Carboplatin and Vinorelbine

Indication
First-line chemotherapy for advanced (stage III/IV) non-adenocarcinoma non-small cell lung cancer (NSCLC), when cisplatin is not appropriate.

ICD-10 codes
Codes pre-fixed with C34

Regimen details

Day	Drug	Dose	Route
1 and 8	Vinorelbine	25 mg/m² (max 60mg)	IV infusion
1	Carboplatin*	AUC 5	IV infusion

* Carboplatin dose calculated using the Calvert equation: **Carboplatin dose (mg) = AUC (CrCl +25)**
The creatinine clearance (CrCl) is calculated using the Cockcroft and Gault equation, however for patients where the creatinine level may not truly reflect renal function (e.g. in extremes of BSA or debilitated patients) an EDTA should be performed.
CrCl should be capped at 125mL/min

Alternatively vinorelbine may be given orally as follows:

Day	Drug	Dose	Route
1 and 8	Vinorelbine	60 mg/m^2 (max 120 mg)	PO
1	Carboplatin	AUC 5	IV infusion

From cycle 2 onwards consider increasing the vinorelbine dose to 30 mg/m² (IV) or 80 mg/m² (PO) if first cycle well tolerated.

Cycle frequency
21 days

Number of cycles
4 cycles

Administration
Vinorelbine is administered in 50 mL sodium chloride 0.9% over 10 minutes, as per national guidance.
Nurse to remain with patient throughout infusion.

Carboplatin is administered in 500mL 5% glucose over 30 minutes.

Oral vinorelbine
Vinorelbine is available as 20mg, 30mg and 80mg capsules. The capsules should be swallowed whole with water and with or after food.

Equivalent doses:

IV vinorelbine	**PO vinorelbine**
25mg/m^2	60mg/m^2
30mg/m^2	80mg/m^2

Oral doses should be prescribed as per the table below:

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

Pre-medication

Antiemetics as per local guidelines.

Emetogenicity

This regimen has moderate emetic potential.

Additional supportive medication

H_2 antagonist or proton pump inhibitor if required.
Laxatives
Mouthwashes as per local policy.

Extravasation

Carboplatin is irritant (Group 3)
Vinorelbine is vesicant (Group 5)

Investigations - pre-first cycle

Investigation	**Validity period** (or as per local practice)
FBC	14 days
U+E (including creatinine)	14 days
LFTs	14 days

Investigations - pre subsequent cycles

Investigation	**Validity period** (or as per local practice)
FBC	96 hours*
U+E (including creatinine)	7 days
LFTs	7 days

*In addition FBC is required within 24 hours of day 8 vinorelbine

Standard limits for administration to go ahead

If blood results not within range, authorisation to administer **must** be given by prescriber/ consultant

Investigation	Limit
Neutrophils	≥1.0 x 10^9/L
Platelets	≥100 x 10^9/L
Creatinine Clearance (CrCl)	> 20 mL/min
Bilirubin	<1.5 x ULN
ALT/AST	<1.5 x ULN
Alkaline phosphatase	<2.5 x ULN

Dose modifications

- **Haematological toxicity**

Day 1

If neutrophils < 1.0 x 10^9/L and/or platelets < 100 x 10^9/L delay by 1 week and recheck FBC.

Day 8

Neutrophils (x 10^9/L)		**Platelets** (x 10^9/L)	**Vinorelbine dose**
≥ 1.0	and	≥ 100	100%
0.5 – 1.0	or	50-99	75%
<0.5	or	< 50	Omit

- **Renal impairment**

Carboplatin is contraindicated if CrCl <20mL/min.

If the calculated creatinine clearance falls by >10% from previous cycle recalculate dose of carboplatin. If the calculated creatinine clearance appears to improve the dose should not be increased unless a clear cause of renal function improvement is documented (e.g. treatment of urinary tract obstruction).

- **Hepatic impairment**

If bilirubin > 1.5-3 x ULN and/or AST/ALT > 5-20 x ULN delay vinorelbine for 7 days and recheck LFTs. Once improved consider dose reduction.

If toxicity persists beyond 3 weeks or bilirubin > 3 x ULN and/or AST/ALT > 20 x ULN discontinue treatment.

No dose modification required for carboplatin.

- **Other toxicities**

Neurotoxicity:

If grade 2 neurotoxicity reduce carboplatin and vinorelbine doses to 50%.

If ≥ grade 3 discontinue treatment.

If any other grade 3-4 toxicity (except mucositis and alopecia) delay until ≤ grade 1 toxicity and reduce doses of carboplatin and etoposide to 75%.

If grade 3-4 constipation omit vinorelbine. Consider switching to carboplatin and gemcitabine protocol.

Adverse effects - for full details consult product literature/ reference texts

- **Serious side effects**

Myelosuppression
Neurotoxicity
Peripheral neuropathy
Hypersensitivity
Nephrotoxicity

- **Frequently occurring side effects**

Myelosuppression
Nausea and vomiting
Mucositis, stomatitis
Constipation

- **Other side effects**

Alopecia
Fatigue
Myalgia
Electrolyte imbalances
Taste disturbance

Significant drug interactions – for full details consult product literature/ reference texts

Warfarin/coumarin anticoagulants: increased or fluctuating anticoagulant effects. Avoid if possible, consider switching patient to a low molecular weight heparin during treatment or if the patient continues taking an oral anticoagulant monitor the INR at least once a week and adjust dose accordingly.
Phenytoin: reduced absorption and efficacy of phenytoin, monitor levels and adjust dose as necessary.

Vinorelbine only:
Itraconazole: increased risk of neurotoxicity.
Aprepitant: potential to increase plasma vinorelbine levels.
CYP3A4 inhibitors (e.g. azole antifungals such as ketoconazole and itraconazole) could increase blood concentrations of vinorelbine.
CYP3A4 inducers (e.g. rifampicin, phenytoin) could decrease blood concentrations of vinorelbine.

Carboplatin only:
Aminoglycoside antibiotics: increased risk of nephrotoxicity and ototoxicity
Clozapine: increased risk of agranulocytosis, avoid concomitant use
Diuretics: increased risk of nephrotoxicity and ototoxicity
Nephrotoxic drugs: increased nephrotoxicity ; not recommended

Additional comments

References

- National Institute of Health and Clinical Excellence Guideline CG121. Lung Cancer. The diagnosis and treatment of lung cancer Accessed 7 June 2017 via www.nice.org.uk
- Summary of Product Characteristics Carboplatin (Hospira) accessed 7 June 2017 via www.medicines.org.uk
- Summary of Product Characteristics Vinorelbine (Pierre Fabre) accessed 7 June 2017 via www.medicines.org.uk
- O'Brien et al. Ann of Oncol 2004; 15(6): 921-927

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