IFOSFAMIDE high dose

INDICATION (ICD10) C40, C41, C49
1. Recurrent and primary refractory high grade sarcoma

REGIMEN
Day 1	MESNA 400mg/m^2 IV bolus 60 minutes before ifosfamide
Days 1 to 5	IFOSFAMIDE 3000mg/m^2/day in 3000ml sodium chloride 0.9% IV infusion over 24 hours
Days 1 to 5	MESNA 3000mg/m^2/day in 3000ml sodium chloride 0.9% IV infusion over 24 hours
Day 5	MESNA 1800mg/m^2 in 1000ml sodium chloride 0.9% IV infusion over 12 hours following final ifosfamide dose

CYCLE FREQUENCY AND NUMBER OF CYCLES
Every 21 days for 4 cycles

ANTI-EMETICS
High emetic risk days 1 to 5 (consider aprepitant)

CONCURRENT MEDICATION REQUIRED
Ifosfamide	Ensure mesna administered. Ensure adequate oral fluid intake.
GCSF	Starting 24 hours after completion final ifosfamide infusion

EXTRAVASATION AND TYPE OF LINE / FILTERS
Ifosfamide – neutral

Central line

INVESTIGATIONS
Blood results required before SACT administration
FBC, U&E and LFTs every week
Neutrophils x 10^9/L ≥1.5
Platelets x 10^9/L ≥100
DTPA at baseline
Creatinine clearance >55ml/min
Serum creatinine every cycle
Haematuria monitoring every specimen
Vitamin D baseline
Hepatitis B status baseline
Baseline weight and every cycle

MAIN TOXICITES AND ADVERSE REACTIONS
Ifosfamide	Ifosfamide encephalopathy. Nephrotoxicity: Irreversible renal failure and tubular damage can occur, and this is more frequent with cumulative doses over 25–50g/m^2 of Ifosfamide Haematuria

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.

DOSE MODIFICATIONS

Non-haematological

Ifosfamide

Neuraland nephrotoxicity grade

Toxicity Grade	GFR (ml/min/1.73m^2)	Tp/C_{crea} (Tm_p/GFR) (mmol/l)	HCO_3* (mmol/l)	Action (apply worst grade)
Grade 0/1	≥60	≥1.00	≥17.0	give 100% dose
Grade 2	40-59	0.8-0.99	14.0-16.9	give 70% dose
Grade 3/4	≤40	≤0.8	≤14.0	**Switch to cyclophosphamide

*Low values of HCO_3 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/m^2/day.

Fractional phosphate clearance calculated

$$Tp/C_{crea}\ [mmol/ml] = Phosphate_{serum} - \frac{Phosphate_{urine} \times creatinine_{serum}}{Creatinine_{urine}}$$

Hepatic impairment

Ifosfamide

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

Renal impairment

Ifosfamide

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

REFERENCES

1. Meazza C, Casanova M, Luksch R, Podda M, Favini F, Cefalo G, et al. Prolonged 14-day continuous infusion of high-dose ifosfamide with an external portable pump: feasibility and efficacy in refractory pediatric sarcoma. Pediatric blood & cancer. 2010;55(4):617-20.
2. Martin-Liberal J, Alam S, Constantinidou A, Fisher C, Khabra K, Messiou C, et al. Clinical activity and tolerability of a 14-day infusional Ifosfamide schedule in soft-tissue sarcoma. Sarcoma. 2013;2013:868973.