Guideline for the Management of Extravasation of a Systemic Anticancer Therapy including Cytotoxic Agents

NHS England and NHS Improvement

West Midlands Cancer Alliance

This sheet is to accompany all documentation agreed by the West Midlands Cancer Alliance Expert Advisory Groups. This will assist the Cancer Alliance to endorse the documentation and request implementation.

EAG name	West Midlands Cancer Alliance Systemic Anticancer Treatment (SACT) Expert Advisory Group	
Document Title	Guideline for the Management of Extravasation of a Systemic Anticancer Therapy Including Cytotoxic Agents	
Published date	16 December 2019	
Document Purpose	The purpose of this guideline is to provide clear guidance on the causes, prevention, recognition and management of an extravasation of a systemic anticancer therapy used in the treatment of malignant disease in the patient over the age of 16 who is being cared for in adult services. Extravasation is an oncology emergency and therefore it is imperative that it is recognised, diagnosed and treated swiftly to minimise the potential for injury.	
Authors	West Midlands Cancer Alliance Systemic Anticancer Treatment (SACT) Expert Advisory Group	
Review Date (must be within three years)	16 December 2022	
Approval Signatures:	**EAG Chair** Sam Toland Date: 16/12/19	**Cancer Alliance Clinical Director** Rob Gornall Date: 16/12/19

This guidance does not override the individual responsibility of health professionals to make appropriate decision according to the circumstances of the individual patient in consultation with the patient and /or carer. Health care professionals must be prepared to justify any deviation from this guidance.

INTRODUCTION

THIS GUIDELINE IS FOR USE BY THE FOLLOWING STAFF GROUPS :
This guideline is relevant to all chemotherapy nursing and medical personnel working with patients over the age of 16 who are being cared for in adult services within the West Midlands Cancer Alliance

Key Amendments to Document

Version	Date	Amendment
0.1	April 2012	Addition of new agents
0.2	May 2012	Minor amendments
0.3	September 2012	Changes to layout and font colourings addition of additional agents
0.4	February 2016	Updated for West Midlands Strategic Network Expert Advisory Group for Chemotherapy
V1	July 2017	Changes agreed by EAG
V2	12 December 2019	Revision of V1 agreed by EAG

Guideline for the Management of Extravasation of a Systemic Anticancer Therapy Including Cytotoxic Agents

This guideline should be read in conjunction with other relevant policies including Cytotoxic Spillage policy, Guidelines for the Administration of Systemic Anticancer Therapy, and other relevant local and Network policies.

Definition

Extravasation is the accidental leakage of any liquid from a vein into the surrounding tissues. In terms of cancer therapy, extravasation refers to the inadvertent infiltration of systemic anticancer therapies (SACT) into the subcutaneous or subdermal tissues surrounding the administration site (Perez-Fidalgo et al, 2012). This term is a generic term for this process however the scope of this guidance is when the substance involved is a systemic anticancer drug (SACT) including cytotoxic agents and monoclonal antibodies used in the treatment of malignant disease.

If extravasation occurs with vesicant drugs, the result may be tissue damage and necrosis – therefore prompt management is required to prevent permanent damage (Dougherty and Oakley, 2011). The extent of injury is determined by the following factors:

- the type of drug which extravasates
- the concentration and volume of drug in the tissue
- the location of the extravasation
- the co-morbidities and other patient factors

Incidence

Incidence rates vary greatly due to the absence of a centralised register but have been estimated at 0.5-6% of patients receiving chemotherapy, and whilst this figure is relatively low, large numbers of patients are at risk since vesicants are commonly administered chemotherapy agents (EONS, 2008).

This guideline has been developed in accordance with the latest scientific understanding and best evidence to date in combination with health professional consensus to ensure that the patient receives optimal treatment. However, this is a complex subject where there is limited evidence due to lack of research and a low incidence of reporting which is difficult to ascertain whether this is a true reflection of the incidence of extravasation and subsequently obtaining consensus can be challenging. This guideline has been developed by reviewing other health care providers' guidelines, national and international guidance, published papers and reviewing individual drug monographs and obtaining specific advice from manufacturers if available.

Classification of cytotoxic agents

Note: The principles of extravasation described in this document can be applied across all clinical settings.

The classification of cytotoxic agents is based on the potential to cause tissue damage if extravasated:

Vesicants: Drugs which are capable of causing pain, inflammation and blistering of the local skin and underlying structures; if left untreated may lead to tissue death and necrosis. These drugs can be sub-classified according to mechanism of action by which they cause damage, but which is also important in that it affects the management strategy.

- **DNA – binding**: these drugs are absorbed locally, enter cells and bind to their DNA, precipitating the death of the cell. Following this, the drug can then be re-released to further destroy healthy cells leading to deeper erosion of cells within the tissue
- **Non-DNA-binding**: These drugs initiate cell death by mechanisms other than binding DNA and are eventually metabolized in the tissue and are more easily neutralized than the DNA-binding vesicants. Injuries resulting from these agents generally remain localized and improve over time.

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 (Ener, Meglathery, Styler 2004).

