Alder Hey Children's
NHS Foundation Trust

GUIDELINES FOR THE PREVENTION AND MANAGEMENT OF CYTOTOXIC DRUG EXTRAVASATION

Contents

1. INTRODUCTION

The purpose of this document is to set out the guidelines for the management of cytotoxic extravasation incidents. Extravasation is the inadvertent leakage of fluid and/or medication from blood vessels into interstitial tissues. It is important that precautions are taken to prevent extravasation, but if it occurs treatment must be initiated immediately.

National/Regional standards and publications have been used to support the development of this guidance.

Additionally, Trust wide policies that support this document and which must be complied with include:

- Intravenous Access Devices in Paediatric Patients – Care and Maintenance Guidelines
- Consent policy (including consent to treatment and photography)
- Operational policy and guidance on the use of cytotoxic drugs for the treatment of malignant disease

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 where available.

2. DEFINITION

Extravasation	Extravasation is defined as the inadvertent leakage of a vesicant solution from its intended vascular pathway (vein) into the surrounding tissue.
Infiltration	Infiltration is the inadvertent leakage of a non-vesicant solution from its intended vascular pathway (vein) into the surrounding tissue.
Vesicant	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.
Irritants	Drugs which are capable of causing inflammation, irritation or pain at site of extravasation but rarely cause tissue breakdown. Some irritants do also have the potential to cause ulceration, but only in the case that a very large amount of the drug is extravasated into the tissue.
Non-vesicant	Inert or neutral compounds that do not cause inflammation or damage. Do not cause ulceration, however they do have the potential to cause pain at and around the injection site and along the vein.
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.

3. SCOPE

The aim of this guideline is to provide a framework for the appropriate management of extravasation injuries for children and young people, based on the best current available evidence.

Drugs that have the potential to cause extravasation may be divided in three categories based upon their propensity to cause extravasation injury (see section 7: Classification of Cytotoxic Drugs). 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.

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.

POTENTIAL CAUSES OF EXTRAVASATION

- 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.
- Clot development above the cannula or development of fibrin sheath/thrombus at the catheter tip.
- Small and fragile veins
- Age – young patients tend to have small mobile veins.
- Obstructed vena cava (elevated venous pressure can cause leakage).
- Unconscious, sedated, confused patients or patients with communication problems may be unable to report any symptoms.
- Obesity

5. PATIENT EDUCATION

- Communication with the patient and parent/carer plays a vital role in the recognition of extravasation.
- Patients/parent/carer must be informed of the potential risk of an extravasation occurring and importance of reporting immediately any symptoms irrespective of how insignificant they might be.

6. PREVENTION OF EXTRAVASATION

1) Cytotoxic drugs should be administered by appropriately trained, competent personnel who have received additional training and are included on the Systemic Anti-Cancer Therapy (SACT) register.

2) All personnel administering cytotoxic drugs should be aware of vesicant agents and the risks of ulceration and necrosis on direct tissue contact; they should have an understanding of the management of extravasation and know the contents and whereabouts of the extravasation kit.

3) Vesicant (high risk of tissue necrosis) drugs should be administered via a central line wherever possible. Where a peripheral route must be used this should be via a newly sited cannula, or a peripheral long line if possible, avoiding the dorsum of the hand or foot and sites over joints. The most vesicant drug(s) should be administered first.

4) The positioning and patency of a central line should be checked prior to the administration of vesicant drugs (e.g. by bleeding/flushing the line). Where this cannot be done, imaging will be required to confirm correct positioning. If in doubt, do not give the drug(s), and arrange contrast studies. Dressings should be taken down from a peripheral line and blood drawn back before and during administration and the site observed for signs of swelling or leakage.

5) Any infusion pump used to administer vesicant drugs must have an in-built pressure sensor to detect increased resistance with an alarm to signal this.

6) Wherever possible, vesicant drugs should not be administered in concentrations higher than the manufacturer's recommendations.

7) The vein should always be flushed after administration of drug.

