

Guidelines for the Management of Extravasation

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“Quality and safety for every patient every time”

Document Control

Prepared By	Issue Date	Approved By	Review Date	Version	Contributors	Comments/ Amendment
Chemo Nurse Group	August 10	Not Approved	Aug 12	1		Initial draft contained reference to specific antidotes, which have been removed as they not routinely available in NECN.
Chemo Nurse Group/ South Tees FT	Feb 2011	NECN Chemo Group	14.2.13	2	Wendy Anderson Steve Williamson	
NECDAG	18.7.11	NECN Chemo Group	18.7.13	3	Steve Williamson	Antidote section added including, dexrazoxane (Savene™) added as an 'option' following NECDAG review on 13/7/11. Table of drugs updated
	Draft 13.2.12	NECN Chemo Group	NA	4	Steve Williamson, Gail Jones	Added in referral pathway for Savene from cancer units to cancer centre
NECN	21.5.12	NECN Chemo Group	25.5.14	5	Steve Williamson Sarah Rushbrooke	Updated and clarified pathway, updated advice on oxaliplatin and hyaluronase. Updated drug list
NECN	13.2.13	NECN Chemo Group	13.2.15	5.2	Steve Williamson	Clarification of pathway point L & change bendamustine to irriatant
NECN	04.05.14	Chairs Action	13.05.15	5.3	Steve Williamson	Review dates added to document control – no other changes
NECN	14.11.14	Chairs Action	14.11.16	5.4	Steve Williamson	Added Savene Referral Form to document (page 8) and updated commissioning advice for savene.
NECN	04.11.16	Chairs Action	04.11.19	5.5	Steve Williamson	Added additional line regarding extravasation with savene and JCUH referral forms. Increased review period to three years.

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What is extravasation?

Extravasation refers to the process by which one substance (e.g., fluid, drug) leaks into the surrounding tissue¹. In terms of cancer therapy, extravasation is defined as the accidental leakage of chemotherapy from its intended compartment (the vein) into the surrounding tissue². A broader definition of extravasation includes the injury which occurs following extravasation. The degree of injury can range from a very mild skin reaction to severe necrosis depending on the type of substance which has extravasated¹⁻⁴.

When does extravasation occur?

Extravasation is not as rare as some people may think. In cancer therapy experts estimate that it accounts for 0.5% to 6.0% of all adverse events associated with treatment⁴. But, when you consider that adverse events with cancer therapy are quite common, the absolute number of extravasations which take place is significant⁵.

Some extravasations are caused by an error in the intravenous (IV) procedure^{4,6}. Cancer patients receiving chemotherapy may have multiple risk factors that make IV infusion difficult. For example, patients with a tendency for thin, fragile and mobile veins are at risk of extravasation⁴. In addition to factors relating to the procedure and to the patient, factors associated with the equipment and material used, concomitant medications and the treatments themselves can also increase the likelihood of extravasation. The most common factors known to increase the risk of extravasation are listed in the guidelines.

What are the implications of extravasation?

Extravasation is to be avoided. Although not all extravasation incidences result in ulcerative and necrotic tissue damage, patients may still experience pain and discomfort as well as indirect consequences such as disruption of treatment and prolonged hospitalisation for the management of extravasation^{3,4}. The specific symptoms of extravasation, as well as their wider consequences, are discussed in this section of the guidelines and these include the initial symptoms, tissue damage, surgery, impact on cancer therapy, and other consequences.

How is extravasation recognised?

It is critical that an extravasation is recognised and diagnosed early. The most effective way to assess extravasation in its early stages is to be aware of and act on all relevant signs and symptoms. Signs and symptoms can be gathered from simple visual assessment of the injection site and careful observation of the IV device.

Once an extravasation is suspected to have occurred, it is important to rule out other possible conditions, such as flare reaction or phlebitis^{4,6}. The quality of the nursing assessment during administration of cytotoxic drugs plays a key role in minimising frequency and severity of extravasations, since delays in the recognition and treatment of vesicant extravasation increase the likelihood of developing tissue damage and necrosis^{4,7}. If there is any doubt as to whether or not an extravasation has occurred, stop the infusion and ask for advice.

