



Title	Management of Systemic Anti-Cancer Therapy (SACT) Extravasation
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NICaN Policy: Management of Systemic Anti-Cancer Therapy (SACT) Extravasation

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SECTION 1: General Information

1.1 Purpose

To help practitioners who are involved in the administration of intravenous (IV) Systemic Anti-Cancer Therapy (SACT) to recognise extravasation and successfully manage it to minimise the risk of injury.

1.2 Summary

Extravasation is defined as the unintended administration of a pharmaceutical into the tissue spaces surrounding a vein during intravenous injection. The consequences are often pain, erythema, inflammation and discomfort. Damage can continue for months and involve nerves, tendons and joints. If left undiagnosed, or if treatment is delayed, surgical debridement, skin grafting, and even amputation may result.

For the purposes of this policy 'SACT' means all intravenous anti-cancer treatments including cytotoxic drugs, monoclonal antibodies and biological agents.

1.3 Differential Diagnosis

Incidents commonly misdiagnosed as extravasation include:

1. Discoloration reactions in the vein (some SACT agents are highly coloured).
2. Venous contraction or spasm due to thermal shock.
3. Phlebitis (inflammation of the vein) due to an irritant component (e.g. etoposide) or because the pH of the formulation is particularly acidic or alkaline (e.g. doxorubicin or epirubicin).
4. Local and / or central hypersensitivity (e.g. taxanes).
5. Anaphylaxis.

1.4 Prevention of Extravasation

The patient is usually the first to be aware of problems with administration due to discomfort. Patient education and co-operation is therefore imperative to ensure early recognition and prompt reporting.

The following groups of patients are at increased risk of extravasation and extra care should be taken:

- Elderly, confused patients, patients with decreased sensitivity, agitated patients
- Vascular and circulatory impairment - patients with fragile veins, sclerosed/thrombosed veins, peripheral vascular disease, on steroid therapy, Raynaud's phenomenon, diabetes, lymphoedematous limbs, obstructed SVC
- Patients with thrombocytopenia or on anticoagulants or antiplatelet drugs
- Other concurrent medications (vasodilators, diuretics, analgesics) may increase the risk by a variety of mechanisms such as increasing blood flow or reducing pain sensation.
- Patients with obesity

- Paediatric patients, those with language barriers, or those on sedation who might not report symptoms early
- Patients who have undergone repeated cannulation/venepuncture attempts
- Patients who mobilise during infusions

The following actions should be considered to prevent an extravasation.

- Patients receiving SACT should be assessed for suitability for a central venous access device (CVAD). This should be done prior to commencement of treatment and assessed at each subsequent treatment.
- If vesicant drugs are administered by a non-ambulatory infusion pump, then the pump must be programmed to alarm for occlusion at a low pressure
- An appropriate venous access device should be selected by a SACT competent practitioner and a suitable placement site selected. Never administer vesicants via the antecubital fossa unless absolutely necessary. If so, this should be authorised and documented by the patients' Consultant.
- Adhere to Guidelines for safe prescribing, handling and administration of SACT (section 12).

1.5 Symptoms of Extravasation

- Burning, stinging, modest or severe pain, or any acute change at the injection site.
- There is a lack of blood return from the cannula. This alone is not sufficient for a definitive diagnosis of extravasation, as lack of blood return can occur without extravasation. Likewise, blood return may be possible even with an extravasation.
- The flow rate is reduced and possible changes in the position of the body (e.g. bending of the wrist or elbow) or cannula supports (e.g. the bandaging) have been excluded.
- Local blistering, mottling and darkening of the skin, induration (abnormal hardening of the tissue), erythema, venous discoloration or swelling.
- If left untreated the surface of the skin may appear very white and cold with no capillary filling. A dry, black eschar may develop.
- Ulceration may occur as a complication of extravasation. (Ulceration is not usually evident until one or two weeks after the injury when the eschar sloughs to reveal the underlying cavity).

Whilst extravasation is possible with IV injection of any SACT agent it is only considered problematic with those compounds which are vesicant, exfoliant or irritant.

It is the responsibility of the person administering SACT to ensure that they are aware of the classification of the drug(s) before they are administered.

