Chemotherapy Protocol

SARCOMA

ETOPOSIDE-IFOSFAMIDE (5 day)

Inpatient Regimen

Regimen

- Sarcoma-InP-Etoposide-Ifosfamide (5 day)

Indication

- Second line treatment of osteosarcoma (palliative)

Toxicity

Drug	Adverse Effect
Etoposide	Hypotension on rapid infusion, hyperbilirubinaemia
Ifosfamide	Haemorrragic cystitis, encephalopathy, nephrotoxicity

The adverse effects listed are not exhaustive. Please refer to the relevant Summary of Product Characteristics for full details.

Monitoring

- FBC, LFTs and U&Es (including uric acid, albumin, calcium, magnesium, bicarbonate and phosphate) prior to day one of treatment
- Urine dip test for blood every four hours the day of and the day after ifosfamide administration
- EDTA or calculated creatinine clearance prior to each cycle
- Fluid balance monitoring every four hours the day of and the day after ifosfamide administration. Urine output should be maintained above 100ml/hour

Dose Modifications

The dose modifications listed are for haematological, liver and renal function and drug specific toxicities only. Dose adjustments may be necessary for other toxicities as well.

Dose/time intensity is regarded as an essential aspect of induction strategy. Please discuss all dose reductions / delays with the relevant consultant before prescribing, if appropriate. The approach may be different depending on the clinical circumstances.

Haematological

Criteria	Eligible Level
Neutrophil	equal to or more than $0.75x10^9$/L
Platelets	equal to or more than $75x10^9$/L

If neutrophils are between 0.5-0.74x10^9/L or platelets are 25-74x10^9/L delay treatment for a week and repeat FBC. If within normal parameters, continue with full dose treatment.

If neutrophils less than 0.5x10^9/L or platelets are less than 25x10^9/L delay treatment for a week and repeat FBC. If within normal parameters, continue with a 25% dose reduction.

Consider blood transfusion or erythropoietin if the patient is symptomatic of anaemia or has a haemoglobin of less than 8g/dL.

Hepatic Impairment

Drug	Bilirubin µmol/L		AST/ALT units/L	Dose (% of original dose)
Etoposide	*30-51	or	60-180	50%
	more than 51	or	more than 180	Clinical decision
Ifosfamide	more than 20	or	more than 2.5xULN	Not recommended
	or ALP more than 2.5xULN			

Renal Impairment

Drug	Creatinine Clearance (ml/min)	Dose (% of original dose)
Etoposide	more than 50	100%
	15-50	75%
	less than15	50%
Ifosfamide	more than 60	100%
	40-59	70% or consider using cyclophosphamide at a dose of 1500mg/m^2
	Less than 40	Clinical decision, consider using cyclophosphamide at a dose of 1500mg/m^2

Other

Etoposide

Where significant reductions in albumin levels occur consider reducing the dose of etoposide.

Ifosfamide

In the case of a NCI-CTC grade 1 neurological toxicity to ifosfamide, consider reducing the dose of ifosfamide for the next cycle. If a NCI-CTC grade 2 neurologic toxicity appears or neurologic toxicity worsens despite dose reduction consider stopping the ifosfamide.

In the case of NCI-CTC grade 3 or 4 mucositis/GI toxicity reduce dose to 80% on first occurrence and to 60% on second occurrence. In the case of NCI-CTC grade 3 or 4 neutropenic sepsis reduce dose to 80% on first occurrence and to 60% on second occurrence. In the case of delayed recovery of greater than 6 days, reduce dose to 80% on first occurrence and to 60% on second occurrence.

Risk factors for CNS toxicity include a low albumin, renal impairment, prior administration of cisplatin, poor performance status, CNS tumour, bulky pelvic disease, concomitant psychotropic drugs and younger age. Methylene blue 50mg four times a day intravenous infusion in 100ml sodium chloride 0.9% over 30 minutes can be used to prevent or treat ifosfamide induced encephalopathy.

Regimen

21 day cycle for 6 cycles

Drug	Dose	Days	Administration
Etoposide	100mg/m^2	1, 2, 3, 4, 5	Intravenous infusion in 1000ml sodium chloride 0.9% over 60 minutes
Mesna	600mg/m^2	1, 2, 3, 4, 5	Intravenous bolus in 100ml sodium chloride 0.9% over 15 minutes
Ifosfamide	1800mg/m^2	1, 2, 3, 4, 5	Intravenous infusion in 1000ml sodium chloride 0.9% over 240 minutes (the ifosfamide and mesna are in the same bag)
Mesna	1800mg/m^2		
Mesna	1200mg/m^2	1, 2, 3, 4, 5	Intravenous infusion in 1000ml sodium chloride 0.9% over 720 minutes beginning at the end of the ifosfamide infusion.