Early detection of an extravasation is often based on the following factors: patient reporting, visual assessment, checking the infusion line, and distinguishing extravasation vs. other conditions.

How is extravasation prevented?

The most important approach to minimising the consequences of extravasation is prevention⁸. Healthcare professionals involved in the handling and administration of IV cancer therapies should become familiar with the extravasation potential of the agents being administered (See Appendix 2), their local procedures and protocols. Healthcare professionals should develop an understanding of the important precautionary steps that should be taken to avoid extravasations and their resulting injuries.

How is extravasation managed?

A pathway for the management of extravasation includes detection, analysis and action is described below and shown as a flow chart in appendix one.

- A. The first course of action is to stop and disconnect the infusion, aspirate as much of the infusate as possible, mark the affected area and then remove the cannula (while continuing to aspirate from the extravasation site).
- B. Elevate the affected limb if required. If possible take a photo of the extravasated area.
- C. Check which category drug belongs to (see appendix Two). Depending on the type of drug, vesicant or non vesicant being infused, the correct protocol should be followed to determine the next steps.
- D. If the drug is a non-vesicant (see appendix 2), application of a cold compress and elevation of the limb may be sufficient to limit the adverse effects.
- E. In contrast, the extravasation of a vesicant requires several steps and differs for the various classes of drug. (see appendix 2 for list)
- F. Anthracycline extravasation needs immediate referral to oncology/haematology (see appendix three) for potential treatment with dexrazoxane (Savene) antidote
- G. Vesicant (non anthracycline) extravasation needs immediate referral to plastic surgeons for potential formal subcutaneous washout of tissues.
- H. Proceed with damage limitation management as below whilst awaiting review
- I. There are two main approaches to limiting the damage caused by extravasation: localisation and neutralisation or dispersion and dilution.
- J. The localise and neutralise strategy involves the use of cold compresses to limit the spread of the extravasation with the potential formal subcutaneous washout of tissues by plastic surgeons to neutralise or use of a specific antidote to neutralise.
- K. Antidotes are agents applied or injected to the extravasated area to counteract the effects of the infiltrated agent. They form an important part of the “localise and neutralise” and the “disperse and dilute” strategies. Antidotes such as Dexrazoxane (SaveneTM) for anthracycline extravasations are an option for use to counteract vesicant actions.

- L. The disperse and dilute strategy involves the initiation of appropriate measures for the extravasation of **vinca alkaloids and non DNA binding agents, e.g taxanes** the use of warm compresses to prompt vasodilatation and encourage blood flow in the tissues which helps to spread the extravasation.
- Note:** Vinca alkaloids are vesicants and therefore require immediate referral to the plastic surgeons as per point G above.
- M. Even if extravasation is identified early, progressive extravasation can give rise to ulcerated and necrotic tissue over time.
- N. Early steps to prevent and manage extravasation such as referral to the plastic surgeons for potential subcutaneous washout of tissues may help to limit the need for surgery.
- O. About one-third of extravasations due to anthracyclines result in ulcerations. In these cases, surgery should not be considered as the initial primary treatment of choice. Surgery to excise damaged tissue is indicated when there is ulceration or continued pain.
- P. Complete the Green National Extravasation Reporting Card and submit to Birmingham. <http://www.extravasation.org.uk/greencard>

Use of Antidotes

Early steps to prevent and manage extravasation such as using antidotes may help to limit the need for surgery. About one-third of extravasations due to anthracyclines result in ulcerations. The only antidote that can be recommended on basis of clinical evidence is dexrazoxane (Savene). NECDAG has recommended dexrazoxane is available as an option for confirmed anthracycline extravasations following assessment and decision to treat by a consultant oncology specialist. The decision to use dexrazoxane must take into account the potential for referral to plastic surgeons.

