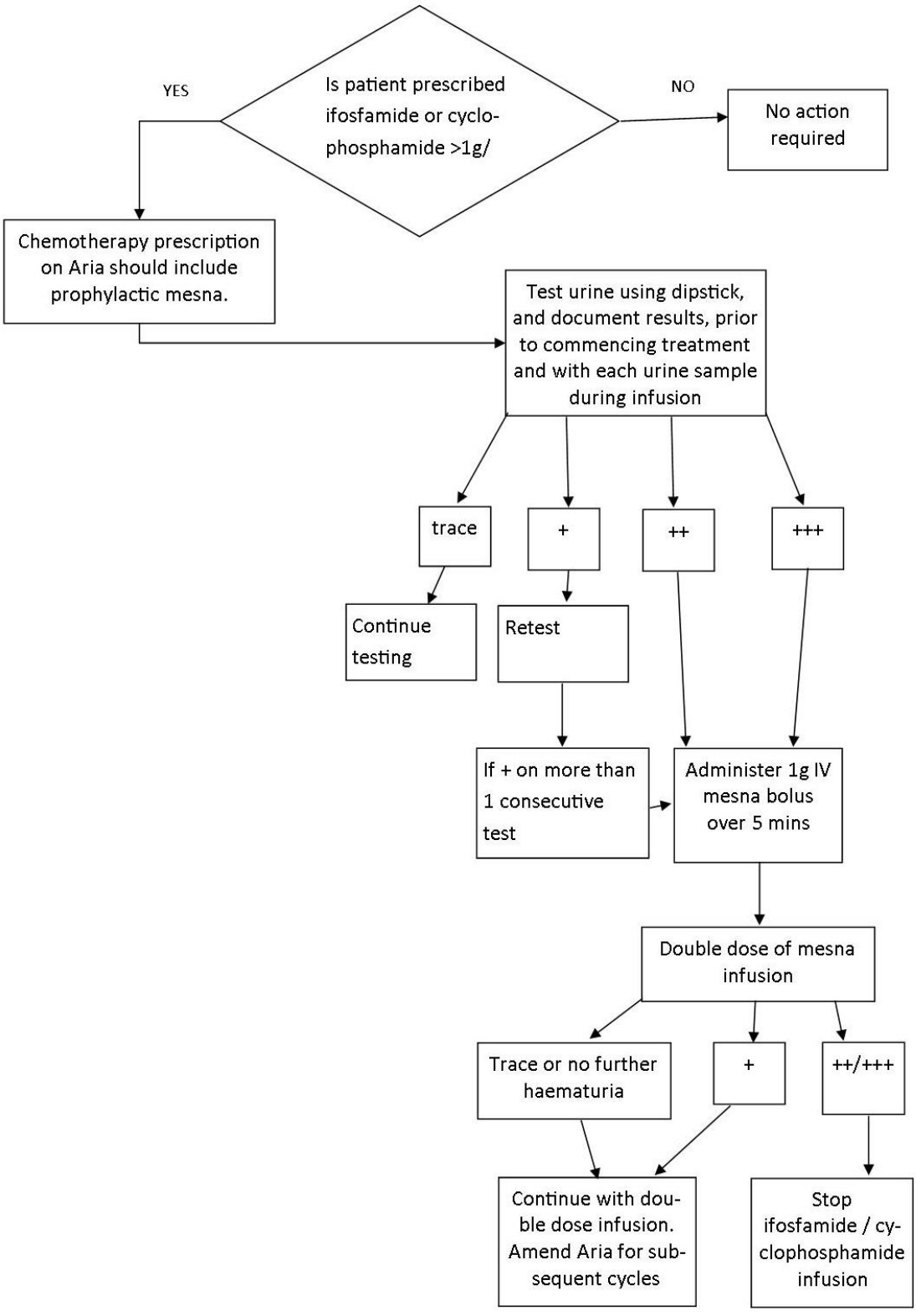
Royal Cornwall Hospitals
NHS Trust

The Administration of Mesna with Ifosfamide and Cyclophosphamide Clinical Guideline