Non-Vesicants: Inert or neutral compounds that do not cause inflammation or damage. Do not cause ulceration, however they do tend to cause pain at, and around the injection site, and along the vein.

(European Oncology Nursing Society (EONS) 2008)

However, any chemotherapy drug has the potential to cause significant symptoms or harm if the volume or concentration of the drug that extravasates is high.
EONS (2008).

Table 1: Classification of drugs commonly used in chemotherapy Regimes

Vesicants	**Irritants**	**Non-Vesicants**
DNA-Binding:		
	Bendamustine Carboplatin Cisplatin Etoposide Fluorouracil Ifosfamide Irinotecan Liposomal Daunorubicin Liposomal Doxorubicin Melphalan Methotrexate Mitoxantrone	Arsenic trioxide Asparaginase Bleomycin Bortezomib Cladrabine Cyclophosphamide Cytarabine Eribulin Fludarabine Gemcitabine Monoclonal antibodies Paclitaxel Albumin

Amsacrine Carmustine Dacarbazine Dactinomycin Daunorubicin Doxorubicin Epirubicin Idarubicin Mechlorethamine (Nitrogen Mustard/ Mustine) Mitomycin Streptozocin Treosulphan	Oxaliplatin Temsirolimus Teniposide Topotecan Trastuzumab Emtansine (Kadcyla) Aflibercept	Pemetrexed Pentostatin Raltitrexed Thiotepa
Non-DNA-Binding:		
Cabazitaxel Docetaxel Paclitaxel Trabectedin Vinblastine Vincristine Vindesine Vinflunine Vinorelbine		

THIS IS NOT AN EXHAUSTIVE LIST: IF AN EXTRAVASATION OCCURS WITH A DRUG NOT LISTED ABOVE PLEASE CONTACT LEAD CHEMOTHERAPY NURSE OR PHARMACIST / ASEPTIC SUITE FOR ADVICE

Identification of Risk Factors

Patient factors

- Small and fragile veins
- Age: very young and elderly patients tend to have small mobile veins with friable skin.
- Cancer patients may have additional risk due to:-
  - multiple cannulations for chemotherapy veins maybe hard or sclerosed.
  - Lymphoedema
  - Previous treatment e.g. mastectomy.
  - Patients with long term side effects from treatment e.g. peripheral neuropathy
  - Previous extravasation injury site
  - Multiple investigations e.g. blood tests
  - Obstructed vena cava (elevated venous pressure can cause leakage).
- Unconscious, sedated, confused patients or patients with communication problems who may be unable to report stinging or discomfort around the cannula site or decreased sensation.
- Patients suffering from co-morbidities which may lead to decreased sensation or poor circulation e.g. diabetes, peripheral vascular disease, cerebral vascular accidents, Raynaud's disease

- Obesity.
- Concurrent medication i.e. analgesics, anticoagulants, anti-fibrinolytics, vasodilators, hormone therapy, steroids, diuretics, anti-histamines, intravenous antibiotics may, depending on the drug increase blood flow, predispose patients to bleeding, suppress the inflammatory response, reduce pain sensation etc (Boulanger et al, 2015).

Cannulation and Infusion Procedure Factors

- Administration of chemotherapy by untrained or inexperienced staff increases the risk of extravasation
- Inferior choice of site for cannulation eg Anti-cubital fossa may increase the risk of a large volume extravasation or may impact on the severity of the injury
- Difficult or multiple attempts at cannulation increase the risk of a subsequent extravasation.
- Steel cannulae must not be used for the administration of chemotherapy
- The size of cannula
- The utilisation of a pre-existing cannula
- The classification of chemotherapy drug
- High flow pressure
- Bolus injections

Equipment Factors

- Inadequate dressings or poor cannula fixation
- Poorly implanted Central Venous Access Devices (CVAD)

Treatment (Drug) Factors

- Ability to bind directly to DNA
- Ability to kill replicating cells
- Ability to cause tissue or vascular dilatation
- pH
- Osmolality
- Characteristics of diluent

(Perez Fidalgo et al, 2012)

Prevention of Extravasation

The following key areas have been identified in minimising the risk of extravasation

Training

Only staff who have completed appropriate training should administer chemotherapy unsupervised. Staff should attend regular chemotherapy updates (either internally or externally facilitated) ideally annually and as a minimum every two years. Competency to administer chemotherapy must be checked annually and should include the demonstration of knowledge regarding

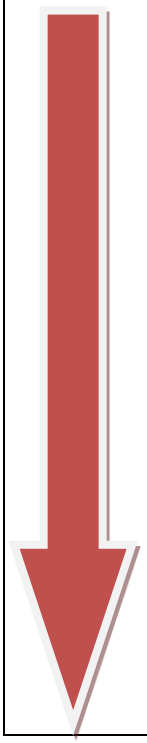
- Assessment of venous access
- Venous access devices
- Administration of chemotherapy
- Prevention, recognition and management of extravasation

- Management of chemotherapy related complications
- A list of authorised staff will be kept and maintained within each Trust.