Should an extravasation occur with CVAD please refer to Section 2.3

1.6 Classification of SACT

Table 1 Classification of SACT agents according to their potential to cause injury when extravasated

Vesicants	Exfoliants	Irritants	Inflammatory Agents	Neutrals	
Amsacrine ♣	Cisplatin ♣	Arsenic Trioxide ♣	Bortezomib ♣	Aflibercept ♣	Ifosfamide ☼
Bendamustine ♣	Daunorubicin (liposomal) ♣	Azacitidine ♣	Etoposide Phosphate ♣	Alemtuzumab ☼	Interferon ☼
Carmustine ♣	Docetaxel ☼	Busulfan ♣	Fluorouracil ♣	Asparaginase ♣	Ipilimumab ☼
Dacarbazine ♣	Doxorubicin (liposomal) ♣	Cabazitaxel ♣	Methotrexate ♣	Bevacizumab ☼	Melphalan ☼
Dactinomycin ♣	Oxaliplatin ☼	Carboplatin ♣	Raltitrexed ♣	Brentuximab ☼	Mifamurtide ♣
Daunorubicin ♣		Etoposide ♣		Bleomycin ☼	Nelarabine ☼
Doxorubicin ♣		Ganciclovir ♣		Blinatumomab ☼	Nivolumab ☼
Epirubicin ♣		Gemtuzumab ♣		Carfilzomib ♣	Obinutuzumab ☼
Idarubicin ♣		Irinotecan ♣		Cetuximab ☼	Ofatumumab ☼
Mitomycin C ♣		Topotecan ♣		Cidofovir ♣	Panitumumab ☼
Mitoxantrone ♣		Trastuzumab emtansine ♣		Cladribine ☼	Pembrolizumab ☼
Nab-Paclitaxel ☼				Clofarabine ☼	Pemetrexed ☼
Paclitaxel ☼				Crisantaspase ☼	Pentostatin ☼
Streptozocin ♣				Cyclophosphamide ☼	Pertuzumab ☼
Trabectedin ♣				Cytarabine ☼	Pixantrone ♣
Treosulfan ♣				Daratumumab ☼	Ramucirumab ☼
Vinblastine ☼				Decitabine ♣	Rituximab ☼
Vincristine ☼				Eculizumab ☼	Temsirolimus ♣
Vindesine ☼				Eribulin ☼	Thiotepa ☼
Vinflunine ☼				Fludarabine ☼	Trastuzumab ☼
Vinorelbine ☼				Gemcitabine ☼	
☼ = heat (warm compression)		♣ = cold (cold compression)		NB. this list is not exhaustive	

HIGH RISK ← → **LOW RISK**

Table 1 is not an exhaustive list of SACT agents. Check [Extant list](#) for latest version. There are other drugs in use which have not yet been classified and for which the risk of extravasation injury is not known. Furthermore, many investigational medical products used in clinical trials are not classified in Table 1. In some instances, information on the risk of extravasation injury or recommended treatments for extravasation of investigational medical products may be available from the trial sponsor or the clinical trials pharmacist.

1.7 Definitions of Classifications

Vesicants

Capable of causing pain, inflammation and blistering of the local skin, underlying flesh and structures, leading to tissue death and necrosis.

Exfoliants

Capable of causing inflammation and shedding of skin, but less likely to cause tissue death.

Irritants

Capable of causing inflammation and irritation, rarely proceeding to breakdown of the tissue.

Inflammatory Agents

Capable of causing mild to moderate inflammation and flare in local tissue.

Neutral

Ostensibly inert or neutral compounds that do not cause inflammation or damage.

