STOP! – Have you got the most up to date version of this policy?

Always Check www.cmscn.nhs.uk before reading further.

Version: 6.0
Owner: Nurse & Pharmacy CNGs
Date first created: October 2011
Date approved: 24TH January 2016
Approved by: Chemotherapy CNG
Review Date: January 2019
## Revision Log

<table>
<thead>
<tr>
<th>Changes and Revisions</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Version 3.0</strong></td>
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<td><strong>Version 4.0</strong></td>
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<td><strong>Version 5.0</strong></td>
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<tr>
<td><strong>Version 6.0</strong></td>
</tr>
<tr>
<td>Definitions expanded</td>
</tr>
<tr>
<td>Localise and neutralise, disperse and dilute drugs identified as red or blue</td>
</tr>
<tr>
<td>Change in management of vesicant drugs to immediate referral to burns assessment unit</td>
</tr>
<tr>
<td>Addition of patient information leaflet</td>
</tr>
</tbody>
</table>

### Policy formulated and developed by the following:

- Alder Hey Children’s NHS Foundation Trust
- Clatterbridge Cancer Centre NHS Foundation Trust
- Countess of Chester Hospital NHS Foundation Trust
- North Cheshire Hospitals NHS Trust
- Royal Liverpool & Broadgreen University Hospitals NHS Trust
- Southport & Ormskirk Hospitals NHS Trust
- St Helens and Knowsley Hospital NHS Trust
- University Hospital Aintree NHS Foundation Trust
- Wirral University Teaching Hospitals NHS Foundation Trust
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1.0 Introduction

The purpose of this document is to set out the guidelines for the management of cytotoxic extravasation incidents within Cheshire and Merseyside Strategic Clinical Networks (CMSCN).

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

- Manual For Cancer Services 2004
- CMSCN Guide to Care and Maintenance of Venous access devices incorporating the Collaborative Intravenous Nursing Service guidelines for venous access devices for Cheshire and Merseyside NHS Northwest
- 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 24 hour telephone advice specification
- 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.

2.0 Definition

Extravasation

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

Vesicant

Vesicants are drugs (cytotoxic or non-cytotoxic) with the potential to cause blistering and ulceration and if left untreated, tissue necrosis

Non-vesicant (also known as infiltrates)

Some non-vesicants may still cause a reaction if they extravasate:
- Exfoliates – inflammation and shredding of the skin
- Irritants – inflammation and irritation
- Inflammatants – mild to moderate inflammation and flare
- Neutrals – inert compounds

Localise and neutralise

Applying a cold source to the extravasation site causes vasoconstriction, localising the drug. An antidote can be used at this stage to neutralise the drug, depending on the drug and volume of extravasation. The drug will then be dispersed via the local vascular and lymphatic systems.

Disperse and dilute

Applying a heat source to the extravasation site causes vasodilation, increasing distribution and absorption and decreasing the local drug concentration
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 requires corrective plastic surgery. Accurate documentation of the incident is essential.

There is no national standard of practice for management of extravasation.

3.0 Scope

The aim of this document is to provide a framework based on current available evidence for the appropriate management of cytotoxic-induced extravasation within the CMSCN (including paediatric practice).

Cytotoxic drugs may be divided in three categories based upon their propensity to cause extravasation injury (appendix 1). However this list may not be exhaustive and it is the practitioner’s responsibility to recognise the potential for injury and appropriate management for any drug which they are administering.

4.0 Evidence Base

Extravasation is a condition that is often under-diagnosed, under-treated and unreported. 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 CMSCN and other network and professional body extravasation documents.

For the evidence base for specific recommendations made in this policy see Appendix 6.0.

5.0 Causes

Potential causes of extravasation include:

- 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.
6.0 Risk Reduction

- Only authorised practitioners who have been trained and are included on a register may administer chemotherapy (see CMSCN Guidance for Ensuring Safety and Quality of Chemotherapy Services incorporating Guidance for Safe Prescribing, Handling and Administration of Cytotoxic Drugs).
- 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.
- Drugs 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 (See Section 9.0).
- 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.