7. CLASSIFICATION OF CYTOTOXIC DRUGS

List of vesicants, irritants and non-vesicants of systemic anti-cancer treatments (EMSO - EONS, 2012)

Vesicants	Irritants	Non-vesicants
Aclarubicin	*Azacitidine*	Aldesleukin (IL-2)
Amsacrine	**Carboplatin**	Allemtuzumab
Bendamustine	*Carmustine*	*Arsenic Trioxide*
Dactinomycin	**Cisplatin**	Asparaginase
Daunorubicin	*Dacarbazine*	**Bleomycin**
Docetaxel	*Etoposide*	*Bortezomib*
Doxorubicin	*Fluorouracil*	**Cladribine**
Epirubicin	**Ifosfamide**	**Cyclophosphamide**
Idarubicin	*Irinotecan*	**Cytarabine**
Mitomycin C	Ixabepilone	*Etoposide phosphate*
Mitoxantrone	*Liposomal doxorubicin*	**Fludarabine**
Paclitaxel	*Liposomal daunorubicin*	**Gemcitabine**
Trabectedin	Mephalan	Interferons
Vinblastine	**Oxaliplatin**	Interleukin-2
Vincristine	*Streptozocin*	*Methotrexate*
Vindesine	Teniposide	Monoclonal antibodies
Vinorelbine	*Topotecan*	**Nelarabine**
		Pemetrexed
		Pentostatin
		Raltitrexed
		Temsirolimus
		Thiothepa

RED = apply warm compress to affected area for 20 mins to disperse and dilute. Repeat this four times in a 24 hour period for up to 48 hours.

BLUE (italics) = apply cold compress to affected area for 20 minutes to localise and neutralise. Repeat this four times in a 24 hour period for up to 48 hours.

The above list is not exhaustive, therefore it is the responsibility of users of this document to ensure they are aware which category new drugs fall into and know the vesicant potential of any drug not on this list and check the Summary of Product Characteristics https://www.medicines.org.uk/emc/
Immunotherapies and other biologically active non-cytotoxic agents are generally classified as non-irritants, although experience of extravasation is limited.

8. RECOGNITION OF EXTRAVASATION

Extravasation should be suspected if:

- Patient complains of burning, stinging pain, numbness or other changes at injection site. Observation of small children and infants is of vital importance as they cannot report such symptoms. Crying and distress during drug administration should always be taken seriously and investigated.

- Induration, swelling, or leaking at injection site.

- Redness or blanching of tissue at site. (It should be noted that doxorubicin may produce a venous flare reaction, with local oedema and streaking over the injection site but this is not usually painful)

- No blood return observed, although blood return may be seen where extravasation has occurred.

- Intravenous infusion does not flow freely. Care needs to be taken when using infusion pumps to administer vesicant drugs. They must always have an alarm to signal increased resistance.

- Resistance is felt when trying to give drugs by bolus.

Monitor children with central lines and investigate immediately for any sign of swelling at the neck, sudden onset of pain in the neck, chest, or local to a port site.

Monitor children with port-a-cath for any pain, leakage or bleeding from needle insertion site.

9. MANAGEMENT OF EXTRAVASATION

General Principles:

- Immediate action is required if extravasation is suspected.

- All personnel who administer Cytotoxic Drugs intravenously must be aware of the extravasation guidelines and the location of the extravasation kit.

- Extravasation guidelines and kit must be available whenever Cytotoxic Drugs are administered intravenously.

NON VESICANTS (neutrals, inflammitants, irritants, exfoliants)

- Tissue damage is unlikely to occur, even when there is local irritation or inflammation.

- Management should be aimed at relieving symptoms.

VESICANTS

There is a high risk of tissue necrosis. Early, aggressive intervention is indicated where significant extravasation has occurred in order to minimise morbidity and should be referred to a plastic surgeon. Management then depends on the type of extravasation.

10. IMMEDIATE MANAGEMENT STEPS

Never apply pressure initially.

