Network Guidance for the Prevention
and Management of Cytotoxic
Extravasation Injuries (October 09)

STOP! – Have you got the most up to date version of this policy?
Always Check www.wales.nhs.uk/nwcn/ before reading further.

Adapted for use in North Wales from original policy developed by
Mersey & Cheshire Cancer Network

Version 2.1 October 2009
NWCN–Tracy Parry, Network Pharmacist
Review October 2010
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1. Introduction

The purpose of this document is to set out the guidelines for the management of cytotoxic extravasation incidents within the North Wales Cancer Network.

National and Regional standards that this document adheres to and should be read in conjunction with include:

- Manual For Cancer Standards 2004
- Reference guide to Consent and Treatment, DH 2001

Additionally, network and local policies that support and comply with this document have been developed. These include:

- Network guidelines for the safe prescribing, handling and administration of cytotoxic drugs
- Network Chemotherapy Formulary
- Local chemotherapy administration policies
- Local consent policies

This policy has been written using the best available current evidence and will be reviewed as other evidence becomes available.

2. Definition

Extravasation is defined as the leakage of a vesicant drug or fluid from a vein into the surrounding tissue during intravenous administration.

Cytotoxic drugs may be divided in 5 categories based upon their propensity to cause extravasation injury. The drugs included in this policy are listed in Appendix 1.

A vesicant is defined as a drug or solution which has the potential to cause blistering, severe tissue damage and even necrosis if extravasated. Vesicants may cause damage to the surrounding tissue nerves, tendons or joints. This may be accompanied by pain, erythema, inflammation and discomfort, which, if left unrecognised or treated inappropriately can lead to necrosis and functional loss of the vein and possibly limb concerned.

Infiltration is the inadvertent administration of a non vesicant solution into surrounding tissues. While this may cause inflammation and discomfort, damage and necrosis rarely occurs.

For clarity the term extravasation will be used to describe the inadvertent leakage of any drug or fluid into surrounding tissues.

Once an extravasation has occurred, the full extent of the injury may be unclear, and damage may continue for weeks or months. Any extravasation should be considered a...
medical emergency and a prompt, appropriate response is essential. The degree of injury can range from apparently insignificant erythema through to blistering, skin sloughing and severe necrosis, which often require corrective plastic surgery. Accurate documentation of the incident is essential. There is no National Standard of Practice.

3. Scope

The aim of this document is to provide a framework based on current available evidence for the appropriate management of cytotoxic chemotherapy induced extravasation within the North Wales Cancer Network.

4. Evidence base

Extravasation is a condition that is often under-diagnosed, under-treated and unreported (Please refer to section 13 for details on reporting extravasation). The relevance of many published articles is difficult to assess because they often refer to isolated incidents that have been treated in an inconsistent way. Treatment recommendations in this policy have been made based on the best available evidence or where such evidence is lacking, based on a consensus of professional opinion from expert pharmacists, nurses, and doctors from the North Wales Cancer Network and other network and professional body extravasation documents. For the evidence base for specific recommendations made in this policy see appendix 3.

5. Causes

- Dislodgement of the distal tip of the cannula into the tissues surrounding the vein.
- Constriction of the blood flow distal to the cannula tip which increases venous pressure and allows fluid to leak from the hole in the vein made by the cannula.
- Inappropriate selection of the position and size of cannula and the length of time which the cannula is left in situ.
- Practitioner unfamiliarity with the drug and the manufacturer’s recommendations for administration.

6. Risk Factors

- Elderly patients can be more at risk of extravasating due to:
  - Interference with the cannula when the patient is confused or agitated.
  - Reduced pain sensation.
  - Fragile skin and veins.
- Patients with communication difficulties of whatever cause will be more at risk of extravasation injuries going unnoticed. Draw attention to these risks with the patient’s carers, parents, partners etc. With patients unable to speak English this must be done through interpreters or relatives.
Repeated venepunctures either due to previous treatments or intravenous drug abuse.

Cancer patients have additional risk due to:
   a) Fragile, mobile veins that are difficult to cannulate.
   b) 'Recall' phenomenon, in patients previously given radiotherapy.
   c) A previous extravasation injury is at risk of further damage when subsequent chemotherapy is given even if administered at a different site.
   d) Limbs with lymphoedema due to poor venous flow.