7.0 Recognition

It is important that extravasation is not misdiagnosed because the treatment itself may involve the administration of drugs which themselves 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 discolouration 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.

**Signs and symptoms of possible extravasation include:**

- Pain, stinging, burning or any other acute change at the injection site.
  - **Please note** – adults or children who are frightened of needing a new cannula may deny pain or discomfort.
- 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 two 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 – please note these may not be seen if using an infusion pump so close observation required.

Central Venous Catheter (CVC) devices
• Aching discomfort in the shoulder/neck – this is the most common
• Pain, burning, aching/discomfort, swelling of chest wall
• Fluid leakage at or around exit site and along subcutaneous canal
### 8.0 Immediate Management (adapted from EONS/UKONS guidance 2007)

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.

<table>
<thead>
<tr>
<th>Step</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Stop the infusion or injection immediately – DO NOT remove the cannula at this point.</td>
</tr>
<tr>
<td>2.</td>
<td>Seek assistance if needed.</td>
</tr>
<tr>
<td>3.</td>
<td>Disconnect the infusion (not the cannula/needle).</td>
</tr>
<tr>
<td>4.</td>
<td>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 site.</td>
</tr>
<tr>
<td>5.</td>
<td>Mark the affected area and take digital images of the site.</td>
</tr>
<tr>
<td>6.</td>
<td>Remove the cannula/needle.</td>
</tr>
<tr>
<td>7.</td>
<td>Collect the extravasation kit (see section 10) and notify the physician/senior nurse.</td>
</tr>
<tr>
<td>8.</td>
<td>Administer pain relief if required. Complete required documentation (<strong>Appendix 3.0</strong>).</td>
</tr>
<tr>
<td>9.</td>
<td>Decide on how the extravasation should be treated (see fig.1 on page.10); <strong>LOCALISE AND NEUTRALISE</strong> OR <strong>DISPERSE AND DILUTE</strong></td>
</tr>
<tr>
<td>10.</td>
<td>For vesicants refer immediately to the burns assessment unit (<strong>Appendix 4.0</strong>).</td>
</tr>
</tbody>
</table>
| 11.  | Provide patient information letter and complete all documentation (appendix 3 to 6);  
- Appendix 3 Extravasation Incident Proforma  
- Appendix 4 Referral to burns assessment unit  
- Appendix 5 GP Notification  
- Appendix 6 Patient Information letter  
- Complete hospital incident form |

In the event of a central venous line extravasation please follow steps 1-5 and discuss immediately with the patient’s consultant. The plastics team should be contacted for further advice to discuss removal of the device and immediate and future treatment as this may differ with each event.
RED = apply warm compress to affected area for 20mins to disperse and dilute 4xdaily for 24-48 hrs
BLUE (italics) = apply cold compress to affected area for 20mins to localise and neutralise 4xdaily for 24-48 hrs

If the drug is a non-vesicant, application of a simple cold compress and elevation of the limb may be sufficient to limit the swelling etc. This list is not exhaustive therefore it is the practitioner’s responsibility to know the vesicant potential of any drug not on this list.
9.0 Extravasation Kits

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 cytotoxic chemotherapy takes place.

Contents

- Topical DMSO (dimethylsulfoxide cream or solution 50%)
- 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 extravasation policy and the extravasation kit.

Location

Kits must be available in all areas where intravenous cytotoxic chemotherapy is given.

It is good practice to laminate a copy of the immediate management of extravasation (section 8 – pages 9 & 10) and make it available in all clinical areas alongside the extravasation kit.

Practitioners should liaise with pharmacy to ensure timely refill of the kit after use.

For Clatterbridge Cancer Centre (CCC) outreach clinics, CCC will be responsible for supplying the extravasation kits for use in the clinic. Local arrangements must be in place if CCC cannot provide any part of the kit e.g. warm/cold packs.

10.0 Documentation and reporting

Follow local procedures for clinical incident reporting. If possible photograph the injury.