SECTION 2: Management of SACT Extravasation

2.1 Immediate Action following an Extravasation

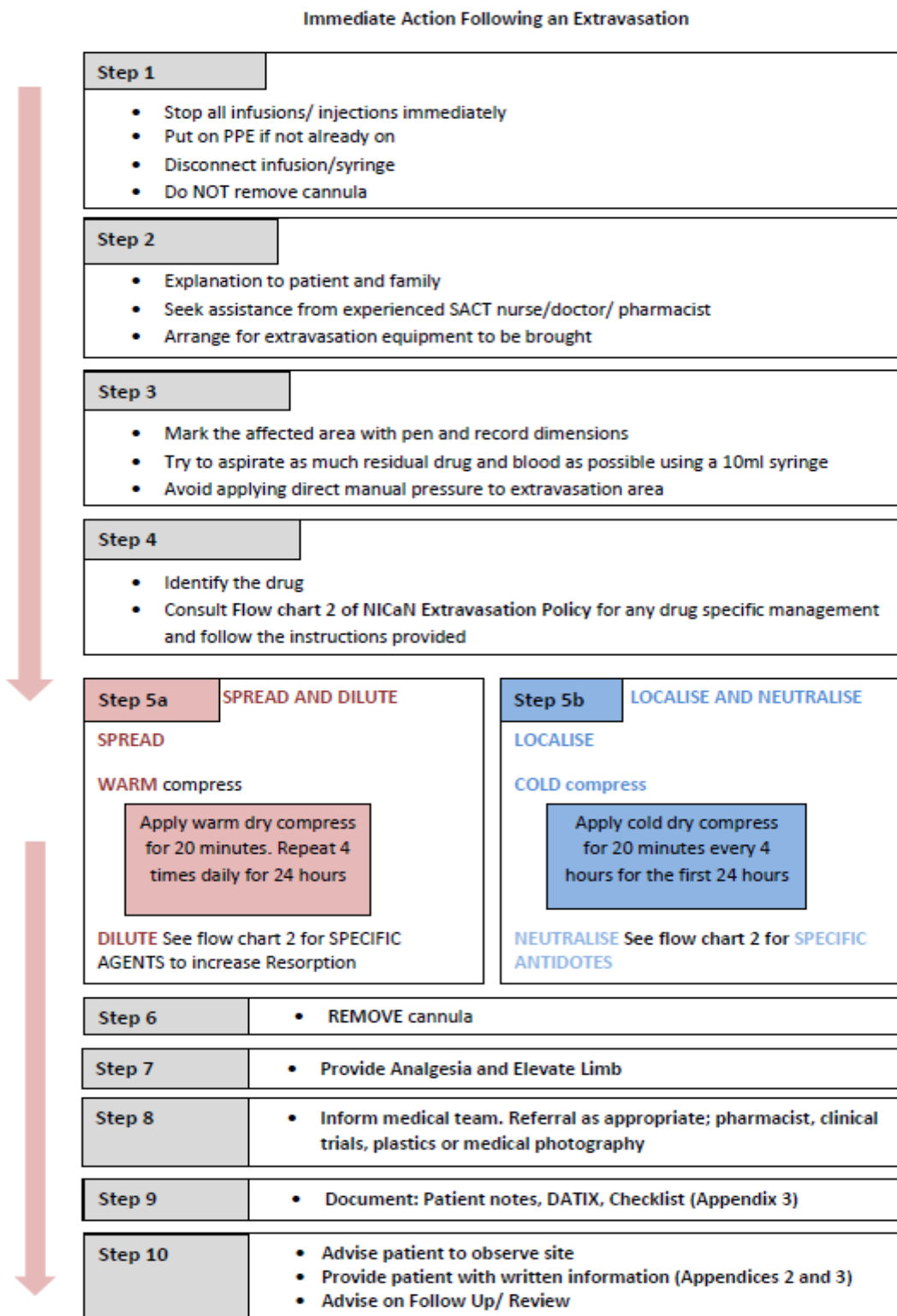


Figure 1 Flow Chart for Immediate Action following an Extravasation

Any extravasation involving vesicant, exfoliant or irritant drugs must be discussed with a member of the medical team and revised after 24 hours and at appropriate intervals until resolution.

2.2 General Procedures for the Management of Mixed Extravasations

In the event of a mixed extravasation of agents from different classifications the following applies:

- The order of precedence of treatment for the different classification is vesicants > exfoliants > irritants > inflammatory agents > neutrals. Vesicant management takes precedence over exfoliants, irritants or inflammatory agents.
- For mixed extravasations from drugs in different classifications, apply the temperature compression of the drug that takes precedence.
- For drugs of the same classification, those requiring cold compression take precedence over applying hot compression – apply cold compression.

2.3 Management of Extravasation from Central Venous Access Devices

While the incidence of extravasation using central catheters is rare, the severity of the injuries that occur may be far greater. This is due to later detection and the potential for greater volumes of a drug with vesicant or exfoliant potential being infused.

