# 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$^2$ once weekly<br>(MAX 120mg) | PO |

## Administration Week 4 onwards

| Day | Drug | Dose | Route and Method of Administration |
|---|---|---|---|
| 1 | Vinorelbine | *80mg/m$^2$ once weekly<br>(MAX 160mg) | PO |
| *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$^2$. | | | |
| Swallow whole with water, without chewing, sucking or dissolving capsule. It is recommended to administer the capsule with some food | | | |
| 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.<br>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<br>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 |

**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 $10^9$/L or severe infection current or recent (within 2 weeks)
- Platelet count < 100 x $10^9$/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

**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 (x10⁹/L) | | Platelets (x10⁹/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 10⁹/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 4th administration: 80mg/m² |
| **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 4th administration: 60mg/m² |

**Table 5: Dose modification of oral vinorelbine Cycle 4 onwards**

| Neutrophil (x10⁹/L) | | Platelets (x10⁹/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/m², Reduce the dose from 80 to 60mg/m² per week during the 3 following administrations. |
| It is possible to re-escalate the dose from 60 to 80mg/m² per week if the neutrophil count does not drop below 0.5 x10⁹/L or more than once between 0.5 -1 x10⁹/L during 3 administrations given at 60mg/m² according to the rules previously defined for the first 3 administrations. | | | |

## 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 |

## Management of adverse effects:

**Table 7: Dose modification schedule based on adverse events**

| Adverse reactions | Recommended dose modification |
|---|---|
| Peripheral neuropathy<br><br>Grade 2<br><br><br><br>Grade 3 | 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$^2$)<br><br>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<br><br>≥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 counselled 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 $H_2$ 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. 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.

## REFERENCES:


1. Freyer G, Delozier M et al. Phase II study of oral vinorelbine in first-line advanced breast cancer chemotherapy. J Clin Oncol 2003; 21(1):35-40
2. Amadori D, Koralewski P et al. Efficacy and safety of navelbine oral (NVBo) in first line metastatic breast cancer (MBC). Eur J Cancer 2001;37(6):S195
3. Depierre A, Freyer J et al. Oral vinorelbine: Feasibility and safety profile Annals of Oncology 2001;12: 1677-1681
4. NCCP Classification Document for Systemic Anti-Cancer Therapy (SACT) Induced Nausea and Vomiting. V3 2021. Available at: https://www.hse.ie/eng/services/list/5/cancer/profinfo/chemoprotocols/nccp-classification-document-for-systemic-anti-cancer-therapy-sact-induced-nausea-and-vomiting.pdf
5. Vinorelbine (Navelbine®) Summary of Product Characteristics HRPA. Accessed July 2021. Available at: https://www.hpra.ie/img/uploaded/swedocuments/Licence_PA0329-011-002_24092019091922.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 |
| 5 | 21/07/2021 | Reviewed | Prof Maccon Keane |

Comments and feedback welcome at oncologydrugs@cancercontrol.ie.