V4.0

October 2025

Summary


Is patient prescribed ifosfamide or cyclo-phosphamide >1g/
YES
NO
No action required
Chemotherapy prescription on Aria should include prophylactic mesna.
Test urine using dipstick, and document results, prior to commencing treatment and with each urine sample during infusion
trace
+
++
+++
Continue testing
Retest
If + on more than 1 consecutive test
Administer 1g IV mesna bolus over 5 mins
Double dose of mesna infusion
Trace or no further haematuria
+
++/+++
Continue with double dose infusion. Amend Aria for subsequent cycles
Stop ifosfamide / cyclophosphamide infusion

1. Aim/Purpose of this Guideline

1.1. The objective of this guideline is to promote consistent clinical practice in relation to the use of mesna in the prevention and treatment of ifosfamide and cyclophosphamide-induced urinary tract toxicity.

1.2. This guideline is relevant to:

1.2.1. Oncology and Haematology doctors.

1.2.2. SACT nurses working on Lowen ward and the Headland Unit.

1.2.3. Pharmacists.

1.3. It is not intended to be used for non-cancer use of cyclophosphamide and ifosfamide (although the general principles may apply to these patients) or to paediatric patients.

1.4. This version supersedes any previous versions of this document.

Data Protection Act 2018 (UK General Data Protection Regulation – GDPR) Legislation.

The Trust has a duty under the Data Protection Act 2018 and UK General Data Protection Regulations 2016/679 to ensure that there is a valid legal basis to process personal and sensitive data. The legal basis for processing must be identified and documented before the processing begins. In many cases we may need consent; this must be explicit, informed, and documented. We cannot rely on opt out, it must be opt in.

Data Protection Act 2018 and UK General Data Protection Regulations 2016/679 is applicable to all staff; this includes those working as contractors and providers of services.

For more information about your obligations under the Data Protection Act 2018 and UK General Data Protection Regulations 2016/679 please see the Information Use Framework Policy or contact the Information Governance Team.

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2. The Guidance

2.1. Background

The overall reported incidence of oxazaphosphorine-induced haemorrhagic cystitis varies considerably due to a lack of agreement for diagnostic criteria, variability in definition of the relevant time frame, and uncertainty regarding the relative contributing factors such as thrombocytopenia, concurrent or previous chemotherapy or radiotherapy, and viral infections.

It is suggested that in patients treated with ifosfamide without urothelial protection the overall incidence of haemorrhagic cystitis ranges from 18% to 40% and is considered dose-limiting.

Among patients treated with high-dose cyclophosphamide with aggressive hydration in the bone marrow transplantation setting, the reported incidence of severe haemorrhagic cystitis ranges from 0.5% to 40%. The incidence of haemorrhagic cystitis is considerably lower with cyclophosphamide as compared with ifosfamide and so mesna use is unnecessary with standard doses of cyclophosphamide i.e.<1g/m2.

2.2. Rationale for the use of mesna

2.2.1. Mesna is a thiol compound, which functions as a regional detoxicant of the oxazaphosphorine metabolites. After oral or intravenous administration, mesna undergoes rapid oxidation in the plasma to dimesna. Only a small portion of the dose remains in the circulation as the physiologically active compound. Both mesna and dimesna are very hydrophilic and therefore remain in the intravascular compartment, where they are rapidly cleared by the kidneys.

2.2.2. The free sulfhydryl (thiol) groups of mesna combine directly with a double bond of acrolein and with other urotoxic 4-hydroxy-oxazaphosphorine metabolites to form stable nontoxic compounds. Because urinary mesna concentration greatly exceeds plasma mesna concentrations regional detoxification of urotoxic oxazaphosphorine metabolites occurs in the urinary system.