Other disease states may increase the risk of extravasation injuries or inhibit their detection, such as:
   a) Peripheral vascular disease.
   b) Raynaud's Phenomenon.
   c) Diabetes.
   d) Superior Vena Cava Syndrome.
   e) Previous Cardiovascular Accidents.
   f) Patients after Cerebrovascular Accidents

Severe extravasation injuries are more associated with the dorsum of the hand and foot, ankle, antecubital fossa and near joints or joint spaces where there is little soft tissue for the protection of underlying structures.

7. Risk Reduction

- Only authorised practitioners who have been trained and are included on a register may administer chemotherapy
- At all times the standards in local and network chemotherapy administration policies must be adhered to.
- Particular care must be taken with the selection and positioning of the cannula.
- Agents with the highest vesicant potential should be given first. All practitioners administering cytotoxic drugs must have an understanding of the management of extravasation and know the contents and whereabouts of the extravasation kit.
- If vesicant drugs are administered by a non ambulatory infusion pump then the pump must have appropriate pressure sensors that will give early warning of an occlusion.

8. Recognition

It is important that extravasation is correctly diagnosed because some of the antidotes used in the management of extravasation can cause further physical trauma to the patient, and may also potentiate extravasation. Early recognition is vital. Misdiagnosis often occurs when the practitioner fails to differentiate discoloration reactions in the vein, venous shock, flare or phlebitis. Some cytotoxic drugs are coloured and if the selected vein lies superficial to the skin, the injection of a red coloured drug may cause local venous discolouration.  

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9. Symptoms

Signs and symptoms of possible extravasation include:

- Pain, stinging, burning or any other acute change at the injection site.
- Induration, erythema, venous discolouration or swelling at the injection site.
- No blood return is obtained. If this is found in isolation, other signs should be looked for, as this can be misleading and has been implicated in a number of serious incidences. There are 2 ways in which the return of blood may be misleading
  - If there has been an extravasation injury and the cannula has become displaced, the act of trying to draw back blood to test for return may move the cannula back into the vein. Thus blood is returned and the vein appears patent. However, there is a hole in the vein wall in the proximity of the cannula tip and when administration of chemotherapy recommences, a larger and more significant extravasation injury will occur.
  - Alternatively, the bevel of the needle can puncture the vein wall during venepuncture, allowing the drug to escape into the tissue while the lumen of the needle may still remain in the blood vessel and allow adequate blood return.

- There is increased resistance to administration once possible positional changes have been discounted
- Changes in infusion rate – NB these may not be seen if using an infusion pump so close observation required.

10. General procedure for the management of extravasation or suspected extravasation

If extravasation is suspected, it is important to act quickly to prevent tissue necrosis. The practitioner who is responsible for the administration of the vesicant should recognise that an extravasation has occurred and initiate the procedure.
1. Ensure patient has regular medical review.
2. Complete Green Card follow-up section.
3. Complete Critical Incident Form
4. Risk of recall in *July* with radiotherapy.
See appendix 3 for evidence base for specific treatments.

11. Treatment principles

- **Localise and neutralise** uses pulsed cold compression with or without a specific treatment to stop the further spread of the drug and prevent further injury.

- **Spread and dilute** uses warm compression with or without hyaluronidase to facilitate dispersal of the extravasated drug thus reducing its concentration and potential for tissue damage.

The practitioner must check the specific antidote table (appendix 2) before proceeding with any intervention.

**Hyaluronidase**: Dilute 1500 units of hyaluronidase in 2 ml of water for injection, or 0.9% sodium chloride. Inject subcutaneously at several areas around the circumference of the extravasated area. Gently massage the area to facilitate dispersal.

**Sodium Thiosulphate**: Infiltrate 1-3 ml of 3% isotonic sodium thiosulphate into the affected area using multiple 'pin cushion' injections. To achieve 3% sodium thiosulphate from the 50% vial in the extravasation kit, dilute 1.2 ml of 50% to 20 ml with water for injection.