Selection of site for cannulation

- The choice of site is paramount when attempting cannulation for chemotherapy. Cannulating over joints, the antecubital fossa or dorsum of the hand should be avoided as tissue damage due to extravasation may have serious consequences as there is little soft tissue for the protection of underlying nerves and tissues. (Allwood &Stanley 2002; Hayden &Goodman, 2005; Weinstein, 2007; Dougherty and Lamb, 2008; RCN 2010).
- Large veins in the forearm are recommended for peripheral administration
- Avoid cannulation where lymphoedema is present, cannulation on the side of a mastectomy is still a matter of discussion (Perez-Fidalgo et al, 2012).
- When choosing a vein to site the cannula a large straight, firm, palpable vein is the ideal choice
- If cannulation attempt fails then further cannulation attempts must be above the previous site to prevent vesicant seepage below the site of recent venepuncture (Sauerland et al, 2006).

Table 2: Vein selection

Assess veins in both arms and hands, do not use veins in compromised limbs or lower extremities		
Criteria for vein selection		**Appropriate choice of venepuncture site**
Most Desirable 	**Ideal vein / best location** large, soft, resilient veins in forearm	Forearm
	Ideal vein / less desirable location large, soft, resilient veins in hand/antecubital fossa	Hand
	Satisfactory vein / best location small, thin veins in forearm	Forearm
	Satisfactory vein / undesirable location small, thin veins in hand; veins in forearm not palpable or visible	Hand
	Unsatisfactory vein / undesirable location small, fragile veins, which easily rupture in forearm/hand	Consider central venous line

Least desirable	**Unsatisfactory vein / undesirable location** veins in forearm/hand not palpable or visible	Consider central venous line

EONS (2008)

Choice of equipment

- A new cannula ideally should be placed prior to the administration of chemotherapy. There is an increased risk of extravasation if a previously placed cannula is utilised.
- It is recommended that the smallest gauge cannula is placed in the biggest vein possible
- Steel winged infusion devices are associated with a higher incidence of extravasation therefore in no circumstances should a metal butterfly needle be utilised to for the administration of chemotherapy
- The vascular access device should be secured utilising a clear dressing that enables visibility whilst maintaining adequate fixation.
- Infusion lines must be secured effectively, however never cover the line with a bandage as the insertion point must be visible at all times.
- For infusion of vesicant drugs of longer duration (e.g. 12-24h) central venous access is highly recommended.

Patient Education

- Communication with the patient plays a vital role in the recognition of extravasation.
- Patients should be informed of the importance of reporting immediately any change in sensation, stinging or burning during the administration of chemotherapy
- For patients with communication difficulties who rely on carers or interpreters, it is important to establish that they understand the significance of reporting symptoms immediately.

Administration

- Consideration should be given to the use of a central venous access device (CVAD) in certain situations i.e. regimes with prolonged infusion of vesicant agents, if the patient has previously had an extravasation or for certain agents an example being Trabectedin where the summary of product characteristics recommends a CVAD.
- Ideally a new peripheral cannula should be sited immediately prior to chemotherapy administration
- Only in exceptional circumstances should a practitioner who is going to administer vesicants or irritants utilise a cannula placed by another practitioner.

- If the practitioner has any doubts in relation to the vascular access device the patient should be re-cannulated proximal to first attempt.
- Ideally a practitioner will only attempt to cannulate a patient twice before handing over to another practitioner.
- Venous access should be assessed and tested immediately prior to and frequently throughout administration of any cytotoxic drugs, checking for backflow, no resistance on syringe plunger on administration and acceptance of free-flowing compatible infusion fluid
- If multiple drugs are prescribed within the chemotherapy protocol, ideally vesicants should be administered first when vein integrity is at its best. However, there are notable exceptions where it is clinically indicated within the protocol that a non-vesicant should be given first.
- If a non-vesicant is administered first for clinical reasons the patency of the cannula should be reassessed prior to administration of vesicants. If there are doubts regarding the integrity of the cannula or the vein the patient should be re-cannulated.
- When administering bolus vesicant agents, they should be administered through the side arm of a fast-flowing compatible fluid drip continually assessing for signs of extravasation.
- Where pumps are utilised for administration of vesicant drugs, these should be specifically designed for this purpose, and an infusion of compatible fluid should be administered simultaneously. The patient should still be continually assessed for any signs of potential extravasation.

- It is known that certain pharmacological and formulation issues such as pH make a difference; volume and temperature are also important, larger volumes will require slower administration and the greater the temperature gradient between the administered drug and physiological 36.8 the greater the degree of ‘venous shock’ and consequential shut down and risk of extravasation.

- Between each intravenous drug administration and on the completion of treatment the cannula should be flushed with compatible fluid.
- A number of regimens may now require patients to receive infusional vesicant agents, Patients receiving vesicant agents in this way should be closely monitored for signs of extravasation as there may be a theoretical increased risk of a larger volume extravasation.
- In particular the Vinca Alkaloids which in response to the NPSA alert RRR004 (NPSA 2008) should only be supplied in the form of minibags for infusion. The Vinca minibag should be infused intravenously over 5 -10 minutes.
- Patients receiving peripheral intravenous infusions of vesicant drugs must not be allowed to leave the clinical area and MUST be observed at all times.
- Night time infusions of potentially vesicant drugs should not be normal practice and should be avoided unless urgent and clinically indicated.