2.2.3. This restriction of mesna to the urinary system implies that mesna neither protects against non-urologic toxicities of oxazaphosphorines nor interferes with their cytotoxic activity. Mesna in doses of up to 70-100mg/kg IV was shown to produce no toxic effect on bone marrow, hepatic, renal or CNS functions. Vomiting and diarrhoea only occurred after doses greater than 80mg/kg.

2.3. Prescribing information for mesna

These are general principles followed for the majority of regimens used at RCHT but they may not represent all regimens currently in use.

2.3.1. Mesna should be used prophylactically for all patients receiving ifosfamide and high dose cyclophosphamide (>1g/m2).

2.3.2. Mesna dosing with ifosfamide - example regimen.

Pre-ifosfamide.

Mesna equivalent of 20% total daily ifosfamide dose given as IV bolus pre-ifosfamide.

During ifosfamide.

Mesna equivalent of 100-120% total daily ifosfamide dose given as IV infusion over 24 hours (mixed in bags with ifosfamide).

Post-ifosfamide.

Mesna equivalent of 60% total daily ifosfamide dose given as IV infusion over 12 hours.

2.3.3. Mesna dosing with high dose cyclophosphamide (>1g/m2).

E.g. HSCT mobilisation (cyclophosphamide 1.5g/m2) day case regimen.

Pre-cyclophosphamide

Mesna equivalent of 40% total daily cyclophosphamide dose given as IV bolus pre-cyclophosphamide.

Post-cyclophosphamide

Mesna 400mg orally 2 hours and 6 hours after the start of the cyclophosphamide infusion.

2.3.4 Bioavailability

After oral administration mesna has a bioavailability of 50-75% and the urinary mesna concentrations are approximately one half of those observed after IV infusion.

N.B. Mesna tablet strengths: 400 mg or 600mg. Round up dose if necessary.

2.4. Haematuria

Haemorrhagic cystitis is generally graded as mild, moderate or severe according to the degree of pain and haematuria. Severe haemorrhagic cystitis typically includes the presence of gross haematuria with clots and occurrence of clinical complications; it can be extremely painful and debilitating, requiring prolonged and expensive hospitalisation.

2.4.1. Monitoring for haematuria

Patients should always have their urine tested by dipstick for blood prior to starting ifosfamide or cyclophosphamide. The result should be documented in the nursing documentation. This will provide a baseline level from which to assess any haematuria that may occur. Thereafter urine should be tested and documented with each sample.

2.4.2. Presentation of haematuria

2.4.2.1. Prior to the start of the ifosfamide or cyclophosphamide infusion

- An unexplained positive test for blood prior to treatment should be investigated. Once other causes of haematuria have been excluded, for example urinary tract infection or menstruation, take a spot urine sample for microscopy for red cells in order to exclude false positive results. Results should be awaited before commencing ifosfamide or cyclophosphamide.

- If cause identified further testing of urine may be unnecessary due to false positive results.

2.4.2.2. Whilst receiving intravenous mesna hydration.

Exclude other causes of haematuria, for example urinary tract infection or menstruation. Take a spot urine sample for microscopy for red cells in order to exclude false positive results and follow the guidelines below

Test result	Action
Trace	Re-test
+	Re-test If '+' on more than one consecutive test give additional bolus mesna
++	Double intravenous mesna
+++	Double intravenous mesna

2.4.2.3 Doubling mesna doses

If the infusion is running containing ifosfamide mixed with mesna, leave this bag running and piggyback an additional bag containing the same amount of mesna.

If the bag running contains mesna only, stop this infusion and replace with a new bag containing double the amount of mesna and run for the time remaining i.e. until a minimum of 12 hours after final ifosfamide infusion.

NB ensure that future bags are prescribed with the increased dose.

2.4.2.4 Whilst receiving oral mesna

Patients who are switched to oral mesna for discharge should be educated to test their urine for up to 12 hours after the end of the ifosfamide/cyclophosphamide infusion.