Thorough documentation is provided in appendices 3, 4 and 5 for use by NHS Trusts in the CMSCN. Documentation should include the drugs involved, size and location of cannula, procedure followed and any specific antidotes used, and outcomes.
11.0 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 or by post from Extravasation Co-ordinator, c/o St Chad’s Unit, City Hospital, Dudley Road, Birmingham B18 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.
Appendix 1.0
List of vesicants, irritants and non-vesicants of systemic anti-cancer treatments (EMSO - EONS, 2012)

<table>
<thead>
<tr>
<th>Vesicants</th>
<th>Irritants</th>
<th>Non-vesicants</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aclarubicin</td>
<td>Carboplatin</td>
<td>Aldesleukin (IL-2)</td>
</tr>
<tr>
<td>Amsacrine</td>
<td>Carmustine</td>
<td>Allemmtuzumab</td>
</tr>
<tr>
<td>Bendamustine</td>
<td>Cisplatin</td>
<td>Arsenic Trioxide</td>
</tr>
<tr>
<td>Doctinomycin</td>
<td>Dacarbazine</td>
<td>Asparaginase</td>
</tr>
<tr>
<td>Daunorubicin</td>
<td>Etoposide</td>
<td>Bleomycin</td>
</tr>
<tr>
<td>Docetaxel</td>
<td>Fluorouracil</td>
<td>Bortezomib</td>
</tr>
<tr>
<td>Doxorubicin</td>
<td>Ifosfamide</td>
<td>Cladribine</td>
</tr>
<tr>
<td>Epirubicin</td>
<td>Irinotecan</td>
<td>Cyclophosphamide</td>
</tr>
<tr>
<td>Idarubicin</td>
<td>Ixabepilone</td>
<td>Cytarabine</td>
</tr>
<tr>
<td>Mitomycin C</td>
<td>Liposomal doxorubicin</td>
<td>Etoposide phosphate</td>
</tr>
<tr>
<td>Mitoxantrone</td>
<td>Liposomal daunorubicin</td>
<td>Fludarabine</td>
</tr>
<tr>
<td>Paclitaxel</td>
<td>Mephalan</td>
<td>Gemcitabine</td>
</tr>
<tr>
<td>Trebectedin</td>
<td>Oxaliplatin</td>
<td>Interferons</td>
</tr>
<tr>
<td>Vinblastine</td>
<td>Streptozocin</td>
<td>Interleukin-2</td>
</tr>
<tr>
<td>Vincristine</td>
<td>Teniposide</td>
<td>Methotrexate</td>
</tr>
<tr>
<td>Vindesine</td>
<td>Topotecan</td>
<td>Monoclonal antibodies</td>
</tr>
<tr>
<td>Vinorelbine</td>
<td></td>
<td>Nelarabine</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Pemtrexed</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Pentostatin</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Raltitrexed</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Temsirolimus</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Thiothepa</td>
</tr>
</tbody>
</table>

RED = apply warm compress to affected area for 20 mins to disperse and dilute 4 x daily for 24-48 hours
BLUE (italics) = apply cold compress to affected area for 20 minutes to localise and neutralise 4 x daily for 24-48 hours

This list is not exhaustive therefore it is the practitioner’s responsibility to know the vesicant potential of any drug not on this list and check the summary of product characteristics https://www.medicines.org.uk/emc/.

Any agent extravasated in high enough concentration may be an irritant. There have been few reports of these agents acting as irritants, but there is no clear evidence for this.

For those medications that are not considered a vesicant but cause prolonged patient discomfort at the infusion site, it is strongly recommended that a central line be placed.
### Appendix 2.0 Specific antidotes in the management of peripheral extravasation