Extravasation may occur in the subcutaneous tissue of the chest wall, neck, or in the mediastinum.

The most frequent symptom of central catheter extravasation is acute thoracic pain.

If a patient complains of changes in sensation, pain, burning, or swelling at any point along the pathway of the catheter or in the ipsilateral chest, or if a change in IV flow rate occurs, then extravasation may have occurred.

A diagnosis of extravasation in the tunnelled subcutaneous section is most readily made if 10mL sodium chloride 0.9% is injected rapidly down the catheter. This will usually raise a bleb at the point of damage or leakage from the catheter, thus allowing targeting of further treatment.

An extravasation in the superficial tunnelled section should be managed in the same way as a peripheral extravasation (see section 2.1).

Extravasation in the deep implanted area is rare but much more serious. If suspected, the patient requires admission for analgesia, parenteral antibiotics and assessment. An extravasation in the deep tissues may require to be surgically managed.

2.4 Definitions for Use in Conjunction with Table 1 and Flow Chart 2

Spread & Dilute

This is a treatment strategy that promotes dispersal of any residual drug to lower its concentration in the tissues, thereby minimising any injury. This typically involves administration of hyaluronidase using the pin cushion technique and the use of warm compression.

Localise & Neutralise

This is a treatment strategy that reduces the dispersal of any residual drug and aims to render it less harmful. This typically involves application of dimethylsulphoxide (DMSO), hydrocortisone cream and the use of cold compression.

Application of Compresses

The drug causing the extravasation injury will determine whether or not a warm or cold compress should be applied. Compresses are never applied on infants (neonates). Compresses are usually applied for 20 minutes at a time every four hours during waking hours for 24 hours. Monitor the patient's skin for any increase in redness, swelling, pain or oedema while using a compress.

Warm Compression

This involves applying firmly, but without undue pressure, a heat source (covered hot water bottle, small electrically heated blanket or hot pack) to the area. The heat source should be tested before applying to ensure it is not too hot and must not be placed directly on the skin. A non-adherent dressing should be laid in between (or wrap the heat source in a light towel). This assists the natural dispersal of the drug through vasodilatation and increased blood flow.

Cold Compression

This involves applying firmly, but without undue pressure, a cold source (crushed ice, flexible cold pack or cold bandage) intermittently (for 20 minutes in every four hours) over the area for the first 24 hours, unless advised otherwise. The cold source should not be placed directly on the skin. A non-adherent dressing should be laid in between (or wrap the cold source in a light towel). Cold compresses will help to reduce pain and local inflammation by causing vasoconstriction and reducing further drug spread. **NB.** Not to be used for vinca alkaloids as may cause further tissue damage.

Pin-Cushion Technique For Hyaluronidase

The 'pin-cushion' technique involves instilling small volumes (0.1-0.2mL) of reconstituted hyaluronidase around and over the area affected by the extravasation. This may cause discomfort to the patient, especially if larger area so consider analgesia. This treatment should be commenced within the first hour following extravasation for best results.

This is done by marking and measuring the circumference of the injury, and then starting at '12 o'clock' and injecting on an imaginary clock face (i.e. 2 o'clock, 4 o'clock etc). This technique is then repeated every 2 hours as required. The injections are administered using a blue (23 gauge x 1 inch), or orange (25 gauge x 5/8 inch) needle, and towards the centre of the clock-face. The needle should be changed after each injection. Gently massage the area to facilitate dispersal.

For large extravasation of greater diameter than 2cm, further injections are made down imaginary radial arms, always moving towards a final injection at the centre of the clock-face. The total volume of reconstituted hyaluronidase is thus determined by the size or spread of the injury. However, it is rare for more than 5mL to be required.

NB. Hyaluronidase increases the absorption of local anaesthetic. If local anaesthetic has been applied to the area (e.g Ametop® gel or EMLA® cream) prior to cannulation, within 6 hours of extravasation, then the patient should be monitored for signs and symptoms of systemic anaesthesia such as increased pulse rate and decreased respirations and medical staff informed immediately.