Step 1 Stop the infusion or injection – DO NOT remove the cannula, longline or gripper needle.

Step 2 Explain the procedure to child and family, seek assistance.

Step 3 Disconnect the infusion (not the cannula/longline/gripper needle).

Step 4 Leave cannula, longline or gripper needle in place and try to aspirate as much of the drug as possible with a 10ml syringe. Avoid applying direct manual pressure to the suspected extravasation site.

Step 5 Mark the affected area and arrange for medical photography to take an image of the site. Patient's consent for photography must be obtained by an ANP/medic using a trust consent form. This should then be stored in the patient's record.

Step 6 Contact the consultant on-call immediately. Make an urgent referral to the plastics registrar on-call through switch board, and to the tissue viability team for assessment. Seek advice from the consultant on-call regarding removal of the device and immediate and future treatment.

Step 7 Remove peripheral cannula, longline or gripper needle only if advised to do so by consultant on-call as may be required to facilitate treatment and administration of any antidote.

Step 8 Collect the extravasation kit.

Step 9 Provide analgesia if required.

Step 10 Decide on how the extravasation should be treated (see Specific Antidotes in the Management of Peripheral Extravasation).

LOCALISE AND NEUTRALISE* OR *DISPERSE AND DILUTE

If the drug is a non-vesicant or non vinca alkaloid, application of a simple cold compress and elevation of the limb may be sufficient to limit the swelling.

Step 11 Provide patient information letter and counsel patient accordingly. Complete all documentation (Appendix 1 to 3).

- Appendix 1 Extravasation/infiltration Injury Proforma
- Appendix 2 GP Notification
- Appendix 3 Patient extravasation information letter
- Complete Ulysses incident form (include ASU and Oncology/ Haematology Pharmacist)

Step 12 Refill extravasation kit – contact Pharmacy ASU.

11. FOLLOW UP

In all cases of extravasation, the affected area should be inspected for signs of erythema, induration, blistering and necrosis. It should be remembered that necrosis and tissue ulceration may occur a considerable time after extravasation has taken place. After initial referral to the plastics registrar and tissue viability team, they should be asked to review any patient with developing signs of tissue necrosis. Good results have been achieved using techniques of saline flush out at an early stage in extravasation injuries.

12. CONTENTS OF EXTRAVASATION KIT

1. Extravasation guidelines
2. Laminated copy of Immediate Management Steps and Specific Antidotes
3. Chemotherapy Extravasation / Infiltration Injury Proforma
4. GP Notification – Extravasation
5. Patient Extravasation Information letter
6. Syringes - 5ml + 2ml
7. Needles - 2 x 21g (drawing up) 2 x 25g (injection)
8. Sodium chloride 0.9% for injection
9. Hyaluronidase 1500 units for injection
10. Chlorhexidine wipes 2%

11. Hydrocortisone cream 1%
12. Sterile gauze
13. Direction to the nearest 'Instant' Cold Pack
    'Instant' Hot Pack
14. Directions to Dimethylsulfoxide (DMSO) (solution 50% to 100% or cream 50%) for topical use – Omnicell ward 3B.

Extravasation Kits are available from the Aseptic Preparation unit.

13. SPECIFIC ANTIDOTES IN THE MANAGEMENT OF PERIPHERAL EXTRAVASATION

NB. This list is not exhaustive therefore it is the practitioner's responsibility to know the vesicant potential of any drug not included on the **list.**