<table>
<thead>
<tr>
<th>Drug/class of drug</th>
<th>Specific antidote</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Vinca Alkaloids</strong></td>
<td></td>
</tr>
<tr>
<td>Vincristine</td>
<td></td>
</tr>
<tr>
<td>Vindesine</td>
<td></td>
</tr>
<tr>
<td>Vinblastine</td>
<td></td>
</tr>
<tr>
<td>Vinorelbine</td>
<td></td>
</tr>
<tr>
<td><strong>Taxanes</strong></td>
<td></td>
</tr>
<tr>
<td>Docetaxel</td>
<td></td>
</tr>
<tr>
<td>Paclitaxel</td>
<td></td>
</tr>
<tr>
<td><strong>Hyaluronidase</strong></td>
<td></td>
</tr>
<tr>
<td>Draw up 150-1500IU hyaluronidase in 1 mL water for injection. 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>
<td></td>
</tr>
<tr>
<td><strong>Anthracyclines</strong></td>
<td></td>
</tr>
<tr>
<td>Daunorubicin</td>
<td></td>
</tr>
<tr>
<td>Doxorubicin</td>
<td></td>
</tr>
<tr>
<td>Epirubicin</td>
<td></td>
</tr>
<tr>
<td>Idarubicin</td>
<td></td>
</tr>
<tr>
<td>Mitoxantrone</td>
<td></td>
</tr>
<tr>
<td>Mitomycin C</td>
<td></td>
</tr>
<tr>
<td><strong>Topical DMSO 50%</strong></td>
<td></td>
</tr>
<tr>
<td>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 DMSO50% 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>
<td></td>
</tr>
<tr>
<td><strong>Bendamustine</strong></td>
<td></td>
</tr>
<tr>
<td><strong>No specific antidote needed</strong></td>
<td></td>
</tr>
<tr>
<td>If signs of erythema persist then <strong>topical 1% hydrocortisone cream</strong> may be used. Apply sparingly to the affected area 4 times a day while symptoms persist.</td>
<td></td>
</tr>
<tr>
<td><strong>Any other cytotoxic drug (appendix 1.0)</strong></td>
<td></td>
</tr>
<tr>
<td><strong>No specific antidote needed</strong></td>
<td></td>
</tr>
<tr>
<td>If signs of erythema persist then <strong>topical 1% hydrocortisone cream</strong> may be used. Apply sparingly to the affected area 4 times a day while symptoms persist. 1% Hydrocortisone cream may be used if erythema occurs.</td>
<td></td>
</tr>
</tbody>
</table>

Not all cytotoxic agents have a specific antidote for extravasation.
### Extravasation Incident Proforma (adapted from EONS/UKONS 2007)

<table>
<thead>
<tr>
<th>Name</th>
<th>Date</th>
<th>Time</th>
</tr>
</thead>
<tbody>
<tr>
<td>Date of Birth</td>
<td>Hosp no</td>
<td></td>
</tr>
<tr>
<td>Cannula used</td>
<td>22g</td>
<td>24g</td>
</tr>
<tr>
<td>Cannula fixated with</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other method i.e. Central line</td>
<td>PICC line</td>
<td>Portacath</td>
</tr>
<tr>
<td>Site of puncture</td>
<td>Left hand/arm</td>
<td>Right hand/arm</td>
</tr>
</tbody>
</table>

Please number and show location of puncture attempts and area of extravasation

#### Extravasation details

<table>
<thead>
<tr>
<th>Name of chemotherapy/drug</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Drug classification:</td>
<td>vesicant</td>
</tr>
<tr>
<td>Date</td>
<td>Time administered</td>
</tr>
<tr>
<td>Time extravasation noticed</td>
<td></td>
</tr>
<tr>
<td>Estimated volume of drug extravasated</td>
<td>ml</td>
</tr>
<tr>
<td>Type of administration</td>
<td>bolus</td>
</tr>
<tr>
<td>How was line patency assessed</td>
<td>Blood return</td>
</tr>
<tr>
<td>Frequency of assessment of insertion site</td>
<td></td>
</tr>
</tbody>
</table>

#### Signs and symptoms (please circle)

<table>
<thead>
<tr>
<th>Pain/stinging</th>
<th>Blistering</th>
<th>Erythema/redness</th>
<th>Discolouration</th>
<th>Induration</th>
<th>Impairment</th>
<th>Ulceration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aspiration possible</td>
<td>Yes</td>
<td>No</td>
<td>Amount in mls</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Initial treatment</td>
<td>localise and neutralise or disperse and dilute</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Area marked</td>
<td>Yes</td>
<td>No</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Area photographed</td>
<td>Yes</td>
<td>No</td>
<td>If no when</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Antidote required</td>
<td>Yes</td>
<td>No</td>
<td>Antidote</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