Documentation

Document clearly the rate of administration, location and condition of the site of infusion, infusion pump pressure, verification of patency, and patient's responses, after giving any systemic anticancer therapy drugs.

Recognition of extravasation

The early recognition and diagnosis of extravasation is critical as delays in the recognition and management of a vesicant extravasation increase the likelihood of tissue damage and necrosis (EONS 2008). The awareness and responsiveness to signs and symptoms is the most effective way to recognise and detect extravasation. If an extravasation is suspected, it is important that a correct diagnosis is established seeking a second opinion is always warranted if in any doubt.

Patient reporting

Patients must be informed of the potential risk of extravasation and the importance of reporting any symptoms below irrespective of how insignificant they may be

- Pain
- Change in sensation
- Burning/tingling
- Stinging
- Discomfort
- Swelling
- Redness
- Other acute changes at the site of administration

Patients must be informed that these symptoms may not be an extravasation, however that a definitive diagnosis will need to be established.

Visual Assessment

Visual signs, while by no means exclusive to extravasation, do provide useful confirmation for patient reporting of symptoms in suspected extravasation. The common signs, occurring at or around the site of the cannula – or, in the case of central line around the Central Venous Access Device and the surrounding area –include:

- **Early symptoms**
  Swelling/oedema
  Redness/erythema

- **Later symptoms**
  Inflammation
  Induration
  Blistering

Importantly, many of these symptoms do not occur immediately upon infusion, induration and blistering, in particular, tend to appear later in the extravasation process. Therefore, careful monitoring of the site should continue during the infusion time and for

some time following an infusion. Patients should be informed of the importance of reporting any pain, swelling, inflammation, blistering around the infusion site that occurs when at home. (EONS 2008).

Warning signs related to the Vascular Access Device

In addition to the patient reporting of symptoms and visual assessment, the following may support a diagnosis of extravasation
Signs of extravasation, in relation to the cannula, include:

- Increased resistance when administering IV drugs
- Slow or sluggish infusion
- Change in infusion flow
- Lack or loss of blood return from the cannula
- Leakage from around the cannula site (EONS 2008)

If there is any doubt of the patency of the vein, STOP the infusion immediately and instigate the extravasation procedure.

Immediate action should be taken if a vesicant has extravasated. Prompt treatment is vital to reduce the amount of tissue damage caused.

All wards and departments who use cytotoxic drugs have an extravasation kit within their department and staff should be familiar with its contents (see Appendix 1)

Distinguishing between Extravasation and other conditions

A definitive diagnosis can be difficult to establish and requires expert clinical judgement. However, a definitive diagnosis enables the initiation of appropriate interventions and management strategies at the earliest possibility opportunity.

Distinguishing between extravasation and other local reactions is an important step in diagnosis. Initially, making the distinction can be very difficult and requires sound clinical judgement. Familiarity with the different symptoms increases the likelihood of appropriate treatment. In the case of extravasation, that means that interventions and management will be initiated at an early stage and help to prevent some of the more serious consequences associated with it.

Other conditions that resemble extravasation include:

- Flare reaction
- Vessel irritation
- Venous shock

See table 4 below for more details

Some chemotherapy drugs, even if correctly administered, can cause a local reaction which resembles an extravasation. This should not be confused with a true extravasation. Signs and symptoms of local non-extravasation reactions include erythema around the cannula site and along the accessed vein (‘flare’), urticaria and local itching. Another potential differential diagnosis is chemical phlebitis. This vein inflammation, frequently followed by a thrombosis or sclerosis of the veins, may cause a

burning sensation at the cannula site and cramping along the vein proximal to the cannula site (Perez Fidalgo et al 2012).

Chemotherapy drugs which may cause a local reaction or chemical phlebitis are listed in **table 3.**

Table 3

Local skin reactions	Chemical phlebitis
Asparaginase Cisplatin Daunorubicin Doxorubicin Epirubicin Fludarabine Mechlorethamine Melphalan	Amsacrine Carmustine Cisplatin Dacarbazine Epirubicin 5-Fluorouracil (as continual infusion in combination with cisplatin) Gemcitabine Mechlorethamine Vinorelbine
Perez Fidalgo et al (2012).	

	Presenting Symptoms	**Colouration**	**Timing**	**Swelling**	**Blood return**
Flare Reaction	Itchy blotches or hives; Pain & burning uncommon	Raised red streak, blotches or 'hive-like' erythema along the vessel; Diffuse or irregular pattern	Usually appears suddenly and dissipates within 30-90 minutes	Unlikely	Usually but not always
Vessel Irritation	Aching and tightness	Erythema or dark discolouration along the vessel	Usually appears within minutes after injection. Colouration may only appear later in the process	Unlikely	Usually but not always

Venous Shock	Muscular wall of the blood vessel in spasm		Usually appears straight after the injection		Often absent
Extravasation	Pain and burning are common at injection site; Stinging may occur during infusion	Erythema around area of needle or around the venepuncture site	Some symptoms start to appear straight after the injection; Symptoms endure	Occurs often Does not dissipate for several days	Usually absent or sluggish

EONS (2008)

Table 4: The following table distinguishes between other possible conditions that resemble extravasation.