For patients experiencing haematuria after discharge on oral mesna the following guide should be followed:

Test result	Action
Trace	Re-test
+	Re-test If '+' on more than one consecutive test give intravenous mesna
++	Admit for intravenous mesna
+++	Admit for intravenous mesna

These test results are all as 'above baseline' results.

An extra dose of oral mesna will be supplied to patients to be taken if an episode of vomiting is experienced while taking their regular oral mesna dose. Consider advising taking this dose (if not already taken) in addition to being admitted to hospital.

An intravenous mesna bolus followed by a continuous infusion as per previous days should be given and continued until haematuria resolved.

Consideration should also be given to the suitability of the patient for oral mesna with further cycles of ifosfamide.

2.5 Subsequent courses

If higher doses of IV mesna or a switch from oral to IV mesna were required during a treatment cycle and were effective at preventing further haematuria, ensure future prescriptions on Aria are amended as appropriate and document on treatment notes.

3. Monitoring compliance and effectiveness

Information Category	Detail of process and methodology for monitoring compliance
Element to be monitored	Appropriate prescribing of mesna.
Lead	Oncology/SACT Governance meeting
Tool	All incidences of haematuria following ifosfamide/ cyclophosphamide to be reported via Datix. Oncology/SACT Governance meeting to review Datix as standing item, and review whether appropriate management occurred.
Frequency	Quarterly via Oncology/SACT Governance meeting.
Reporting arrangements	Oncology/SACT Governance meeting Recorded in meeting minutes.
Acting on recommendations and Lead(s)	Oncology/SACT Governance meeting.
Change in practice and lessons to be shared	Required changes to practice will be identified and actioned within one month. A lead member of the team will be identified to take each change forward where appropriate. Lessons will be shared with all the relevant stakeholders.

4. Equality and Diversity

4.1. This document complies with the Royal Cornwall Hospitals NHS Trust service Equality and Diversity statement which can be found in the Equality Diversity And Inclusion Policy or the Equality and Diversity website.

4.2. Equality Impact Assessment

The Initial Equality Impact Assessment Screening Form is at Appendix 2.

Appendix 1. Governance Information

Information Category	Detailed Information
Document Title:	The Administration of Mesna with Ifosfamide and Cyclophosphamide Clinical Guideline V4.0
This document replaces (exact title of previous version):	The Administration of Mesna with Ifosfamide and Cyclophosphamide Clinical Guideline V3.0
Date Issued/Approved:	October 2025
Date Valid From:	October 2025
Date Valid To:	October 2028
Directorate/Department responsible (author/owner):	Emma Nicholls, Lead Cancer Pharmacist
Contact details:	07876 217568
Brief summary of contents:	Recommendations for the prescribing and administration of mesna with ifosfamide and cyclophosphamide for adult cancer patients.
Suggested Keywords:	Mesna, cyclophosphamide, ifosfamide, cystitis.
Target Audience:	**RCHT:** Yes **CFT:** No **CIOS ICB:** No
Executive Director responsible for Policy:	Chief Medical Officer.
Approval route for consultation and ratification:	Oncology/SACT Governance Group.
Manager confirming approval processes:	Ian McGowan.
Name of Governance Lead confirming consultation and ratification:	Suzanne Atkinson.
Links to key external standards:	None required.
Related Documents:	None required.
Training Need Identified?	No.

Information Category	Detailed Information
Publication Location (refer to Policy on Policies – Approvals and Ratification):	Internet and Intranet.
Document Library Folder/Sub Folder:	Clinical / Cancer Services.

Version Control Table

Date	Version Number	Summary of Changes	Changes Made by
2/11/15	V1.0	Initial issue	Emma Nicholls Lead Cancer Pharmacist
3/10/19	V2.0	Updated with minor amendments to flow chart, Sections 2.3.3 and 2.4.1..	Emma Nicholls Lead Cancer Pharmacist
18/10/22	V3.0	New Trust template.	Emma Nicholls Lead Cancer Pharmacist
21/10/25	V4.0	New Trust template.	Emma Nicholls Lead Cancer Pharmacist

All or part of this document can be released under the Freedom of Information Act 2000.