**Topical DMSO**: apply 50% solution topically every 2 hours to the extravasation site for 24 hours. Avoid contact with good skin. Do not cover the area. If blistering occurs discontinue use and seek further advice.

**Surgical excision**: Wide excision with use of grafts may be indicated if persistent pain 1-2 weeks after injury. Inadequate excision is associated with continuing necrosis at the margins, poor granulation and failure of engraftment.

**Hypodermoclysis**: Administering fluids under the skin.

**Warm Compression W.C.C.** Warm Continuous Compression. Apply firmly but without undue pressure a heat source (hot water bottle or small electrically heated blanket) to the area continuously for 24 hours. The heat source should not be in direct contact with the skin and a piece of dry gauze should be laid in between. This assists the natural dispersal of the drug.

**Cold Compression**: Apply firmly but without undue pressure a cold source (crushed ice, flexible cold pack or cold bandage), intermittently for 30 minutes in every 2 hours over the area for the first 24 hours, unless advised otherwise. The cold source should not be placed directly on the skin. Place a piece of dry gauze between the skin and the cold source.
Acidic Extravasations: If the extravasation has been misdiagnosed or the volume extravasated wrongly assessed, the treatment could lead to an alkali extravasation. If this secondary extravasation occurs, it is far more serious and the consequence far more devastating than those associated with venous extravasation. Caution and expert advice should be exercised before proceeding with this specific management.

Sodium Bicarbonate: Infiltrate with 1-3 ml of 2.1% sodium bicarbonate. 8.4% sodium bicarbonate must be diluted as follows. To achieve 2.1% sodium bicarbonate take 5ml of 8.4% sodium bicarbonate, add 5ml of water for injection, discard 5ml of this new solution and add a further 5ml of water for injection. Sodium bicarbonate is not in the extravasation kit. Do not use this antidote unless recommended by an expert. (Plastic surgeon)

Adapted from the National Extravasation Information Service 2004

Steroids
Many guidelines recommend the use of subcutaneous or intradermal steroids. However many reviews state that inflammation is not prominent in the aetiology of tissue necrosis. There is also evidence that subcutaneous or intradermal steroids may be harmful in high doses, are ineffective in certain extravasations and may increase the skin toxicity of vinca alkaloids. For this reason, this policy does not recommend the routine use of subcutaneous steroids and injectable steroids are not included in the extravasation kit.

Topical hydrocortisone 1% cream applied cream every six hours for 7 days or for as long as erythema continues, may reduce nonspecific inflammation, except in vinca-alkaloid injuries. 5

12. Extravasation Kits
Both the policy and the extravasation kit should be simple and easy to follow to reduce the risk of inflicting further damage. It is necessary to hold a complete set of antidotes and hot and cold facilities in all areas where the administration of chemotherapy takes place.

12.1 Contents

- Hyaluronidase 1500 units injection
- Hydrocortisone 1% cream
- Sodium chloride 0.9% injection
- Water for injection
- Selection of needles, syringes, alcohol wipes, sterile gauze
- Directions to the nearest hot/cold pack
- Guide to immediate management including use of specific antidotes

It is the responsibility of the practitioner to ensure that they are familiar with the general policy and the extravasation kit.
NB
Specific antidotes e.g. Topical DMSO (dimethylsulfoxide solution 50%) are available on prescription from pharmacy

12.2 Location

Kits must be available in any area where intravenous chemotherapy is given. A laminated copy of the immediate management of extravasation should be available in all clinical areas and with the extravasation kit. Practitioners should liaise with pharmacy to ensure timely refill of the kit after use. For outreach clinics, the Acute Trust will be responsible for supplying the extravasation kits for use in the clinic.

13. Documentation and reporting

Follow local procedures for documentation and clinical incident reporting. If possible photograph the injury. Documentation should include the drugs involved, size and location of cannula, procedure followed and any specific antidotes used, and outcomes.

13.1 Green Card Reporting

Most information about the treatment of extravasation is anecdotal. The “Green Card” scheme should be used for reporting extravasation incidences, treatments and outcome. This scheme is coordinated through the St.Chad's Unit, City Hospital, Birmingham. Green cards can be filled in online.