Management of Extravasation

The management of an extravasation is dependent upon a number of contributing factors:

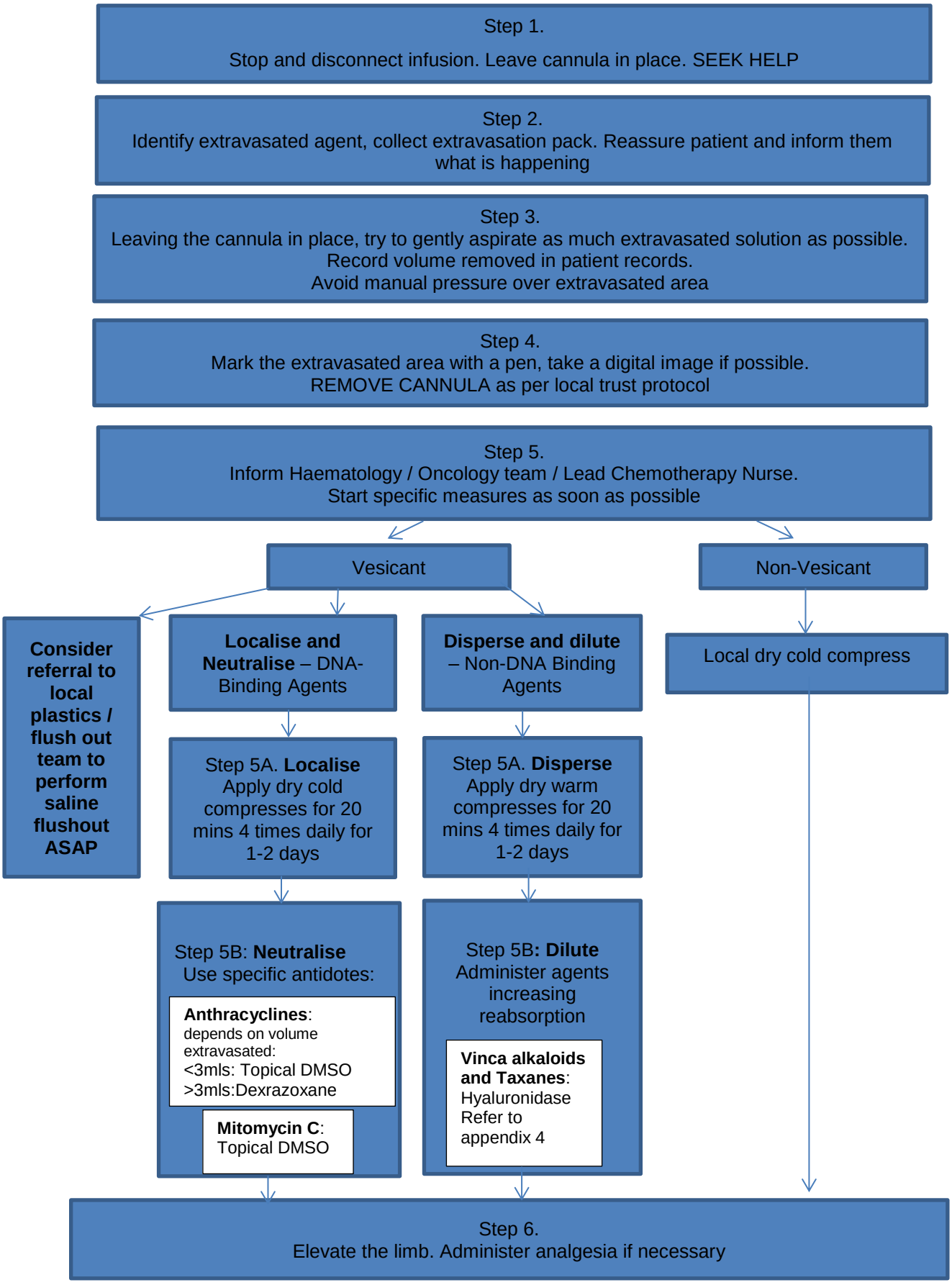
- The drug involved – i.e whether it is DNA-binding or Non-DNA binding
- The volume extravasated
- The site of the extravasation

The early initiation of treatment reduces the potential for tissue damage and necrosis and therefore is a critical part in the management of extravasation. However, in some cases an extravasation injury may not become apparent until a number of days or weeks later.

Extravasation is an oncology emergency and treatment should be initiated as soon as extravasation is suspected.

If an extravasation is suspected the most senior / appropriately trained nurse / Lead Chemotherapy Nurse should co-ordinate the management of the extravasation. A doctor should be informed of the incident immediately; in the case of vesicants or an extravasation via a CVAD a consultant should be informed. Where relevant, local plastics or flush out team should also be consulted

Management of Extravasation via peripheral cannula



Rationale

The ‘Disperse and dilute’ pathway utilises warm compresses to promote vasodilation and encourage blood flow in the tissues therefore spreading the extravasated agent.

Hyaluronidase may be utilised with the aim of promoting drug diffusion and enhancing drug absorption.