Dexrazoxane is given as a three day course of treatment: 1000mg/m² IV as soon as possible (no later than 6 hours) after extravasation on day 1; 1000mg/m² IV on day 2 and 500mg/m² IV on day 3. Due to the potential need to administer over a weekend and the cytotoxic nature of the drug it is recommended that the treatment be given in cancer centres or units that are able to administer chemotherapy at weekend.

Other products such as topical DMSO (99%), sodium thiosulfate and hyaluronidase have been suggested as possible antidotes in many literature sources. Hyaluronidase while having limited evidence, is licensed and may be considered an option to assist dispersal where dispersal is indicated (e.g. vinca-alkaloids). When hyaluronidase is used 1500iu of hyaluronidase should be dissolved in 1ml of water for injection or sodium chloride 0.9% and infiltrated into the affected area using multiple subcutaneous injections as soon as possible after extravasation is detected. The use of DMSO and sodium thiosulfate is not recommended as they are not licenced.

Extravasation of dexrazoxane (Savane)

An extravasation with dexrazoxane is possible. Dexrazoxane is an irritant and treatment would include stopping the infusion, initiate cooling and elevate the affected area. Observation should be made for redness and the patient asked to report any pain or discomfort. There is no antidote for extravasation with dexrazoxane.

As the infusion will have been stopped it will be necessary to insert a new cannula for the remaining dexrazoxane treatment which should be completed to treat the anthracycline extravasation. The site chosen for cannulation should be in a different extremity / area other than the ones affected by either extravasation.

Local Trust Responsibilities

Local Trusts are responsible to ensure they have established a referral pathway to the cancer centre for administration of dexrazoxane (Savane) antidote (see appendix three) and that they have established a pathway for referral to plastic surgery. Cancer Centres administering dexrazoxane (Savane) can recharge the cost of the drug to the referring patients PCT/CCG.

Local Trusts are responsible for the adoption of these guidelines via their own Trust Chemotherapy Multi Disciplinary Meetings and for ensuring the most up to date version is in use.

Conclusion

Managing extravasation in accordance with the latest scientific understanding and medical consensus allows for optimal treatment of the patient. By following current protocols and policies nurses can contribute to improving the standard of care in cancer therapy. By learning how to effectively recognise extravasation and by becoming familiar with local protocols for dealing with it, nurses can help to minimise the incidence of this complication of cancer treatment and, subsequently, play a crucial role in expanding the use of best practice. By implementing guidelines in their practice setting, nurses can provide best practice based on clinical evidence.

GUIDELINES FOR THE MANAGEMENT OF EXTRAVASATION

Step 1: STOP the infusion immediately. DO NOT remove the cannula

Step 2: Disconnect the infusion (not the cannula/needle)

Step 3: Leave the cannula/needle in place and try to aspirate as much of the drug as possible from the cannula with a 10ml syringe. Avoid applying direct manual pressure to suspected extravasation area

Step 4: Collect the extravasation kit, (cold/ warm compresses)

Step 5: Mark the affected areas and take digital images of the site (if possible)

Step 6: Remove cannula

Step 7: Check which category drug belongs to (see appendix Two)

Anthracycline extravasation needs immediate referral to oncology/haematology (see appendix three) for potential treatment with dexrazoxane (Savene) antidote (see step 11 below)

Vesicant (non anthracycline) extravasation needs immediate referral to plastic surgeons for potential formal subcutaneous washout of tissues.