#### Checklist

| Trust risk assessment completed | Yes | No |
| Green card completed | Yes | No |
| Referred to burns assessment unit | Yes | No |
| Extravasation proforma attached to referral | Yes | No |
| Patient information letter given | Yes | No |
| Link nurse informed | Yes | No | Who |
| Follow up organised | Yes | No | Details |
| GP letter sent | Yes | No |
| Print name | Signature | Date |
Appendix 4.0  Referral to Burns Assessment Unit - Extravasation of cytotoxic agents

Referral to the burns assessment unit – St Helens and Knowsley Hospitals NHS Trust
(Exception paediatrics that refer to own team in Alder Hey)

Tel: 0151 430 1540    Fax: 0151 430 1508

Please phone direct to make an appointment and then fax the referral including incident proforma

Dear Dr…………………………………………….. Date………………………………………………………………………………

Patient Details

…………………………………………………………………………………………………………………………………..…….………
……………………………………………………………………………………………………………………………………….………..

The patient detailed above is receiving chemotherapy and suffered an extravasation on
date…………………………………………time……………………………………at……………………………………hospital

We have attached the proforma explaining the incident.

We would be very grateful if you could review the patient urgently advising on future treatment.

Please send correspondence to the consultant & link nurse as detailed below:

Referring Consultant/Team……………………………………………………………………………………………………...

Link Nurse / CNS………………………………………………………………………………………………………………

Referring hospital………………………………………………………………………………………………………………

Address………………………………………………………………………………………………………………………………

Postcode……………………………………………………………………………………………………………………………..

Contact number………………………………………………………………………………………………………………..

GP Name…………………………………………………………………………………………………………………………

Practice………………………………………………………………………………………………………………………………

Address……………………………………………………………………………………………………………………………..

If you require any further information please do not hesitate to contact the link nurse / consultant as
detailed above or

Out of hours haematology – on call haematologist at relevant hospital

Out of hours oncology – on call registrar/triage Clatterbridge Cancer Centre on
0151 334 1155 bleep 5555

Name of referrer…………………………………………….. Signature……………………………………………………………..

Contact Number………………………………………………………………………………………………………………


Appendix 5.0  GP Notification - Extravasation of cytotoxic agents

Date: -

Dear Doctor

In reference to your patient:

Your patient is currently receiving a course of cytotoxic chemotherapy under the care of:

Dr.................................................................

Chemotherapy was administered on date...................time.............. using the following drugs.

................................................................................................................................................................................

................................................................................................................................................................................

Unfortunately they have experienced an extravasation illustrated on the below diagram.

Right hand / arm  Left hand / arm  Additional information:

![Diagram of extravasation]

This has been treated according to our local policy and documented within the case notes.

Follow up has been arranged with Dr/Team..............................................on date...............time..................

Any further referrals will be made as appropriate, i.e. physiotherapy or the plastics team.

If you require any further information please do not hesitate to contact the link nurse/consultant below or

**Out of hours haematology** – on call haematologist at relevant hospital

**Out of hours oncology** – on call registrar Clatterbridge Cancer Centre 0151 334 1155

Consultant Name......................................................  Link Nurse.................................................................

Address..............................................................................  Address.................................................................

Contact number..........................................................  .................................................................

Yours sincerely

Print name ..................................................  Signature.....................
Appendix 6.0  Patient Information letter
(Leakage of chemotherapy outside of the vein called extravasation)

Name ........................................... Date ......................
Hospital number ..............................
Address ...............................

Following/during your chemotherapy today ......................, you are displaying symptoms of an extravasation, the following explains what this is and how to manage it.

What is extravasation? The drug leaks outside the vein. If this happens when you’re having chemotherapy, it can damage the tissue around the vein. This is called extravasation. You may have noticed stinging, pain, redness or swelling around the vein. Extravasation is not common but if it happens it’s important that it’s dealt with quickly. It may lead to pain, stiffness and tissue damage.

