

## Chemotherapy Protocol

### SARCOMA

#### IFOSFAMIDE (2 day)

#### Inpatient Regimen

#### Regimen

- Sarcoma-InP-Ifosfamide (2 day)

#### Indication

- Advanced or metastatic soft tissue sarcoma

#### Toxicity

Drug	Adverse Effect
Ifosfamide	Haemorrhagic 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 $1 \times 10^9/L$
Platelets	equal to or more than $100 \times 10^9/L$

If neutrophils are between  $0.5-1 \times 10^9/L$  or platelets are between  $25-100 \times 10^9/L$  delay treatment for seven days and repeat FBC. If within normal parameters, continue with full dose treatment. If a fourteen day is required to allow counts to recover then treatment may be continued with a 25% dose reduction. If the neutrophils are less than  $0.5 \times 10^9/L$  and the platelets are less than  $25 \times 10^9/L$  then delay treatment until the counts recover and 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 $\mu\text{mol/L}$		AST/ALT units/L	Dose (% of original dose)
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)
Ifosfamide	more than 60	100%
	40-59	70% or consider using cyclophosphamide at a dose of $1500\text{mg/m}^2$
	Less than 40	Clinical decision, consider using cyclophosphamide at a dose of $1500\text{mg/m}^2$

### Other

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

In the case of CTCAE grade 3 or 4 mucositis/GI toxicity reduce dose to 80% on first occurrence and to 60% on second occurrence. In the case of CTCAE 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

The dose of ifosfamide can vary. The dose can be between 2000mg/m<sup>2</sup> per day for two days to 3000mg/m<sup>2</sup> per day for three days. Check the dose with the relevant consultant before prescribing.

Drug	Dose	Days	Administration
Mesna	400mg/m <sup>2</sup>	1, 2	Intravenous bolus in 100ml sodium chloride 0.9% over 15 minutes
Ifosfamide	2000mg/m <sup>2</sup>	1,2	Intravenous infusion in 1000ml sodium chloride 0.9% over 240 minutes (the ifosfamide and mesna are in the same bag)
Mesna	2000mg/m <sup>2</sup>		
Mesna	1200mg/m <sup>2</sup>	1, 2	Intravenous infusion in 1000ml sodium chloride 0.9% over 720 minutes

## [Dose Information](#)

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

## [Administration Information](#)

Extravasation

- 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 3 days oral or intravenous
- metoclopramide 10mg three times a day for 3 days then when required oral or intravenous
- ondansetron 8mg twice a day for 3 days oral or intravenous
- Growth factors according to local formulary choice. For example:
  - filgrastim or bioequivalent 30million units once a day from day 5 subcutaneous
  - lenograstim or bioequivalent 33.6million units once a day from day 5 subcutaneous
  - pegfilgrastim, lipegfilgrastim or bioequivalent 6mg once only on day 3 subcutaneous
- Ciprofloxacin 500mg twice a day for 7 days starting on day 7 of the cycle

- The final dose of mesna on day 2 may be replaced with oral mesna at a dose of 800mg/m<sup>2</sup> (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<sub>2</sub> antagonist may be considered in patients considered at high risk of GI ulceration or bleed.

#### Coding

- Procurement – X70.5
- Delivery – not required

#### References

1. van Osterom AT, Mouridsen HT, Nielson OS et al. Results of randomised studies of the EORTC soft tissue and bone sarcoma group (STBSG) with two different ifosfamide regimens in first and second line chemotherapy in advanced soft tissue sarcoma patients . Eur J Cancer 2002; 38 (18): 2397-2404

## REGIMEN SUMMARY

### InP-Ifosfamide (2 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

##### 1. Warning – Check supportive medication prescribed

###### Administration Instructions

1. Dexamethasone 4mg twice a day for 3 days oral or intravenous
2. Metoclopramide 10mg three times a day for 3 days oral or intravenous
3. Ondansetron 8mg twice a day for 3 days oral or intravenous
4. Ciprofloxacin 500mg twice a day days 7-14 oral
5. Growth factor according to local formulary choice. For example;
  - filgrastim or bioequivalent 30million units once a day for 7 days from day 5 subcutaneous
  - lenograstim or bioequivalent 33.6million units once a day for 7 days from day 5 subcutaneous
  - pegfilgrastim, lipegfilgrastim or bioequivalent 6mg once only on day 3 subcutaneous
6. Consider gastric protection
7. Consider mouthwashes

2. Mesna 400mg/m<sup>2</sup> intravenous bolus in 100ml sodium chloride 0.9% over 15 minutes

3. Ifosfamide 2000mg/m<sup>2</sup> and mesna 2000mg/m<sup>2</sup> intravenous infusion in 1000ml sodium chloride 0.9% over 240 minutes

###### Administration Instructions

Please check the dose with the relevant consultant. There are regimens where 2000mg/m<sup>2</sup> to 3000mg/m<sup>2</sup> of ifosfamide per 24 hours for 2 to 3 days are used. The mesna dose will also need adjusting if this regimen is altered.

4. Mesna 1200mg/m<sup>2</sup> intravenous infusion in 1000ml sodium chloride 0.9% over 720 minutes

###### Administration Instructions

On day 2 of the cycle (after the last of the ifosfamide infusions) this may be substituted by oral mesna at a dose of 800mg/m<sup>2</sup> rounded upwards to the nearest 400mg capsule 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 which occur as a result of following these guidelines.