Proceed with damage limitation management as below whilst awaiting review

Step 8: Administer pain relief as required

Step 9: Decide on Appropriate Damage Limitation Management
(**Cold** compress to localise or **Hot** compress to disperse)

COLD COMPRESS

Actinomycin D	Amsacrine
Bendamustine	Carmustine
Carbazitaxel	Darcarbazine
Dactinomycin	Daunorubicin
Doxorubicin	Epirubicin
Idarubicin	Mitomycin C
Mitoxantrone	Mustine
Streptozotocin	Treosulphan

Step 10: LOCALISE

Apply cold pack to the affect area for 20 minutes 4 times daily for 1-2 days

Step 11: NEUTRALISE

(Anthracyclines only) Assess for potential administration dexrazoxane (Savene)

HOT COMPRESS

Docetaxel
Oxaliplatin
Paclitaxel
Vinblastine
Vincristine
Vindesine
Vinflunine
Vinorelbine

Only use heat those listed above

Step 10: DISPERSE

Apply a warm compression to the affect area for 20 minutes, 4 times daily for 1-2 days

Treatment of a non-vesicant extravasation

Step 10: Elevate the limb. Consider applying cold compression if local symptoms occur. Arrange necessary follow up for patient.

Step 12: Notify doctor in charge of patient's care. Complete documentation

If presents after 24 hours with vesicant extravasation, needs referral to plastic surgeons for management of potential blistering or soft tissue necrosis

Document incident including completion of a green card <http://www.extravasation.org.uk/greencard>

Appendix Two: Classification of drugs

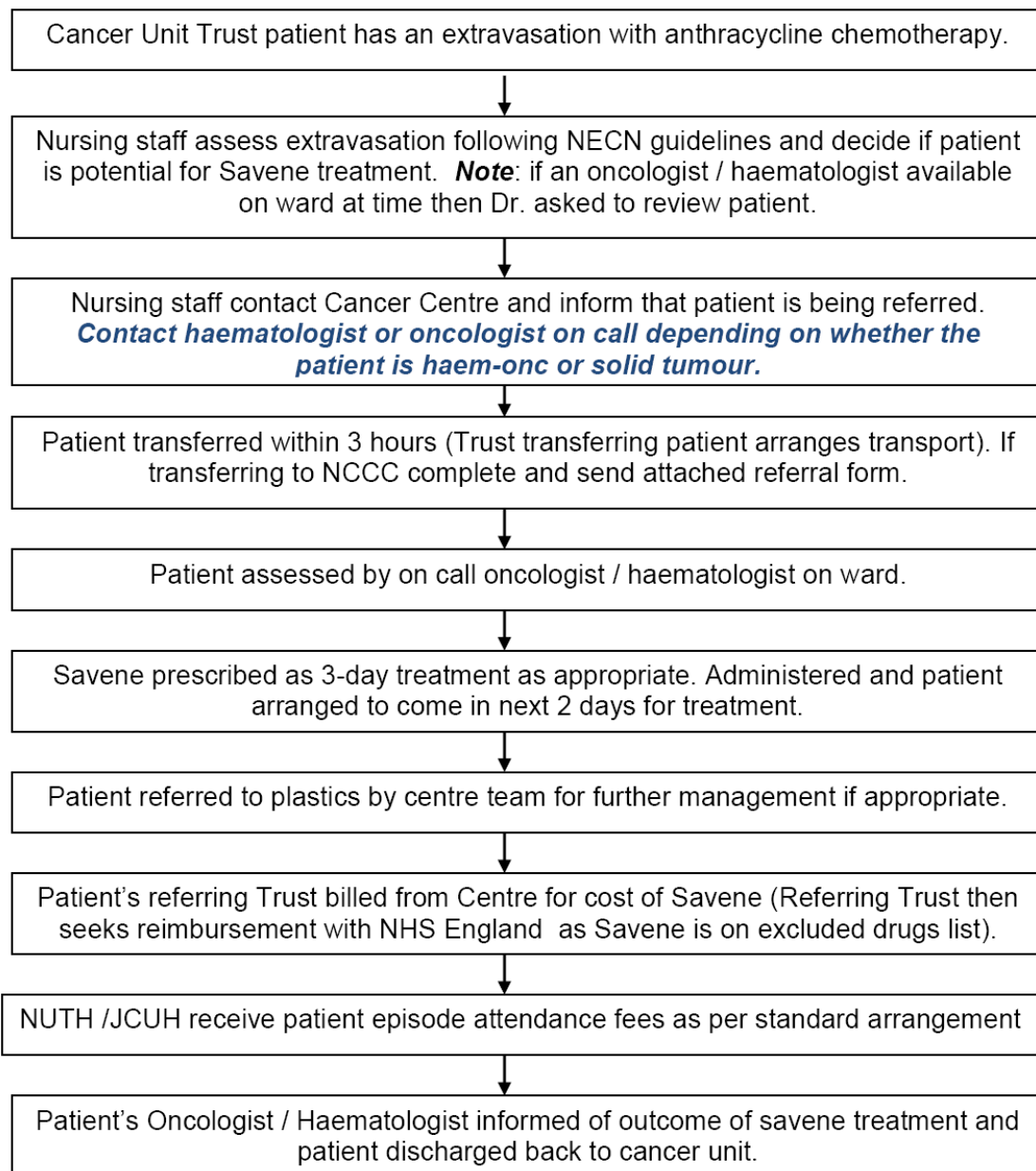
Vesicant	Irritant	Non Irritant
Aclarubicin	Bendamustine	Asparaginase
Actinomycin D	Cisplatin	Bleomycin (if painful treat as irritant)
Amsacrine	Cladribine	Bortezomib
Carmustine	Cyclophosphamide	Carbplatin
Cabazitaxel	Cytarabine	Eribulin
Dacarbazine	Docetaxel	Etoposide
Dactinomycin	Fludarabine	Fluorouracil
Daunorubicin	Gemcitabine	Irinotecan
Liposomal-Daunorubicin	Ifosfamide	Methotrexate
Doxorubicin	Melphalan	Pemetrexed
Liposomal-Doxorubicin	Oxaliplatin*	Ralitrexed
Epirubicin	Paclitaxel	Tenoposide
Idarubicin	Pentostatin	Topotecan
Mitomycin	Thiotepa	Monoclonal antibodies (MAB's)**
Mitoxantrone		• Alemtuzumab
Mustine		• Bevacizumab
Treosulphan		• Bortezomib
Vinblastine		• Cetuximab
Vincristine		• Rituximab
Vindesine		• Trastuzumab
Vinflunine		
Vinorelbine		