The ‘localise and neutralise’ pathway utilises cold compresses to limit the spread of the extravasated agent. It is proposed that the cellular uptake of the agent into the tissues is reduced when cold compresses are utilised. The cold compresses also may reduce local discomfort.

There are a number of antidotes available for certain cytotoxic agents and these are drug/group specific, these should be considered to reduce the potential for severe tissue damage or injury.

Specific measures (antidotes)

Clinicians should consider the utilisation of antidotes where available. These antidotes when utilised appropriately may help to prevent progression to ulceration and severe tissue damage. This decision will be based on a holistic assessment of the individual patient, their treatment protocol, the suspected extravasated drug, their co-morbidities and concurrent medications. The evidence to support the utilisation of antidotes is often inconclusive and any decision to utilise these antidotes should be carefully considered.

Various suggestions of specific antidotes have been published with possible topical or injected pharmacologic methods for some vesicant drugs, however many of these are considered ineffective or may further damage the extravasated area (Perez-Fidalgo et al, 2012).

The table below summarises some of the drugs most frequently used with their suggested specific antidotes:

Extravasated Drug	Suggested antidote	Level of evidence	Advice
Anthracyclines	Savene (Dexrazoxane) The only licensed antidote. Savene neutralises anthracyclines	Efficacy in biopsy confirmed anthracycline extravasation has been confirmed in clinical trials	3-day course of treatment Day 1 (within 6 hours of extravasation) 1000mg/m^2. Day 2 1000mg/m^2. Day 3 500mg/m^2.
Anthracyclines	Topical DMSO (99%) It is proposed this prevents ulceration by its property of scavenging free radicals.	Suggested as a possible antidote in many literature sources.	Apply locally as soon as possible. Repeat every 6 hours for 7 days stop if blistering occurs

Extravasated Drug	Suggested antidote	Level of evidence	Advice
Mitomycin C	Topical DMSO (99%) It is proposed this prevents ulceration by its property of scavenging free radicals	Suggested as a possible antidote in many literature sources.	Apply locally as soon as possible. Repeat every 6 hours for 7 days stop if blistering occurs
Vinca alkaloids	Hyaluronidase Breaks down hyaluronic acid ("cement") in connective/soft tissue, allowing for dispersion of the extravasated drug, thereby reducing the local concentration of the damaging agent and increasing its rate of absorption	Suggested as a possible antidote in many literature sources	150–1500 IU subcutaneously around the area of extravasation
Taxanes	Hyaluronidase Breaks down hyaluronic acid ("cement") in connective/soft tissue, allowing for dispersion of the extravasated drug, thereby reducing the local concentration of the damaging agent and increasing its rate of absorption	Suggested as a possible antidote in many literature sources.	150–1500 IU subcutaneously around the area of extravasation

Specific advice for Carboplatin, Cisplatin and Oxaliplatin:
If treatment is administered within 24 hours then a warm pack and Hyaluronidase would be the treatment of choice, however for cisplatin and carboplatin, if the injury is not treated within 24 hours a cold pack and hydrocortisone cream would then be the appropriate management (not in the case of Oxaliplatin where the cold may risk development of other symptoms)

If DMSO 99% is not available, the 50% solution can be used as an alternative

Appendix 2, 3, 4 detail the specific individual drug management instructions for Savene, DMSO and Hyaluronidase.

Follow Up

- All patients must have a review of their extravasation injury within 1 week, this appointment must be arranged prior to the patient leaving clinic

- Advise the patient of the importance of contacting the 24-hour helpline if there is any deterioration in the affected limb.

Surgical management

- Treatment of unresolved tissue necrosis or pain lasting more than 10 days is surgical debridement; this is generally for those patients who have suffered a severe extravasation in whom conservative therapy has not been appropriately initiated. Once this has been performed, skin grafting is usually applied.

Documentation

- Ensure all extravasations are reported in the local incident reporting system to enable monitoring and review of incidents.
- Ensure that the extravasation injury is recorded in line with the NMC standards for record keeping. The suggested documentary requirements for an extravasation injury are detailed in Appendix 5.

References

Allwood M, Stanley A, Wright P (Eds) (2002) The Cytotoxic Handbook, 4th Edition, Radcliffe Medical Press Ltd.

J. Boulanger, A. Ducharme, A. Dufour, S. Fortier and K. Almanric (2015) Management of the extravasation of anti-neoplastic agents, Supportive Care in Cancer(Vol. 23, Issue 5.)

Dougherty, L & Lamb J (2008) Intravenous Therapy in Nursing Practice, 2nd edition, Blackwell Oxford

Dougherty L & Lister, S (2008) The RMH Manual of clinical Nursing Procedures, Wiley Blackwell, Oxford 7th edition

Dougherty L & Oakley, C (2011) Advanced Practice in the Management of Extravasation, Cancer Nursing Practice 10 (5)

Ener, R.A; Meglathery, S.B; Styler, M (2004) Extravasation of systemic haemato-oncological therapies, Annals of Oncology 15 (6)

European Oncology Nursing Society (2008) Extravasation Guidelines. European Oncology Nursing Society

Hayden, MK & Goodman, M (2005) Chemotherapy: Principles of Administration Cancer Nursing – Principles and practice, Edited by Henke Yarbro, C et al

Hughes CB. Giving cancer drugs IV: some guidelines. American Journal of Nursing 1986;**86**(1):34–38.