Drug / Class of drug	Warm / Cold compression	Specific antidote
Vinca Alkaloids **Vincristine,Vindesine** **Vinblastine,Vinorelbine** **Taxanes** **Paclitaxel, Docetaxel**	**Warm** compression - apply for 20 minutes, four times daily for 24 to 48 hours. Place a piece of dry gauze between skin and warm pack.	**Hyaluronidase 1500 IU** Draw up 1500IU hyaluronidase in 1ml Sodium Chloride 0.9% for injection. Inject 0.1 to 0.2ml subcutaneously at points of the compass around the circumference of the area of extravasation. Gently massage the area to facilitate dispersion.
Anthracyclines **Daunorubicn** **Doxorubicin** **Epirubicin, Idarubicin** **Mitoxantrone** **Other** **Mitomycin C**	Apply cold pack intermittently for 20 minutes, four times daily for 24 to 48 hours. Place a piece of dry gauze between skin and cold pack. Elevate the limb.	**Topical DMSO** (solution 50% to 100% or cream 50% Apply Topical DMSO 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 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.
Actinomycin D **Carmustine** **Dacarbazine** **Bendamustine** **Amsacrine**	Apply cold pack intermittently for 20 minutes, four times daily for 24 to 48 hours. Place a piece of dry gauze between the skin and cold pack. Elevate the limb.	**No specific antidote needed** If signs of erythema persist, then **topical 1% hydrocortisone cream** may be used. Apply sparingly to the affected area 4 times a day while symptoms persist.
Any other cytotoxic drug	Tissue damage is unlikely to occur, even when there is local irritation or inflammation. Automatic cold or warm compression is **not** required. However if symptoms warrant it, then this can be used. Refer to Classification of Cytotoxic Drugs Table.	**No specific antidote needed** If signs of erythema persist, then **topical 1% hydrocortisone cream** may be used. Apply sparingly to the affected area 4 times a day while symptoms persist. Hydrocortisone cream may be used if erythema occurs.

14. SOURCES CONSULTED

- Cheshire and Merseyside Strategic Clinical Networks. Network Guidance for the prevention and management of extravasation injuries v.6.0.Review date January 2019

- Perez-Fidalgo, JA; Garcia Fabregat, L; Cervantes, A; Marguiles, A; Vidall, C; Roila, F;(2012) on behalf of the ESMO Guidelines working group, Management of chemotherapy extravasation: ESMO-EONS clinical practice guidelines, European Journal of Oncology Nursing; 16 (2012) 528-534

- European Oncology Nursing Society (2007) Extravasation Guidelines

- Implementation Toolkit

- Manual for Cancer Services Chemotherapy measures 2011

Appendix 1 2014

CHEMOTHERAPY EXTRAVASATION / INFILTRATION INJURY PROFORMA

Please complete this document as your legal record of actions in the event of an extravasation event, and stored in the patient record

NHS Alder Hey Children's NHS Foundation Trust

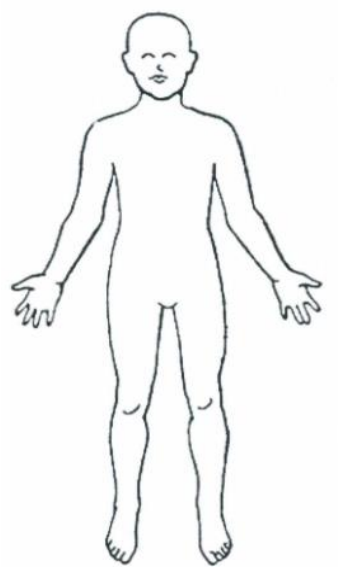
Date of event	____ / ____ / _____
Time of event	_____ : _____

Name:

Hospital Number:

or attach patient label

Insertion site: *(record detailed anatomical descriptors & mark on body chart)*



Grade of Injury	
1	Pain at infusion site
2	Pain at infusion site Swelling No skin blanching Normal capillary refill and peripheral pulsation
3	Pain at infusion site Swelling Skin blanching Cool blanched area Normal capillary refill and peripheral pulsation
4	Pain at infusion site Swelling Skin blanching Cool blanched area Reduced capillary refill +/- arterial occlusion +/- blistering

Line access: CVL❒ Port❒ Longline❒ Peripheral (specify) _____

Administration by IV bolus ❒ Infusion ❒ Rate: _____ mls/hour

Appearance of infusion site: (eg puffy, swollen, red, blistered, mottled, dark, black)

