Cisplatin and Vinorelbine

Indication

First-line chemotherapy for advanced (stage III/IV) non-adenocarcinoma non-small cell lung cancer (NSCLC).

Adjuvant chemotherapy for resected NSCLC.

ICD-10 codes

Codes pre-fixed with C34.

Regimen details

Day	Drug	Dose	Route
1 and 8	Vinorelbine*	25 -30 mg/m² (max 60mg)	IV infusion
1	Cisplatin	80mg/m^2	IV infusion

Alternatively vinorelbine may be given orally as below:

OR

Day	Drug	Dose	Route
1 and 8	Vinorelbine	60 mg/m^2 (max 120 mg) or 80 mg/m² (max 160mg)	PO
1	Cisplatin	80mg/m^2	IV infusion

Cycle frequency

21 days

Number of cycles

4 cycles

Administration

Day 1

Vinorelbine is administered in 50 mL sodium chloride 0.9% over 10 minutes, as per national guidance.
Nurse to remain with patient throughout infusion.
Cisplatin is administered in 500mL sodium chloride 0.9% over 60 minutes following the pre and post hydration protocol below.

Infusion Fluid & Additives	Volume	Infusion Time
Sodium Chloride 0.9%	1000mL	60 minutes
Mannitol 20% **OR** Mannitol 10%	200mL 400mL	10 minutes 15 minutes
Ensure urine output > 100mL / hour prior to giving cisplatin. Give a single dose of furosemide 20mg iv if necessary.		
Cisplatin	500mL	60 minutes
Sodium Chloride 0.9% + 2g $MgSO_4$ + 20mmol KCl	1000mL	2 hours
TOTAL	**2700 or 2900mL**	**4 hours 10 minutes or 4 hours 15 minutes**

Note: Patients with magnesium or potassium below the normal range should have 2g $MgSO_4$ and 20mmol KCl added to the pre-hydration bag and the duration of the infusion increased to 2 hours

Patients should be advised to drink at least 2 litres of fluid over the 24 hours following cisplatin.

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**
30mg/m^2	80mg/m^2
25mg/m^2	60mg/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

Day 8

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

Pre-medication

Antiemetics as per local guidelines.

Emetogenicity

Day 1 has high emetic potential.
Day 8 has moderate - low emetic potential.

Additional supportive medication

H_2 antagonist or proton pump inhibitor if required.
Laxatives if required.
Mouthwashes as per local policy.
If magnesium levels < normal reference range refer to local magnesium replacement guidelines.

Extravasation

Cisplatin – exfoliant (Group 4)
Vinorelbine – 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
Calcium	14 days
Magnesium	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
Magnesium	7 days
Calcium	7 days

In addition FBC is required within 48 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)	> 60 mL/min
Bilirubin	<1.5 x ULN
ALT/AST	<3 x ULN or < 5 x ULN in presence of liver metastases
Alkaline phosphatase	<2 x ULN or < 5 x ULN in presence of liver metastases

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

CrCl (mL/min)	**Cisplatin dose**	**Vinorelbine dose**
≥ 60	100%	100%
50 - 59	75%	100%
40 – 49	50% (or switch to carboplatin AUC 5)	100%
< 40	Omit	100%*

*If CrCl <30mL/min consider vinorelbine dose reduction.

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

- **Other toxicities**

Toxicity	Definition	Cisplatin dose	Vinorelbine dose
Neurotoxicity	≤Grade 1	100%	100%
	Grade 2	50%	100%
	Grade 3	Omit	100%
	Grade 4	Discontinue	Discontinue
Other toxicities (except alopecia or nausea and vomiting)	≤Grade 2	100% (with or without treatment delay)	100% (with or without treatment delay)
	≤Grade 3	Delay until recovery then consider dose reduction (consultant decision)	Delay until recovery then consider dose reduction (consultant decision)

If grade 3-4 constipation omit vinorelbine and consider switching to gemcitabine.

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

- **Serious side effects**

Myelosuppression
Neurotoxicity
Infertility
Ototoxicity
Cardiotoxicity
Nephrotoxicity

- **Frequently occurring side effects**

Myelosuppression
Nausea and vomiting
Mucositis, stomatitis
Constipation

- **Other side effects**

Alopecia
Fatigue
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: cisplatin and vinorelbine reduce absorption and efficacy of phenytoin, monitor levels and adjust dose as necessary.

Vinorelbine only:
Itraconazole: increased risk of neurotoxicity.

Cisplatin only:
Aminoglycoside antibiotics: increased risk of nephrotoxicity and ototoxicity when given within 2 weeks of cisplatin.
Diuretics: increased risk of nephrotoxicity and ototoxicity
Nephrotoxic drugs: increased nephrotoxicity ; not recommended
Ototoxic drugs: increased risk of ototoxicity
Anti-gout agents: cisplatin may increase plasma concentration of uric acid therefore dose adjustments may be required to control hyperuricaemia and gout.

Additional comments

References

- National Institute of Health and Clinical Excellence Guideline CG121. Lung Cancer. The diagnosis and treatment of lung cancer Accessed 29 October 2014 via www.nice.org.uk
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- 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: Pg.92-8
- Douillard J.Y., et al. Adjuvant vinorelbine plus cisplatin versus observation in patients with completed resected stage IB-IIIA NSCLC. Lancet Oncol. 2006 Sep;7(9):719-27

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