The aims of the Green Card are:
- to obtain accurate statistical information on the number of incidents categorised by extravasating drug and type of treatment to collect data on treatment methods and antidotes being used for extravasation incidents
- to obtain accurate information on the outcome of incidents
- to feedback information on the treatment and its effectiveness

Green Cards ask for the following information:
- the drug or drugs involved
- how was it detected
- the extent of the problem
- drugs used in the treatment of the extravasation
- the procedure for treatment
- type of cannula used for the administration of the chemotherapy
- location and extent of the extravasation
- outcome

These reporting cards are user friendly. The information given can remain anonymous for the reporter, the patient and the Centre involved. Reporting can be done online at http://www.extravasation.org.uk/Greenmenu.htm
Green cards should be available alongside the extravasation kit and can be obtained from [http://www.extravasation.org.uk/Greenmenu.htm](http://www.extravasation.org.uk/Greenmenu.htm) or by post from Extravasation Co-ordinator, c/o St Chad’s Unit, City Hospital, DudleyRoad, Birmingham B1 8 7QH
If reporting online please print a copy of the form before submitting and send to the network pharmacist. If using a green card please make a copy and send to your trust pharmacist who will send it to the network pharmacist.

14. References and suggested further reading

5. UKCCSG extravasation policy (2005)
APPENDIX I

CLASSIFICATION OF CYTOTOXIC AGENTS ACCORDING TO THEIR POTENTIAL TO CAUSE SEVERE NECROSIS WHEN EXTRAVASATED

<table>
<thead>
<tr>
<th>VESICANTS Group 5</th>
<th>EXFOLIANTS Group 4</th>
<th>IRRITANTS Group 3</th>
<th>INFLAMMITANTS Group 2</th>
<th>NEUTRALS Group 1</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vincristine</td>
<td>Cisplatin</td>
<td>Carboplatin</td>
<td>Etoposide Phosphate</td>
<td>Asparaginase</td>
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<tr>
<td>Vinblastine</td>
<td>Docetaxel</td>
<td>Etoposide</td>
<td>Fluorouracil</td>
<td>Bleomycin</td>
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<tr>
<td>Vinorelbine</td>
<td>Liposomal Daunorubicin</td>
<td>Irinotecan</td>
<td>Methotrexate</td>
<td>Cladribine</td>
</tr>
<tr>
<td>Carmustine</td>
<td>Liposomal Doxorubicin</td>
<td>Mylotarg</td>
<td>Raltitrexed</td>
<td>Cyclophosphamide</td>
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<tr>
<td>Dacarbazine</td>
<td>Mitoxantrone</td>
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<td>Cytarabine</td>
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<td>Amsacrine</td>
<td>Oxaliplatin</td>
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<td>Fludarabine</td>
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<td>Daunorubicin</td>
<td>Topotecan</td>
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<td>Gemcitabine</td>
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<td>Doxorubicin</td>
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<td>Ifosfamide</td>
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<td>Epirubicin</td>
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<td>Melphalan</td>
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<td>Idarubicin</td>
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<td>Pentostatin</td>
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<td>Mitomycin</td>
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<td>Rituximab</td>
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<td>Paclitaxel</td>
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<td>Trastuzemab</td>
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<td>Streptozocin</td>
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<td>Bortezomib</td>
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<td>Dactinomycin</td>
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<td>Alemtuzumab</td>
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<td>Bevacizumab</td>
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<td>Cetuximab</td>
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**NB** this list is not exhaustive. It is the practitioner’s responsibility to know the vesicant potential of any drug not on this list.
## APPENDIX 2