Notes

- a. Oxaliplatin extravasation has been associated with increased risk of pain, oedema and neurological symptoms. These symptoms can develop more slowly than with other agents, so careful monitoring is required. It is classified as an irritant but as a non-DNA binding drug can be safely treated with a warm compress to avoid the risk of paraesthesia which can be precipitated by cold.
- b. Monoclonal antibodies (MAB's) and other biologically active non-cytotoxic agents are generally classified as non-irritants, though experience is limited with their extravasation.
- c. The above list does not claim to be a comprehensive list of all chemotherapy products, new treatments are approved on a frequent basis therefore it is the responsibility of users of this document to ensure they are aware which category new drugs fall into

Appendix Three: Referral Pathway for Dexrazoxane

Referral Pathway for Dexrazoxane (Savene)



Cancer Units referring to Newcastle (NCCC)	Cancer Units referring to South Tees (JCUH)
<ul style="list-style-type: none"> • <i>Northumbria – Hexham, North Tyneside, Wansbeck</i> • <i>Gateshead</i> • <i>Sunderland</i> • <i>South Tyneside</i> • <i>Durham Hospital</i> 	<ul style="list-style-type: none"> • <i>Darlington</i> • <i>North Tees - Stockton and Hartlepool</i> • <i>Friarage</i>

Note: Cumbria have own Savene kit

Note: A different locally agreed referral pathway will be needed in each trust for referral to plastic surgery

North East Cancer Network
Adult Referral Pathway for the Treatment of an Anthracycline Extravasation with
SAVENE to the Northern Centre for Cancer Care,
Cancer Services & Clinical Haematology, Freeman Hospital