All Policies, Strategies and Operating Procedures, including Business Plans, are to be kept for the lifetime of the organisation plus 6 years.

This document is only valid on the day of printing.

Controlled Document.

This document has been created following the Royal Cornwall Hospitals NHS Trust The Policy on Policies (Development and Management of Knowledge Procedural and Web Documents Policy). It should not be altered in any way without the express permission of the author or their Line Manager.

Appendix 2. Equality Impact Assessment

Section 1: Equality Impact Assessment (EIA) Form

The EIA process allows the Trust to identify where a policy or service may have a negative impact on an individual or particular group of people.

For guidance please refer to the Equality Impact Assessment Policy (available from the document library) or contact the Equality, Diversity, and Inclusion Team rcht.inclusion@nhs.net

Information Category	Detailed Information
Name of the strategy/policy/proposal/service function to be assessed:	The Administration of Mesna with Ifosfamide and Cyclophosphamide Clinical Guideline V4.0
Directorate and service area:	Cancer Services.
Is this a new or existing Policy?	Existing.
Name of individual completing EIA (Should be completed by an individual with a good understanding of the Service/Policy):	Emma Nicholls, Lead Cancer Pharmacist.
Contact details:	07876 217568

Information Category	Detailed Information
1. Policy Aim - Who is the Policy aimed at? (The Policy is the Strategy, Policy, Proposal or Service Change to be assessed)	Prescribers, nurses and pharmacists managing cancer patients being treated with ifosfamide or cyclophosphamide.
2. Policy Objectives	Safe and effective prescribing of cyclophosphamide, ifosfamide and mesna.
3. Policy Intended Outcomes	Ensure that all patients are prescribed required mesna and that staff are aware of action to be taken in the event of haematuria.
4. How will you measure each outcome?	Annual review.
5. Who is intended to benefit from the policy?	Adult cancer patients at the Royal Cornwall Hospital.

Information Category	Detailed Information
6a. Who did you consult with? (Please select Yes or No for each category)	• Workforce: Yes • Patients/visitors: No • Local groups/system partners: No • External organisations: No • Other: No
6b. Please list the individuals/groups who have been consulted about this policy.	**Please record specific names of individuals/groups:** Oncology/SACT Governance Group.
6c. What was the outcome of the consultation?	Approved.
6d. Have you used any of the following to assist your assessment?	**National or local statistics, audits, activity reports, process maps, complaints, staff, or patient surveys:** No.

7. The Impact

Following consultation with key groups, has a negative impact been identified for any protected characteristic? Please note that a rationale is required for each one.

Where a negative impact is identified without rationale, the key groups will need to be consulted again.

Protected Characteristic	(Yes or No)	Rationale
Age	No	
Sex (male or female)	No	
Gender reassignment (Transgender, non-binary, gender fluid etc.)	No	
Race	No	
Disability (e.g. physical or cognitive impairment, mental health, long term conditions etc.)	No	
Religion or belief	No	
Marriage and civil partnership	No	

Protected Characteristic	(Yes or No)	Rationale
Pregnancy and maternity	No	
Sexual orientation (e.g. gay, straight, bisexual, lesbian etc.)	No	

A robust rationale must be in place for all protected characteristics. If a negative impact has been identified, please complete section 2. If no negative impact has been identified and if this is not a major service change, you can end the assessment here.

I am confident that section 2 of this EIA does not need completing as there are no highlighted risks of negative impact occurring because of this policy.

Name of person confirming result of initial impact assessment:

Emma Nicholls, Lead Cancer Pharmacist.

If a negative impact has been identified above OR this is a major service change, you will need to complete section 2 of the EIA form available here:
Section 2. Full Equality Analysis