### SPECIFIC ANTIDOTES IN THE MANAGEMENT OF CYTOTOXIC EXTRAVASATION

<table>
<thead>
<tr>
<th>Drug/class of drug</th>
<th>Warm/Cold compression</th>
<th>Specific antidote</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Vinca Alkaloids</strong>&lt;br&gt;Vincristine&lt;br&gt;Vinblastine&lt;br&gt;Vinorelbine</td>
<td>Apply firmly but without undue pressure a heat source (hot water bottle, flexible heat pack or small electric blanket) continuously for 24 hours. The heat source should not be placed directly on the skin. Place a piece of dry gauze between the skin and the heat source.</td>
<td><strong>Hyaluronidase 1500 IU</strong>&lt;br&gt;Draw up 1500IU hyaluronidase in 1 to 2ml water for injection or 0.9% sodium chloride. Inject 0.1 to 0.2ml subcutaneously at points of the compass around the circumference of the area of extravasation. Gently massage area to facilitate dispersal.</td>
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<tr>
<td><strong>Anthracyclines</strong>&lt;br&gt;Daunorubicin&lt;br&gt;Doxorubicin&lt;br&gt;Epirubicin&lt;br&gt;Idarubicin&lt;br&gt;Mitomycin&lt;br&gt;Mitoxantrone</td>
<td>Apply firmly but without undue pressure a cold source (crushed ice, flexible cold pack or cold bandage), intermittently for 30 minutes in every 2 hours over the area for the first 24 hours, unless advised otherwise. The cold source should not be placed directly on the skin. Place a piece of dry gauze between the skin and the cold source.</td>
<td><strong>Topical DMSO 50%</strong>&lt;br&gt;Apply Topical DMSO 50% using a cotton bud every 2 hours at the extravasation site for 24 hours. Avoid contact with good skin. For the next 7 days apply DMSO 50% every 6 hours alternating with topical hydrocortisone 1% cream every 3 hours. Do not use an occlusive cover. If blistering occurs, stop DMSO and seek further advice.</td>
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<td><strong>Taxanes</strong>&lt;br&gt;Docetaxel&lt;br&gt;Paclitaxel</td>
<td>Apply firmly but without undue pressure a heat source (hot water bottle, flexible heat pack or small electric blanket) continuously for 24 hours. The heat source should not be placed directly on the skin. Place a piece of dry gauze between the skin and the heat source.</td>
<td><strong>Hydrocortisone and Chlorphenamine</strong>&lt;br&gt;Using 0.2ml “pin cushion” injections, infiltrate the area with 1 to 3ml of a mixture of 100mg hydrocortisone and 4mg Chlorphenamine in 10ml. Alternate warm compression with the application of any topical anti-histamine cream. In particularly severe cases, administer 1g of oral sodium cromoglycate.</td>
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<tr>
<td><strong>Oxaliplatin</strong></td>
<td>Apply firmly but without undue pressure a heat source (hot water bottle, flexible heat pack or small electric blanket) continuously for 24 hours. The heat source should not be placed directly on the skin. Place a piece of dry gauze between the skin and the heat source.</td>
<td>Infiltrate the site with 1500 units of hyaluronidase in 1ml Water for Injection. Inject subcutaneously at several areas around the circumference of the extravasated area. The area should be warmed to aid dispersion.</td>
</tr>
<tr>
<td><strong>Cisplatin If Small Volume (&lt;20ml) or Solution &lt;0.5mg/mL</strong>&lt;br&gt;Carboplatin</td>
<td>Apply firmly but without undue pressure a heat source (hot water bottle, flexible heat pack or small electric blanket) continuously for 24 hours. The heat source should not be placed directly on the skin. Place a piece of dry gauze between the skin and the heat source.</td>
<td>Infiltrate the site with 1500 units of hyaluronidase in 1ml Water for Injection. Inject subcutaneously at several areas around the circumference of the extravasated area. Gently massage the area to facilitate dispersion. Apply topical hydrocortisone 1% cream every six hours for the next 7 days or for as long as erythema continues.</td>
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<tr>
<td><strong>Cisplatin if Large Volume (&gt;20ml) or Solution &gt;0.5mg/mL</strong></td>
<td><strong>Sodium Thiosulphate 3%</strong></td>
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<tr>
<td>Apply firmly but without undue pressure a heat source (hot water bottle, flexible heat pack or small electric blanket) continuously for 24 hours. The heat source should not be placed directly on the skin. Place a piece of dry gauze between the skin and the heat source.</td>
<td>Infiltrate the site with 1-3ml of 3% sodium thiosulphate into the affected area using multiple ‘pin cushion’ injections at several areas around the circumference of extravasated area. Infiltrate the site with 1500 units of hyaluronidase in 1ml Water for Injection. Inject subcutaneously at several areas around the circumference of the extravasated area. Gently massage the area to facilitate dispersion. Apply topical hydrocortisone 1% cream every six hours for the next 7 days or for as long as erythema continues.</td>
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APPENDIX 3