2.5 Drug Specific Management Procedures: Identify Drug below and treat as directed. KEY ☼ = HEAT ☐ = COLD

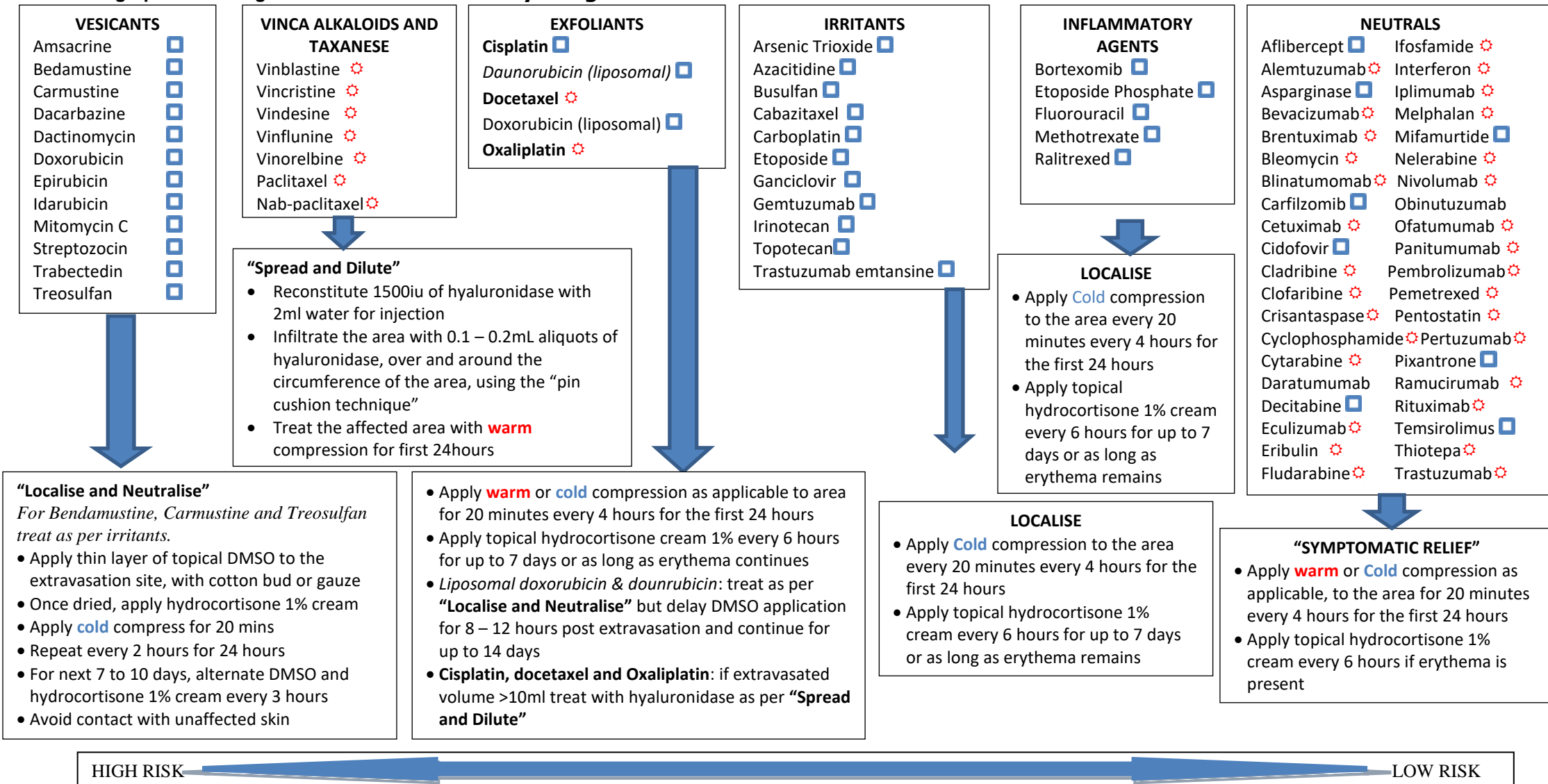


Figure 2: Flow Chart for Drug Specific Management of SACT

Dexrazoxane (Savene®) has recently been licensed as a specific antidote for use with anthracyclines and is recommended by some authorities (Jackson et al 2006; Mouridsen, Lager et al 2007). There is some limited evidence from clinical trial to support its use. It has been considered by the Scottish Medicines consortium and the All Wales Medicines Strategy Group, neither of which supported its use. Its use is not currently supported by Northern Ireland Cancer Network

SECTION 3: IMPLEMENTATION OF POLICY

3.1 Dissemination

This policy has been agreed by the relevant medical teams and the SACT Multi-professional team (MPT) and disseminated at haematology and oncology meetings. It will be available on the BHSCT intranet for use by all medical, pharmacy and nursing staff.