Jones L, Coe P. Extravasation. European Journal of Oncology Nursing 2004; **8:355**–358

National Patient Safety Agency. Rapid Response Report NPSA/2008/RRR04 Using Vinca Alkaloid Minibags (adult /adolescent Units) 2008 available at www.npsa.nhs.uk.

NMC (2014) The code, NMC London

NMC (2010) Record Keeping: Guidance for nurse and midwives, NMC London

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

Polovich M, Whitford J,Olson M .Chemotherapy and Biotherapy Guidelines and Recommendations for practice, 3rd edition .Oncology Nursing Society, 2009.

RCN (2010) Standards for Infusion Therapy, London

Sauerland C, Engelking C, Wickham R, Corbi D (2006) Vesicant extravasation part 1: Mechanisms of pathogenesis, and nursing care to reduce risk. Oncology Nursing Forum, 33, 1134-1141

Schrijvers DL. Extravasation: a dreaded complication of chemotherapy. *Annals of Oncology 2003*; **14**(Suppl3):iii26-iii30.

Spepharm: Healthcare professionals' clinical guide: Management of Anthracycline Extravasation with Savene® (dexrazoxane)

Summary of product characteristics: Savene accessed November 2010.

Weinstein, S (2007) Antineoplastic therapy, Plumers principles and Practices of Intravenous Therapy, 8th edition, Lippincott. Philadelphia

Acknowledgements
Local and Alliance guidelines were reviewed in the development of this document.

Appendix 1: An Example of an Extravasation Kit

- Copy of extravasation guideline (also available on the intranet)
- 10ml syringes
- Green needles, orange needles
- Water for injection
- Alcohol wipes
- Sterile gauze and cotton wool
- Cold and hot packs (available within chemotherapy units)
- Hyaluronidase 1500 units x 2 (administration instructions appendix 4 in extravasation guideline)
- DMSO (administration instructions appendix 3 in extravasation guideline)
- Hydrocortisone 1% cream-labelled with instructions for use to reduce local trauma and irritation
- Non-occlusive dressing
- Savene Kit available in aseptic suite (administration instructions appendix 2 in extravasation
- Indelible Pen

Appendix 2: Administering Savene (Dexrazoxane)

THE DECISION TO UTILISE EITHER SAVENE OR DMSO FOR AN ANTHRACYCLINE EXTRAVASATION MUST BE UNDERTAKEN BY A SENIOR CLINICIAN BASED ON AN ASSESSMENT OF THE INDIVIDUAL'S COMORBIDITIES AND CONCURRENT MEDICATIONS

Indication

Savene is indicated for the treatment of extravasation by one of the following anthracycline agents: **Doxorubicin, Epirubicin, Idarubicin and Daunorubicin.**

DMSO must not be used concurrently

Steps for administration.

1. Follow localise and neutralise pathway for extravasation (pg 17).
2. The indicated dose should be administered as an intravenous infusion over 1-2 hours into a large vein in an extremity / area other than the one affected by the extravasation. The first infusion should be initiated as soon as possible and within the first six hours after the incident.
3. Cooling procedures such as ice packs should have been removed from the area at least 15 minutes prior to Savene administration in order to allow sufficient blood flow. **DMSO should not be used concurrently**.
4. Savene will be reconstituted during normal working hours within the aseptic suite (where the Savene kit will be stored) or by nurses where applicable according to local trust policies
5. Savene should be given once daily for three consecutive days. The patient will need to be re-cannulated for each infusion as Savene is classified as a cytotoxic agent
6. The recommended dose according is:
   a) Day 1: 1000mg/m^2
   b) Day 2: 1000mg/m^2
   c) Day 3: 500mg/m^2
7. For patients with a body surface area of more than 2 m^2 the single dose should not exceed 2000 mg
8. Treatment on Day 2 and Day 3 should start at the same hour (+/- 3 hours) as on the first day.
9. The Savene kit contains 10 vials of Savene powder each containing 500mg Dexrazoxane and 3 bags of Savene diluent
10. The kit must be stored at less than 25°C
11. After reconstitution Savene should be stored for no longer than 4 hours at 2-8°C.

.

For full prescribing information, contraindications, precautions and warnings please refer to summary of product characteristics and Clinigen health professionals' guide

Appendix 3: Administering Dimethyl Sulfoxide (DMSO)

THE DECISION TO UTILISE EITHER SAVENE OR DMSO FOR AN ANTHRACYCLINE EXTRAVASATION MUST BE UNDERTAKEN BY A SENIOR CLINICIAN BASED ON AN ASSESSMENT OF THE INDIVIDUAL'S CO-MORBIDITIES AND CONCURRENT MEDICATIONS.

Dimethyl Sulfoxide (DMSO) is an unlicensed option for the treatment of extravasation with anthracyclines including Doxorubicin, Idarubicin, Epirubicin, Daunorubicin; it can also be used to treat extravasation with Mitomycin C, Mitoxantrone, Dactinomycin, Liposomal Daunorubicin and Liposomal Doxorubicin.