EXTRAVASATION – EVIDENCE BEHIND RECOMMENDATIONS

Controversy continues about appropriate antidote therapy and the situation is complicated by the inability to conduct controlled studies on human subjects. Ethical constraints and differences in tissue structure between human and animal skin are two of the biggest obstacles of antidote research. In this section the evidence behind the recommendations made in the monographs will be graded according to the definitions derived from US Agency for Health Care Policy and Research below.

<table>
<thead>
<tr>
<th>Type and level of evidence</th>
<th>Type of evidence</th>
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<tbody>
<tr>
<td><strong>Level</strong></td>
<td><strong>Type of evidence</strong></td>
</tr>
<tr>
<td>Ia</td>
<td>Evidence obtained from meta-analysis of randomised controlled trials.</td>
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<tr>
<td>Ib</td>
<td>Evidence obtained from at least one randomised controlled trial.</td>
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<tr>
<td>IIA</td>
<td>Evidence obtained from at least one well-designed controlled study without randomisation.</td>
</tr>
<tr>
<td>IIb</td>
<td>Evidence obtained from at least one other type of well-designed quasi-experimental study.</td>
</tr>
<tr>
<td>III</td>
<td>Evidence obtained from well-designed non-experimental descriptive studies, such as comparative studies, correlation studies and case control studies.</td>
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<tr>
<td>IV</td>
<td>Evidence from expert committee reports or opinions and/or clinical experiences of respected authorities.</td>
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<tr>
<th>Grade of Recommendation</th>
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<tr>
<td>Grade</td>
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<td>B</td>
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<td>C</td>
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Unfortunately, no antidote has so far received a clear validation in controlled clinical trials. Therefore, case reports and uncontrolled studies are still the only evidence for the role of antidotes in the clinical setting and, in some cases they do provide relevant cumulative experience. Due to the volume of the above studies the authors of this policy decided to use only reviews as evidence. The authors also reviewed other policies from the UK and contacted the manufacturer of each drug asking for their recommendations for the treatment of an extravasation with that particular drug. As a result most of the recommendations contained in this policy will be Grade B or C and will be a result of evidence obtained from reviews, other UK extravasation policies, and manufacturers.
<table>
<thead>
<tr>
<th>Treatment Recommendations</th>
<th>Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>A. Cleanse the area with Water for Irrigation sachets.</td>
<td>Cleansing the area will allow for better assessment and documentation of the injury.</td>
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<tr>
<td>B. Apply firmly but without undue pressure a cold source (crushed ice, flexible cold pack or cold bandage), intermittently for 30 minutes in every 2 hours over the area for the first 24 hours, unless advised otherwise. The cold source should not be placed directly on the skin. Place a piece of dry gauze between the skin and the cold source.</td>
<td>Application of cold to the site is thought to decrease toxicity of the agent to the area. It is believed this causes vasoconstriction, localising the extravasation and perhaps allowing time for local vascular and lymphatic systems to disperse the agent as well as shunting blood away from the area and reducing cellular metabolism. The application of cold to vinca-alkaloid induced injuries has been shown to increase ulcer formation in animal studies and therefore the use of cold should be reserved only for the treatment of non vinca alkaloid vesicant injuries. Intermittent local cooling for up to 24 hours appears to be the recommended schedule. The evidence supporting this treatment consists entirely of III or IV reports but is sufficiently extensive that this can be recommended at Grade B.</td>
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<tr>
<td>C. Apply topical hydrocortisone 1% cream every six hours for the next 7 days or for as long as erythema continues.</td>
<td>Many guidelines recommend the use of subcutaneous or intradermal steroids. However, many of the reviews found argued that inflammation is not prominent in the aetiology of tissue necrosis. There is also evidence that subcutaneous or intradermal steroids may be harmful in high doses and may increase the skin toxicity of vinca alkaloids. Therefore this guideline recommends that topical hydrocortisone 1% is used, which can do little harm and may bring down non-specific inflammation, except in vinca-alkaloid injuries. The evidence supporting this treatment consists entirely of III or IV reports but is sufficiently extensive that this can be recommended at Grade B.</td>
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<tr>
<td>D. Infiltrate the site with 1500 units of hyaluronidase in 1ml Water for Injection. Inject subcutaneously at several areas around the circumference of the extravasated area. Gently massage the area to facilitate dispersion.</td>
<td>Hyaluronidase has been reported to be an effective antidote for vinca alkaloids and Etoposide. Animal studies have also shown hyaluronidase to be of potential benefit in paclitaxel extravasations. It is believed injection of hyaluronidase promotes the permeability of tissue, improving the absorption of infiltrated cytotoxic. Tissue injury is decreased secondary to the dilution of the cytotoxic across a larger tissue area. The guideline therefore recommends that the use of hyaluronidase is</td>
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</table>
unlikely to cause harm and recommends its use where a policy of “spread and dilute” is indicated. The evidence supporting this treatment consists entirely of III or IV reports but is sufficiently extensive that this can be recommended at Grade B.

