

A Guideline for Managing Positive Blood on Urine dips for Inpatients on Ifosfamide

Introduction

Ifosfamide is a cytotoxic chemotherapy drug used in various regimens on the oncology ward for treating sarcomas. (1) It can be an extremely effective drug and is used in high doses. Unfortunately one of its many side effects includes haemorrhagic cystitis. This occurs more frequently with higher doses and mesna is used alongside the drug to prevent this.(2)

Mechanism of Action

Ifosfamide is a prodrug and is metabolised to form a powerful alkylating agent which makes DNA cross links damaging the cancer cells. One of its metabolites includes acrolein which is renally excreted but is also toxic to the bladder. This can result in haemorrhagic cystitis. Mesna is used as the antidote to acrolein. It forms a complex producing a non-toxic by product which is excreted harmlessly. (2,3)

Monitoring

All patients' urine is collected throughout treatment and each bottle should be tested using the urine testing strips provided on the ward. (Siemens Multistix 8SG)

Grading system

- 0 – No symptoms of bladder irritability or haemorrhage
- 1 – Microscopic haematuria
- 2 – Macroscopic haematuria
- 3 – Macroscopic haematuria with small clots
- 4 – Massive macroscopic haematuria requiring instrumentation for clot evacuation and/or causing urinary obstruction.

If there is **ONE** positive + 1 blood urine dip then continue to monitor the patient carefully. There is no need to take further action. Make sure fluids **and in particular the MESNA** are running correctly and encourage oral fluid intake.

If there are **TWO** or more positive +1 blood urine dip results then action should be considered.

Treatment

A bolus of mesna at 600mg/m² in 250mls of sodium chloride 0.9% over 30 minutes can be started if the patient requires intervention (5). Following this another infusion of mesna should to be given at double dose. For example: to increase mesna from 3000mg/m² over 12 hours to 6000mg/m² over 12 hours, the extra 3000mg/m² of Mesna can be put into a separate 1 Litre bag of 0.9% sodium chloride and run alongside the mesna and ifosfamide bag. (3,5) This treatment can be started straight away, however it is important to discuss this with the treating sarcoma team as soon as possible.

Written by S.Whiting, C. Orman May 2016

Checked by L.Spiers, S.Pratap

Review Date May 2018

It is important to continue the separate mesna infusion until the patient is reviewed **and for 24 hours after the ifosfamide infusion has finished** (5). The patient needs to be monitored for blood in further urine dips. If positive dips persist or if there is grade 2 or greater haematuria then ifosfamide infusion should be stopped and the sarcoma team should be consulted for **further management advice**. There may be other causes for the haematuria such as ureteric stent placement and therefore if ifosfamide is stopped the sarcoma team should be involved in making this decision.

The sarcoma team should be informed of all positive blood dips in the urine during normal working hours, ideally prior to them reviewing the patient on the ward. All results need to be documented on EPR.

Should treatment be required outside of normal working hours the registrar on-call should be contacted and informed the patient has reached the threshold for treatment. The sarcoma team is available to discuss this out of hours also.

Side Effects of Mesna

The most commonly occurring Mesna side effects include headache, infusion site reactions, abdominal pain/colic, lightheadedness, lethargy/drowsiness, pyrexia, rash, diarrhoea, nausea, flushing, and influenza-like illness.(4) The most severe adverse reactions (but rare) associated with use of mesna are: bullous skin reactions, anaphylaxis, and drug rash with eosinophilia and systemic symptoms (DRESS).

Cyclophosphamide

The above guideline can also be applied to cyclophosphamide given to inpatients on oncology ward under the sarcoma team.

References

- (1) Ifosfamide Summary of Product Characteristics
<http://www.medicines.org.uk/emc/medicine/30184> [Accessed 02/02/2016]
- (2) Haemorrhagic Cystitis : A challenge to the urologist Indian J Urol. 2010 Apr-Jun; 26(2): 159–166. <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2938536/> [Accessed 02/02/2016]
- (3) EURAMOS 1 regimen (MAPIE) from ARIA Planner (now out of date)
- (4) Mesna Summary of product Characteristics [Accessed 04/02/16]
<https://www.medicines.org.uk/emc/medicine/30187>
- (5) EuroEwing 2012 Trial protocol from ARIA