As this is an unlicensed indication patient details must be recorded when DMSO is utilised

Steps for administration:

1. Follow steps for localisation and neutralisation of extravasation (page 17)
2. Draw around the area with indelible pen.
3. Put gloves on
4. Carefully apply a thin layer of DMSO topically to the marked area avoiding contact with unaffected areas
5. Allow it to dry,
6. This should be applied ideally within 10 – 25 minutes,
7. Check for erythema caused by DMSO.
8. Repeat administration of DMSO every 6 hours for 7 days
9. Advise patient to stop using DMSO and contact chemotherapy unit if blistering occurs

Note:
Please refer to DMSO prescribing information for a full list of contraindications, precautions and warnings.

(EONS 2008)

Appendix 4

Administering Hyaluronidase

Hyaluronidase has been suggested as a possible antidote for some extravasations in many literature sources. It works by breaking down hyaluronic acid (“cement”) in connective/soft tissue, allowing for dispersion of the extravasated drug, thereby reducing the local concentration of the damaging agent and increasing its rate of absorption. (Schrijvers 2003)

Steps for administration:

1. Follow steps for dispersion and dilution of extravasation (page 17)

2. Administration of hyaluronidase should begin within 1 hour of extravasation for best results.

3. Dilute 150 – 1500 IU of hyaluronidase in 1 ml of sterile water,

4. Subcutaneously (or intradermally) inject 1 ml (150 IU) of hyaluronidase as 5 separate 0.2 ml injections around the periphery of extravasation site.

5. To ensure adequate coverage, the 4 compass points can be utilised first, followed by a further injection into the middle of the site

Note:
Please refer to hyaluronidase prescribing information for a full list of contraindications, precautions and warnings.

(EONS 2008)

Appendix 5: Documentation Requirements

Each incident of extravasation must be thoroughly documented and reported. (Dougherty & Lister 2008)

Documentation serves several purposes:

- To provide an accurate account of what happened (in the event that there is litigation)
- To protect the healthcare professionals involved (showing they followed procedure)
- To gather information on extravasations, how and when they occurs – for audit purposes
- Highlight any possible deficits in practice which require review.

Following an extravasation, the following details should be documented: (Dougherty & Lister 2008, Polovich et al 2006)

- Patient name and number
- Clinical area
- Date and time of extravasation
- Name of drug which has extravasated
- Signs and symptoms
    - Colour of surrounding skin
    - Size of extravasation
- Description of the IV access
    - Venepuncture site
    - Size and position of cannula
    - Number of attempts at obtaining venous access and positions
    - Drugs administered and the sequence
    - Drug administration technique (bolus or infusion)
    - Blood return
- Extravasation area
    - Approximate amount of the drug extravasated
    - Photograph of extravasated area
    - Size (diameter, length and width) of extravasation area
    - Appearance of extravasation area
- Step-by step management with date and time of each step performed and medical notification
    - Aspiration possible (including amount) or not, location (venous and/or subcutaneous) and amount
    - Cold/heat
    - Antidote
    - Referral details (if any)
- Patient's complaints, comments, statements
- Indication that patient's information sheet given to patient
- Follow-up instructions given (to patient, nurse, physician, etc.)
- Names of all professionals involved in the patient management
- Signature of nurse

All follow up care should be documented in the notes and all visual assessments should be recorded.

Appendix 6: Patient Information

What is extravasation?

Extravasation is a term used when a small amount of a drug has accidently leaked from the vein into the surrounding tissues. You may have noticed pain; stinging, swelling or other changes to the skin at the site of drug administration, or the nurse may have noticed that the drug was not flowing in easily.
The extent of the injury depends on the chemotherapy involved and can vary from a mild reaction with irritation and inflammation to in some cases the drug which has leaked causing local pain, stiffness and tissue damage.

Why did this happen?

Extravasation is a rare but known complication of intravenous chemotherapy. Despite all possible measures to prevent this happening sometimes it is impossible. The important thing is that it has been detected and treated.

What treatment have I received to prevent tissue damage?

The nurse has treated the extravasation with the recommended treatment for the particular drug involved. Although this treatment may help to minimise the chance of further problems occurring we ask that you monitor the area daily

Checking the area

Once a day, check the area for the following:

- Has the area changed colour or increased in redness?
- Is the area blistering, peeling or flaking?
- Is the area more uncomfortable?
- Is the pain making it difficult for you to exercise the arm or hand?

What else do I need to do?

Follow the specific instructions written in the box below by the nurse

- Gently exercise the affected arm or hand.
- Take mild painkillers if required.
- Do not apply any other lotions, creams or ointments unless you have been instructed to do so by a doctor or nurse.
- Do not expose the area to strong sunlight.
- Avoid wearing tight clothing around the affected area.
- Protect the affected area when bathing (or having a shower) so that it does not get wet.

When should I contact you?

If you answered **YES** to any of the questions in the checklist above, or if you have any other concerns, then you must contact someone at this hospital who is experienced in extravasation.

Contact Telephone Number ……