### E. Apply firmly but without undue pressure a heat source (hot water bottle, flexible heat pack or small electric blanket) continuously for 24 hours. The heat source should not be placed directly on the skin. Place a piece of dry gauze between the skin and the heat source.

Application of heat is thought to induce vasodilation, which facilitates increased systemic absorption and distribution of the cytotoxic. It is thought to aid the dispersal of the vinca-alkaloids. The application of heat to anthracycline induced injuries increases tissue damage and therefore the use of heat should be reserved only for the treatment of vinca alkaloid and non-vesicant induced injuries where a policy of “spread and dilute” is indicated\(^1,2,3,4\). The evidence supporting this treatment consists entirely of III or IV reports but is sufficiently extensive that this can be recommended at Grade B.

### F. Apply topical Dimethyl Sulfoxide (DMSO) 50% (v/v), by painting on with a ‘cotton bud’, every 2 hours at the extravasation site for 24 hours. Avoid contact with good skin. If blister forms stop DMSO and seek further advice.

This is recommended for the anthracyclines and Mitomycin \(^1,2,3,4,5,6,7\). The use seems well supported, and seems unlikely to cause any harm. The optimal schedule and duration of DMSO applications is unclear but should probably be at least every 6 hours for a minimum of 3 days. It should be noted that DMSO is not licensed for this use. The evidence supporting this treatment consists entirely of III or IV reports but is sufficiently extensive that this can be recommended at Grade B.

### G. For the next 7 days apply DMSO every 6 hours, alternating with topical hydrocortisone 1% cream every 6 hours (a preparation applied every 3 hours on an alternate basis). Do not use an occlusive cover. If required cover once the area is dry. If blister forms stop DMSO and seek further advice.

This is recommended for the anthracyclines and Mitomycin \(^1,2,3,4,5,6,7\). The use seems well supported, and seems unlikely to cause any harm. The optimal schedule and duration of DMSO applications is unclear but should probably be at least every 6 hours for a minimum of 3 days. It should be noted that DMSO is not licensed for this use. The evidence supporting this treatment consists entirely of III or IV reports but is sufficiently extensive that this can be recommended at Grade B.

### H. Infiltrate the site with 1-3ml of 3% sodium thiosulphate into the affected area using multiple ‘pin cushion’ injections at several areas around the circumference of extravasated area.

This is recommended for extravasations due to large concentrated solutions of Cisplatin \(^1,2,3\). The use seems well supported, and seems unlikely to cause any harm. It should be noted that sodium thiosulphate is not licensed for this use. The evidence supporting this treatment consists entirely of III or IV reports but is sufficiently extensive that this can be recommended at Grade B.

### I. Monitor patient closely for “recall

Anthracyclines administered after radiotherapy
have been shown in a reactivation of skin toxicity known as a “recall reaction”. A similar reaction may be seen in patients who have had previous extravasations. This reaction has also been shown with paclitaxel. The evidence for this approach in patients on anthracyclines and Paclitaxel is very limited (level IV) and the confidence with which it can be recommended is Grade C.