

IFOSFAMIDE ETOPOSIDE (5 day)

INDICATION (ICD10) C40

1. Relapsed / refractory osteosarcoma

REGIMEN

Day 1 ETOPOSIDE 100mg/m²* in 500ml sodium chloride 0.9% IV infusion over 2 hours
 Mesna 1000mg/m² in 500ml sodium chloride 0.9% IV infusion over 60 minutes
 IFOSFAMIDE 2800mg/m² and Mesna 1400mg/m² in 1000-2000ml sodium chloride 0.9% IV infusion over 4 hours
 Mesna 1400mg/m²* in 1000ml sodium chloride 0.9% IV infusion over 17 hours

Day 2 ETOPOSIDE 100mg/m²* in 500ml sodium chloride 0.9% IV infusion over 2 hours
 Mesna 1000mg/m² in 500ml sodium chloride 0.9% IV infusion over 60 minutes
 IFOSFAMIDE 2800mg/m² and Mesna 1400mg/m² in 1000-2000ml sodium chloride 0.9% IV infusion over 4 hours
 Mesna 1400mg/m²* in 1000ml sodium chloride 0.9% IV infusion over 17 hours

Day 3 ETOPOSIDE 100mg/m²* in 500ml sodium chloride 0.9% IV infusion over 2 hours
 Mesna 1000mg/m² in 500ml sodium chloride 0.9% IV infusion over 60 minutes
 IFOSFAMIDE 2800mg/m² and Mesna 1400mg/m² in 1000-2000ml sodium chloride 0.9% IV infusion over 4 hours
 Mesna 1400mg/m²* in 1000ml sodium chloride 0.9% IV infusion over 17 hours

Day 4 ETOPOSIDE 100mg/m²* in 500ml sodium chloride 0.9% IV infusion over 2 hours
 Mesna 1000mg/m² in 500ml sodium chloride 0.9% IV infusion over 60 minutes
 IFOSFAMIDE 2800mg/m² and Mesna 1400mg/m² in 1000-2000ml sodium chloride 0.9% IV infusion over 4 hours
 Mesna 1400mg/m²* in 1000ml sodium chloride 0.9% IV infusion over 17 hours

Day 5 ETOPOSIDE 100mg/m²* in 500ml sodium chloride 0.9% IV infusion over 2 hours
 Mesna 1000mg/m² in 500ml sodium chloride 0.9% IV infusion over 60 minutes
 IFOSFAMIDE 2800mg/m² and Mesna 1400mg/m² in 1000-2000ml sodium chloride 0.9% IV infusion over 4 hours
 Mesna 1400mg/m²* in 1000ml sodium chloride 0.9% IV infusion over 17 hours

*doses 48mg to 88mg in 250ml, 200mg to 360mg in 1000ml sodium chloride 0.9%

CYCLE FREQUENCY AND NUMBER OF CYCLES

Every 21 days for up to 5 cycles

ANTI-EMETICS

Moderate emetic risk days 1 to 5

CONCURRENT MEDICATION REQUIRED

Ifosfamide	Ensure mesna administered Ensure adequate oral fluid intake.
GCSF	GCSF starting at least 24 hours after chemotherapy

EXTRAVASATION AND TYPE OF LINE / FILTERS

Etoposide - irritant

Ifosfamide – neutral

Central line

INVESTIGATIONS

Blood results required before SACT administration
 FBC, U&E, Ca⁺⁺, PO₄⁻ and LFTs every week
 Neutrophils x 10⁹/L ≥0.25
 Platelets x 10⁹/L ≥50
 Creatinine clearance ≥70ml/min
 Bilirubin <1.25xULN
 Haematuria monitoring every specimen
 DTPA baseline
 Serum creatinine every cycle
 Creatinine clearance every cycle
 Vitamin D baseline
 Hepatitis B status baseline
 Baseline weight and every cycle

MAIN TOXICITIES AND ADVERSE REACTIONS

Ifosfamide	Ifosfamide encephalopathy. Nephrotoxicity - Irreversible renal failure and tubular damage can occur, more frequent with cumulative doses over 25–50g/m ² of ifosfamide. Haematuria
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INTERACTIONS WHICH MAY REQUIRE DOSE MODIFICATIONS (not exhaustive list check SPC/BNF/Stockleys)

Ifosfamide	Aprepitant and fosaprepitant are predicted to increase the exposure to ifosfamide. Caution.
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DOSE MODIFICATIONS

Non-haematological

Ifosfamide

Neural toxicity grade

Toxicity Grade	Tp/C _{crea} (T _{mp} /GFR) (mmol/l)	HCO ₃ [*] (mmol/l)	Action (apply worst grade)
Grade 0/1	≥1.00	≥17.0	give 100% dose
Grade 2	0.8-0.99	14.0-16.9	give 70% of total dose
Grade 3/4	≤0.8	≤14.0	**Switch to cyclophosphamide 1500mg/m ²

*Low values of HCO₃ should be re-checked when the patient is clinically stable (to rule out infection as a cause, etc) before modifying treatment.

**Discuss with consultant before and to confirm substitution of ifosfamide with cyclophosphamide 1500mg/m²/day day 1

Fractional phosphate clearance calculated

$$Tp/C_{crea} [\text{mmol/ml}] = \frac{\text{Phosphate}_{\text{serum}} - \text{Phosphate}_{\text{urine}} \times \text{creatinine}_{\text{serum}}}{\text{Creatinine}_{\text{urine}}}$$

Hepatic impairment

Etoposide

Bilirubin ≥50micromol/L or decreased albumin	give 50% dose
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Ifosfamide

Bilirubin >17 micromol/L or AST and ALP >2.5xULN	discuss
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Renal impairment

Etoposide

CrCl >50ml/min	give 100% dose
CrCl 15-50ml/min	give 75% dose
CrCl <15ml/min	Further dose reduction

Ifosfamide

CrCl >50ml/min	give 100% dose
CrCl <50ml/min	Clinical decision

REFERENCES