorelbine-7days	Published: 29/04/2015 Review: 19/06/2021	Version number: 4
Tumour Group: Breast/Lung NCCP Protocol Code: 00259	ISMO Contributor: Prof Maccon Keane	Page 1 of 5

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Table 2: Dose of vinorelbine (PO) required for appropriate ranges of body surface area (BSA).

BSA (m ²)	60mg/m ²	80mg/m ²
	Dose (mg)	Dose (mg)
0.95 to 1.04	60	80
1.05 to 1.14	70	90
1.15 to 1.24	70	100
1.25 to 1.34	80	100
1.35 to 1.44	80	110
1.45 to 1.54	90	120
1.55 to 1.64	100	130
1.65 to 1.74	100	140
1.75 to 1.84	110	140
1.85 to 1.94	110	150
≥1.95	120	160

ELIGIBILITY:

- Indications as above.
- ECOG status 0-2.
- Life expectancy > 3 months.

EXCLUSIONS:

- Hypersensitivity to vinorelbine or other vinca alkaloids
- Disease significantly affecting absorption
- Previous significant surgical resection of stomach or small bowel
- Patients requiring long term oxygen therapy
- Pregnancy
- Breast feeding

USE WITH CAUTION:

- Neutrophil count < 1.5 x 10⁹/L or severe infection current or recent (within 2 weeks)
- Platelet count < 100 x 10⁹/L

PRESCRIPTIVE AUTHORITY:

The treatment plan must be initiated by a Consultant Medical Oncologist.

TESTS:

Baseline tests:

- FBC, renal and liver profile.
- Assessment of peripheral neuropathy

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Tumour Group: Breast/Lung NCCP Protocol Code: 00259	ISMO Contributor: Prof Maccon Keane	Page 2 of 5
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Regular tests:

- FBC before each treatment
- Renal and liver profile at start of each cycle

Disease monitoring:

Disease monitoring should be in line with the patient’s treatment plan and any other test/s as directed by the supervising Consultant.

DOSE MODIFICATIONS:

- Any dose modification should be discussed with a Consultant

Haematological:

Dosing should be determined by haematological status.

Table 3: Dose modification of oral vinorelbine during first three administrations at 60mg/m² (Cycle 1-3)

	Neutrophil (x10 ⁹ /L)		Platelets (x10 ⁹ /L)	Dose modification
Cycle 1-3	<1.5	and/or	≤100	Delay until recovery

Table 4: Dose determination criteria for cycle 4

Cycle 4	Neutrophils (x 10 ⁹ /L)-		Dose modification
Neutrophil count during the first 3 administrations of 60mg/m²/week	> 1	≥ 0.5 and < 1 (1 episode)	Recommended starting dose for 4 th administration : 80mg/m ²
Neutrophil count during the first 3 administrations of 60mg/m²/week	≥ 0.5 and < 1 (2 episodes)	< 0.5	Delay until recovery Recommended starting dose for 4 th administration : 60mg/m ²

Table 5: Dose modification of oral vinorelbine Cycle 4 onwards

Neutrophil (x10 ⁹ /L)		Platelets (x10 ⁹ /L)	Dose Modification
<1.5	and/or	≤100	Delay until recovery
≥ 0.5 and < 1 (2 episodes) or < 0.5	and/or	any	Delay until recovery For patients that have increased to 80mg/m ² , Reduce the dose from 80 to 60mg/m ² per week during the 3 following administrations.
It is possible to re-escalate the dose from 60 to 80mg/m ² per week if the neutrophil count does not drop below 0.5 x10 ⁹ /L or more than once between 0.5 -1 x10 ⁹ /L during 3 administrations given at 60mg/m ² according to the rules previously defined for the first 3 administrations.			

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Tumour Group: Breast/Lung NCCP Protocol Code: 00259	ISMO Contributor: Prof Maccon Keane	Page 3 of 5

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Renal and Hepatic Impairment:

Table 6: Dose modification of vinorelbine in renal and hepatic impairment

Renal Impairment	Hepatic Impairment			
No dose reduction necessary	AST +/-or ALT		Bilirubin	Dose
	1.5 -2.5 x ULN	and	< 1.5 x ULN	60mg/m ²
	Any	and	1.5 – 3 x ULN	50mg/m ²
	Any	and	> 3 x ULN	Discontinue

Other Toxicity:

Table 7: Dose modification schedule based on adverse events

Adverse reactions	Recommended dose modification
Peripheral neuropathy Grade 2	Withhold treatment until recovery to grade 1 then reduce the dose to 60mg/m ² (or to 50mg/m ² if already on 60mg/m ²)
Grade 3	Discontinue treatment
Constipation ≥Grade 3	See Adverse Effects below. May consider reducing the dose to 60mg/m ² (or to 50mg/ m ² if already on 60mg/m ²)
Other toxicities ≥Grade 3	Defer therapy for 1 week until resolved to ≤ grade 1. Discuss with consultant if >1week delay.

SUPPORTIVE CARE:

EMETOGENIC POTENTIAL: Moderate (Refer to local policy)

PREMEDICATIONS: None

OTHER SUPPORTIVE CARE:

- Patients should be counseled on the risk of constipation associated with the use of vinca alkaloids. Dietary interventions or prophylactic laxatives may be required.
- Gastric protection with a proton pump inhibitor or a H₂ antagonist may be considered in patients considered at high risk of GI ulceration or bleed.

ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS:

The adverse effects listed are not exhaustive. Please refer to the relevant Summary of Product Characteristics for full details.

- **Cardiac toxicity:** Special care should be taken when prescribing for patients with history of ischemic heart disease.
- **Neutropenia:** The dose limiting adverse reaction is mainly neutropenia. This effect is non-cumulative, having its nadir between 7 and 14 days after the administration and is rapidly reversible within 5 to 7 days. Fever or other evidence of infection must be assessed promptly and treated appropriately.
- **Constipation:** Constipation should at a grade 1-2 be managed with dietary interventions or laxatives.

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Tumour Group: Breast/Lung NCCP Protocol Code: 00259	ISMO Contributor: Prof Maccon Keane	Page 4 of 5

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Laxatives and careful monitoring of bowel mobility are recommended in patients receiving concomitant morphine or opioid analgesics.

- **Fructose intolerance:** Due to sorbitol content, patients with rare hereditary problems with fructose intolerance should not take the capsules.

DRUG INTERACTIONS:

- Risk of drug interactions causing increased concentrations of vinorelbine with CYP3A inhibitors. Patients should also be counselled with regard to consumption of grapefruit juice.
- Risk of drug interactions causing decreased concentrations of vinorelbine with CYP3A inducers.
- Current drug interaction databases should be consulted for more information.

ATC CODE:

Vinorelbine L01CA04

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5. Navelbine ®Summary of Product Characteristics HRP. Last updated: 08/02/2017 Accessed May 2019 Available at https://www.hpra.ie/img/uploaded/swedocuments/LicenseSPC_PA1287-001-004_08022017140058.pdf

Version	Date	Amendment	Approved By
1	29/04/2015		Dr Maccon Keane
2	14/06/2017	Updated with new regimen template	Prof Maccon Keane
3	19/06/2019	Clarification of haematological dose modification	Prof Maccon Keane
4	18/09/2019	Update of emetogenic potential	Prof Maccon Keane

Comments and feedback welcome at oncologydrugs@cancercontrol.ie.

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Tumour Group: Breast/Lung NCCP Protocol Code: 00259	ISMO Contributor: Prof Maccon Keane	Page 5 of 5
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