Why did this happen? Extravasation is a rare but known complication of intravenous chemotherapy. It may be difficult to prevent this even though we take all possible precautions. The important thing is that it has been detected and treated.

Treatment The nurse has given you the recommended treatment for the extravasation. This will help to minimise the chance of developing further problems, however please check the area every day for:
- Changes in colour or increase in redness
- Blistering, peeling or flaking
- Increasing discomfort or pain making it difficult for you to exercise your arm or hand
If yes to any of the above please contact your nurse specialist / link nurse on contact number:

Practical tips that will help you manage extravasation include:

DO
- Elevate the affected arm
- Remove any jewellery
- Take mild painkillers if required i.e. paracetamol

DON’T
- Apply any other lotions, creams, ointments or dressings unless you have been instructed to do so by a doctor or nurse
- Expose the area to strong sunlight
- Wear tight clothing around the affected area

Follow up
Chemotherapy may be delayed to allow healing to occur. This will be decided by your consultant (oncologist / haematologist). You may be required to see different professionals to help treat the extravasation. This may include the burns team and/or physiotherapy team. An appointment has been made for you with

<table>
<thead>
<tr>
<th>Team</th>
<th>Date</th>
<th>Time</th>
<th>NOTE: All patients (with the exception of St Helens and Knowsley) must attend A&amp;E to register and then you will be transferred to Ward 4D</th>
</tr>
</thead>
<tbody>
<tr>
<td>Burns Assessment Unit (Ward 4D)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Whiston Hospital</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Nurse name ........................... Signature ........................... Tel ..............................
Appendix 7.0  Evidence behind the 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 is graded according to the University of Oxford Centre for Evidence Based Medicine. The 2011 levels of evidence table and introductory notes are available from http://www.cebm.net/index.aspx?o=5513

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\(^1\),\(^2\),\(^3\),\(^4\). 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\(^1\),\(^2\),\(^3\),\(^4\). Intermittent local cooling for up to 24 hours appears to be the recommended schedule\(^2\).

The evidence supporting this treatment consists entirely of non-randomised or case reports and is recommended at Level 4.

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 non-randomised or case reports and is recommended at Level 4.

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\(^1\),\(^2\),\(^3\),\(^4\),\(^5\),\(^6\),\(^7\). There is also evidence that subcutaneous or intradermal steroids may be harmful in high doses\(^2\), are ineffective in certain extravasations\(^2\) and may increase the skin toxicity of vinca alkaloids\(^2\),\(^3\). 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 non-randomised or case reports but is sufficiently extensive that this can be recommended at Level 4.

Hyaluronidase has been reported to be an effective antidote for vinca alkaloids and etoposide\(^2\),\(^3\),\(^4\). Animal studies have also shown hyalouronidase to be of potential benefit in paclitaxel extravasations. It is believed injection of hyalouronidase 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 hyalouronidase is 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 non-randomised or case reports but is sufficiently extensive that this can be recommended at Level 4.

Application of DMSO is recommended for the anthracyclines and mitomycin\(^2\),\(^3\),\(^6\),\(^7\). 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\(^6\). It should be noted that DMSO is not licensed for this use.

The evidence supporting this treatment consists entirely of non-randomised or case reports and is recommended at Level 4.
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 supporting this treatment is recommended at Level 5.

Dexrazoxane (Savene™) has recently been licensed as a specific antidote for use with anthracyclines and is recommended by some authorities (Jackson, Butler et al 2006; Mouridsen, Langer et al 2007). There is some limited evidence from clinical trials to support its use. It has recently been considered however by both the Scottish Medicines Consortium and its Welsh counterpart, neither of which supported its use. Its use is not currently supported by Cheshire & Merseyside Strategic Clinical Network.

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Appendix 8.0  References and suggested further reading


De Lemos, M Role of dimethylsulfoxide for management of chemotherapy extravasation J Oncol Pharm Pract December 2004 vol. 10 no. 4 197-200


How, C and Brown J. (1998) Extravasation of cytotoxic chemotherapy from peripheral veins European Journal of Oncology Nursing 2 (1) 51-58