Chemotherapy drug administered:

Estimated volume of drug extravasated (mls):

Consultant on call notified ☐ Time notified ____ : ____ Name of doctor:

Information discussed / advice received:

Plastics Team consultation Yes☐ No☐

Outcome of consultation (if applicable)

Tissue Viability Nurse contacted Yes☐ No☐ by meditech referral ☐ via bleep ☐

Techniques used to manage the extravasation:

Antidotes/ treatments (if applicable)
Description of wound care provided:
Grade / extent of injury :1❒ 2❒ 3❒ 4❒
Medical Photography contacted for photographs Yes☐ No☐ Photographs filed in notes Yes☐ No☐
Description of follow-up measures:
Patient / parent / carer information / education: ❒Informed that extravasation is suspected / has occurred ❒Patient extravasation information leaflet given ❒Informed of possible cause of extravasation ❒Informed about action/ treatment required ❒Informed about follow-up arrangements ❒Informed that an incident form will be completed ❒GP Notification sent
Patient / parent / carer comments:
Nurse comments:
Incident form completed on Ulysses Yes❒ No❒
Nurse (name) Band / job title: Signature:

Other staff involved:
Name: Job title: Signature:

Appendix 2

GP Notification – Extravasation

Dear Doctor

In reference to your patient:

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

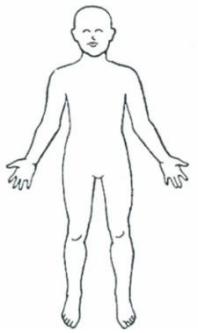
Dr……...

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

……

……

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



This has been treated according to our trust policy and documented in the patient's record

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

Consultant Name……..

Nurse……..

Alder Hey Oncology/Haematology Unit 0151 252 5212
Yours sincerely

Print name ……..… Signature…… Date ……

Appendix 3

Alder Hey Children's NHS Foundation Trust

Patient/Parent Extravasation Information letter

Name ……..

Date…… Hospital number……..

Address……

Following/during your/your child's chemotherapy today……..…, there are 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 a patient has chemotherapy, it can damage the tissue around the vein. This is called extravasation. You/your child 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/your child 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 the Oncology/Haematology Unit 0151 252 5212

Practical tips that will help you manage extravasation include: DO

- Elevate the affected arm
- Remove any jewellery
- Take painkillers provided by Oncology/Haematology Unit if required

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/your child's consultant. You/your child may be required to see different professionals to help treat the extravasation. This may include the plastic team, tissue viabilityand/or physiotherapy team.

Nurse name:..……Signature:.……

Oncology/Haematology Unit 0151 252 5212

GUIDELINES FOR THE PREVENTION AND MANGEMENT OF CYTOTOXIC DRUG EXTRAVASATION	
Version:	3
Ratified by:	Medicines Management and Optimisation Committee (MMOC)
Date ratified:	21st February 2023 (agCA)
Name of originator/author:	Caroline Osborne (Principal Oncology Pharmacist), Laura Healy (Practice Educator)
Name of responsible committee:	Chemotherapy Group
Date issued:	21st February 2023
Review date:	February 2026

Version Control Table				
Version	Date	Author(s)	Status	Comment(s)
3	February 2023	Caroline Osborne/Becky Evans/Lucy Crooks (Oncology)	Current	
2.1	June 2022	Caroline Osborne Laura Healy	Archived	3 month extension agreed by MMOC
2	June 2019	Caroline Osborne Laura Healy	Archived	
1	2011	D and T approved	Section archived	V 3.1 Sep 2012 section 14, MMC Operational policy on cytotoxic drugs for treatment of malignant disease

Review and Revision(s) Log *Record of revision(s) made to guidelines since Version 1*			
Section Number	Page Number	Revision(s) made	Reason for revision(s)
		Refer to archive	Full review due
6 10	6 9	Removed butterfly as not used	No longer used
7	7	Added Azacitidine	New drug