Contact: Consultant Haematologist on call for haematology patients, Consultant Oncologist for oncology patients. Switchboard 0191 2336161
 Chemotherapy Day Unit Ward 36 0191 2137036 or out of hours Ward 34 0191 2137033

Indications for Use

The treatment of Doxorubicin or Epirubicin anthracycline extravasation.
 The use of Savene in anthracycline extravasations other than Epirubicin or Doxorubicin is at the discretion of the prescriber. (Idarubicin, Daunorubicin, Dactinomycin, Mitomycin)

Patient Addressograph Label
Name:
Hospital No:
DOB:

SAVENE is to be administered within 6hrs of extravasation

Referral Unit:

Referred by:

Consultant:

Regimen prescribed:

Drug extravasated:

Approximate amount extravasated:

Time of extravasation:

Time patient referred to NCCC:

Height:

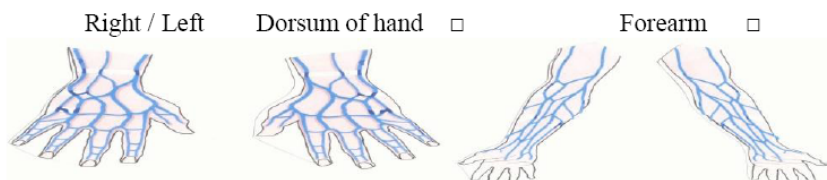
Weight:

Date of blood results:

Hb	Wbc	Neuts	Plts	Bilirubin	S. Creat	ALT/AST
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History of injury & procedures carried out post extravasation:

Mark site of injury on diagram:



Transport:

Time injury reviewed within Northern Centre for Cancer Care:

Form completed by:

Contact Number:

Appendix Five. JCUH dexrazoxane (Savene™) Referral Form

**North East Cancer Network
Adult Referral Pathway for the Treatment of an Anthracycline Extravasation with
SAVENE to James Cook University Hospital Middlesbrough**

Contact: Consultant Haematologist on call for haematology patients, Consultant Oncologist for oncology patients. Switchboard 01642 850850

Haematology Day Unit 01642 835996 or out of hours Haematology Ward 01642 835 996
Chemotherapy Day Unit 01642 835502 or out of hours Oncology Ward 01642 854019

Indications for Use

The treatment of Doxorubicin or Epirubicin anthracycline extravasation.
The use of Savene in anthracycline extravasations other than Epirubicin or Doxorubicin is at the discretion of the prescriber. (Idarubicin, Daunorubicin, Dactinomycin, Mitomycin)

Patient Addressograph Label
Name:
Hospital No:
DOB:

SAVENE is to be administered within 6hrs of extravasation

Referral Unit:

Referred by:

Consultant:

Regimen prescribed:

Drug extravasated:

Approximate amount extravasated:

Time of extravasation:

Time patient referred to James Cook:

Height:

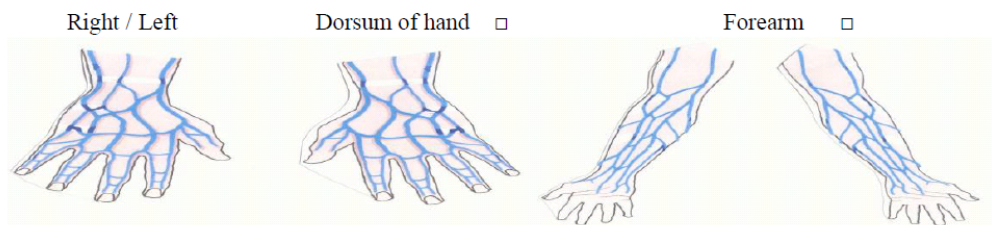
Weight:

Date of blood results:

Hb	Wbc	Neuts	Plts	Bilirubin	S. Creat	ALT/AST
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History of injury & procedures carried out post extravasation:

Mark site of injury on diagram:



Transport:

Time injury reviewed within James Cook University Hospital:

Form completed by:

Contact Number:

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