Vincristine, Doxorubicin & Cyclophosphamide (VDC) (Sarcoma)

Indication
Treatment of newly diagnosed Ewing's sarcoma family of tumours as an alternative to VDC/IE in older patients.

ICD-10 codes
C40, C49

Regimen details
NOTE: in patients whose surface area is > 2m^2 consider capping the dose.

VDC

Day	Drug	Dose	Route
1	Vincristine	2mg	IV infusion over 10 mins
1	Doxorubicin[#]	60mg/m^2*	IV bolus or IV infusion over 1 hour
1	Mesna	240mg/m^2	IV bolus
1	Cyclophosphamide	1200mg/m^2*	IV infusion over 1 hour
1	Mesna At 2 hours and 6 hours post end of cyclophosphamide infusion	480mg/m^2	Oral

*For older patients or those with co-morbidities consider starting at a dose reduction – doxorubicin 50mg/m^2 and cyclophosphamide 900mg/m^2.
[#]If LVEF < 50% substitute with dactinomycin 1.5mg/m^2 (capped at 2mg).

Cycle frequency
21 days

Number of cycles
6 cycles

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

Doxorubicin may be administered as an IV bolus, or IV infusion in 250mL Sodium Chloride 0.9% over 1 hour. The latter is preferred as it may reduce the risk of cardiotoxicity.

Cyclophosphamide is administered in 500mL sodium chloride 0.9% over 1 hour. 1000mL sodium chloride 0.9% with 20mmol potassium chloride over 2 hours should be administered immediately following cyclophosphamide administration and patients should maintain an oral intake of 2L of fluid on treatment day

Mesna is administered as an IV bolus immediately prior to cyclophosphamide. Oral mesna is then administered at 2 hours and 6 hours post the end of the cyclophosphamide infusion. Mesna is available as 400mg and 600mg tablets and doses should be rounded up to the nearest tablet size.

Pre-medication
Nil

Emetogenicity

This regimen has high emetic potential – refer to local policy.

Additional supportive medication

Antiemetics as per local policy
Benzydamine mouthwash as required
Proton pump inhibitor on days where steroids given
Laxatives as required
GCSF for 5-7 days, starting on day 6

Extravasation

Vincristine – vesicant
Doxorubicin – vesicant
Cyclophosphamide – neutral

Investigations – pre first cycle

Investigation	Validity period
FBC	14 days
U&E (including creatinine)	14 days
LFTs	14 days
Echocardiogram	3 months

Investigations – pre subsequent cycles

Investigation	Validity period
FBC	96 hours
U&E	7 days
LFTs	7 days
Echocardiogram	As clinically indicated

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
Bilirubin	≤ ULN (see dose modifications for hepatic toxicity below)
Creatinine Clearance	> 20 mL/min
Left ventricular ejection fraction	≥ 50% and less that 10% decline from baseline

Dose modifications

- **Haematological toxicity**

If neutrophils <1.0 x 10^9/L or platelets <100 x10^9/L delay treatment until count recovery then reduce doxorubicin and cyclophosphamide doses by 20% for future cycles.

If further haematological toxicity despite dose reduction, reduce doses by a further 20%.

- **Renal impairment**

Vincristine – no dose adjustment is expected.

Doxorubicin – no dose adjustment is expected.

Cyclophosphamide:

Creatinine Clearance	Cyclophosphamide dose
>20 mL/min	100%
10-20 mL/min	75%
<10 mL/min	50%

- **Hepatic impairment**

Bilirubin (mmol/L)	Vincristine dose	Doxorubicin dose	Cyclophosphamide dose
21-50	100%	50%	Full dose
51-86	50%	25%	Use full dose with caution, potential reduced efficacy
>86	Omit	Omit	

- **Other toxicities**

Toxicity	Definition	Dose adjustment
Decline in left ventricular ejection fraction (LVEF)	LVEF < 50% or a decline in LVEF by 10 percentage points or more from baseline	Hold chemo and repeat echocardiogram in 7 days. patients should be started on a beta-blocker (e.g. bisoprolol 1.25mg od) and an angiotensin-converting enzyme (ACE) inhibitor (e.g. ramipril 1.25mg od), and referred to a cardiologist. If no improvement switch to actinomycin-D 1.5mg/m^2 (capped at 2mg) on day 1 only. Repeat cardiac imaging prior to next cycle and if normalised, re-commence doxorubicin at usual dose
Mucositis	Grade 3: severe pain interfering with oral intake *or* Grade 4: life threatening, urgent intervention needed	Reduce subsequent doxorubicin doses to 75%

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

- **Serious side effects**

Myelosuppression
Neutropenic sepsis
Haemorrhagic cystitis
Peripheral neuropathy
Nephrotoxicity

- **Frequently occurring side effects**

Neutropenia
Thrombocytopenia
Anaemia

- **Other side effects**

Alopecia
Infertility

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 or DOAC during treatment, or if the patient continues taking an oral anticoagulant monitor the INR at least once a week and adjust dose accordingly.

Vincristine:
Itraconazole, voriconazole, posaconazole: increase severity of neuromuscular side effects. Avoid for 72 hours either side of vincristine dose if concurrent use cannot be avoided.

Doxorubicin:
Ciclosporin: reduced clearance of doxorubicin due to CYP3A4 and P-gp inhibition. Monitor closely for toxicity.

Cyclophosphamide:
Amiodarone: increased risk of pulmonary fibrosis – avoid if possible
Clozapine: increased risk of agranulocytosis – avoid concomitant use
Digoxin tablets: reduced absorption – give as liquid form
Indapamide: prolonged leucopenia is possible - avoid
Itraconazole: may increase adverse effects of cyclophosphamide
Phenytoin: reduced absorption - may need to increase dose of phenytoin
Grapefruit juice: decreased or delayed activation of cyclophosphamide. Patients should be advised to avoid grapefruit juice for 48 hours before and on day of cyclophosphamide dose.

Additional comments

The maximum cumulative dose of doxorubicin is 450-550mg/m^2. In patient with cardiac risk factors the maximum cumulative dose is 400mg/m^2.

References

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- Summary of Product Characteristics Vincristine (Hospira) accessed 26 June 2025 via www.medicines.org.uk
- Summary of Product Characteristics Doxorubicin (Accord) accessed 26 June 2025 via www.medicines.org.uk
- Summary of Product Characteristics Cyclophosphamide (Sandoz) accessed 26 June 2025 via www.medicines.org.uk

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Date: June 2025