Dose Information

- Etoposide will be dose banded according to the agreed bands
- Ifosfamide will be dose banded according to the agreed bands
- Mesna will be dose banded according to the agreed bands

Administration Information

Extravasation

- Etoposide - irritant
- Ifosfamide – neutral

Additional Therapy

This is an inpatient regimen please ensure all supportive and take home medicines are prescribed on the inpatient chart or general electronic prescribing system.

Antiemetics

Starting 15-30 minutes prior to chemotherapy

- dexamethasone 4mg twice a day for 6 days oral or intravenous
- metoclopramide 10mg three times a day for 6 days then when required oral or intravenous
- ondansetron 8mg twice a day for 6 days oral or intravenous

- Growth factors according to local formulary choice. For example:

  - filgrastim or bioequivalent 30million units once a day for 7 days from day 7 subcutaneous
  - lenograstim or bioequivalent 33.6million units once a day for 7 days from day 7 subcutaneous
  - pegfilgrastim, lipegfilgrastim or bioequivalent 6mg once only on day 5 subcutaneous

- Ciprofloxacin 500mg twice a day for 7 days starting on day 10 of the cycle

- The final dose of mesna on day 3 may be replaced with oral mesna at a dose of 1200mg/m^2 (rounded upwards to the nearest 400mg capsule) at 0, 2 and 6 hours after the end of the ifosfamide infusion.

- Mouthwashes according to local or national policy on the treatment of mucositis

- Gastric protection with a proton pump inhibitor or a H_2 antagonist may be considered in patients considered at high risk of GI ulceration or bleed.

Coding

- Procurement – X71.2

- Delivery – not required

References

REGIMEN SUMMARY

InP-Etoposide-Ifosfamide (5 day)

Other than those listed below, supportive medication for this regimen will not appear in Aria as prescribed agents. The administration instructions for each warning describes the agents which must be prescribed on the in-patient chart or general electronic prescribing system

Day 1, 2, 3, 4, 5

1. Warning – Check supportive medication prescribed
   Administration Instructions
   1. Dexamethasone 4mg twice a day for 6 days oral or intravenous bolus
   2. Metoclopramide 10mg three times a day for 6 days oral or intravenous bolus
   3. Ondansetron 8mg twice a day for 6 days oral or intravenous bolus
   4. Ciprofloxacin 500mg twice a day days 10-17 inclusive of the cycle oral
   5. Growth factor according to local formulary choice. For example;
      - filgrastim or bioequivalent 30million units once a day for 7 days from day 7 subcutaneous
      - lenograstim or bioequivalent 33.6 million units once a day for 7 days from day 7 subcutaneous
      - pegfilgrastim, lipegfilgrastim or bioequivalent 6mg once only on day 6 subcutaneous
   6. Consider gastric protection
   7. Consider mouthwashes

2. Etoposide 100mg/m^2 intravenous infusion in 1000ml sodium chloride 0.9% over 60 minutes

3. Mesna 600mg/m^2 intravenous bolus in 100ml sodium chloride 0.9% over 15 minutes

4. Ifosfamide 1800mg/m^2 and mesna 1800mg/m^2 intravenous infusion in 1000ml sodium chloride 0.9% over 240 minutes

5. Mesna 1200mg/m^2 intravenous infusion in 1000ml sodium chloride 0.9% over 720 minutes
   Administration Instructions
   On day 5 of the cycle (after the last of the ifosfamide infusions) this may be substituted by oral mesna at a dose of 1200mg/m^2 rounded upwards to the nearest 400mg tablet given 0, 2 and 6 hours after the end of the ifosfamide infusion.

DOCUMENT CONTROL

Version	Date	Amendment	Written By	Approved By
1	February 2016	None	Dr Deborah Wright Pharmacist	Dr Nicola Keay Consultant Medical Oncologist

This chemotherapy protocol has been developed as part of the chemotherapy electronic prescribing project. This was and remains a collaborative project that originated from the former CSCCN. These documents have been approved on behalf of the following Trusts;

Hampshire Hospitals NHS Foundation Trust
NHS Isle of Wight
Portsmouth Hospitals NHS Trust
Salisbury NHS Foundation Trust
University Hospital Southampton NHS Foundation Trust
Western Sussex Hospitals NHS Foundation Trust

All actions have been taken to ensure these protocols are correct. However, no responsibility can be taken for errors that occur as a result of following these guidelines.