SECTION 4: CONSULTATION PROCESS

Consultation for this policy was through the SACT multi professional group, which includes medical, pharmacy, nursing and senior management representation. In addition, relevant oncology and haematology medical teams were consulted.

SECTION 5: EQUALITY STATEMENT

In line with duties under the equality legislation (Section 75 of the Northern Ireland Act 1998), Targeting Social Need Initiative, Disability discrimination and the Human Rights Act 1998, an initial screening exercise to ascertain if this policy should be subject to a full impact assessment has been carried out.

The outcome of the Equality screening for this policy is:


Major impact

Minor impact

No impact.

SIGNATORIES

(Policy – Guidance should be signed off by the author of the policy and the identified responsible director).



Author

Date: 27 September 2019



Date: 27 September 2019

APPENDICES

Appendix 1: Patient Information on Extravasation

You have been given this information sheet because it is suspected that you may have had an extravasation during administration of your systemic anti- cancer therapy.

What is extravasation?

Extravasation is the accidental leakage of a drug into the tissue surrounding a vein during intravenous administration. You may experience pain, stinging, redness, swelling or other changes to the skin at the site of drug administration.

Extravasation is a rare occurrence and can be difficult to diagnose as the signs are similar to other problems that may occur with the administration of intravenous drugs.

Extravasation can be a serious problem if it is not treated properly. However, when recognised early, most extravasations can be dealt with easily and do not result in any lasting problems.

What treatment is required?

The initial treatment for your suspected extravasation will have been completed in the hospital. In some cases no further treatment is required.

However, occasionally it may be necessary to use additional treatment for a few days afterwards. If you need to use any additional treatment you will be provided with the necessary medicines and given information on how to use them properly.

In addition to using any recommended treatments you should keep the affected limb elevated for the first 48 hours. This may be done by simply using some pillows to support it in a raised position.

It may be necessary for the hospital to check how things are the following day. In many cases this can be done by contacting you by telephone. However, in some cases it may be necessary for you to attend the hospital so that the affected area can be examined. You will be told what arrangements have been made for you.

It is also important to note that the effects of the leakage of some drugs may not appear immediately but may develop over the following seven to 10 days. If this should occur, you should contact the Oncology /Haematology telephone helpline.

Checking the area

Once a day check the area for the following:

- A change in colour or an increase in redness
- Blistering, peeling or flaking
- Increased discomfort
- Increasing pain which limits your ability to exercise the area

What else do I need to do?

- Gently exercise the affected arm
- Take mild painkillers if required
- Do not apply any lotions, creams or ointments unless you have been advised to do so
- Do not expose the area to strong sunlight
- Avoid wearing tight clothing around the affected area

If at any stage, you are concerned that your extravasation is not healing or is getting worse, you should contact the Oncology/Haematology telephone helpline.

Does extravasation affect any future treatment that I need?

Extravasation should not stop you from completing your planned course of treatment. However, if you are returning to have further treatment (including more chemotherapy or radiotherapy), please tell the staff looking after you that you have previously been treated for a suspected extravasation.

Appendix 2: Use of Dimethylsulphoxide (DMSO) and Hydrocortisone 1% Cream for Treatment of a Suspected Extravasation Injury

Extravasation occurs when a drug leaks out of the vein. You are being treated for a suspected extravasation injury. This treatment will help to prevent or lessen any further problems.

You will need to apply a liquid (DMSO) and a cream (hydrocortisone 1%) to the affected area for a further 7 to 10 days. Apply DMSO every six hours, alternating with hydrocortisone cream, so that the treatment is being applied every three hours on an alternating basis for example:-

10am – apply DMSO
3 hours later, at 1pm – apply hydrocortisone cream
3 hours later, at 4pm – apply DMSO
3 hours later, at 7pm – apply hydrocortisone cream

It is not necessary to wake during the night to apply the DMSO liquid or 1% hydrocortisone cream. You will be told if you need to attend the hospital during this time.

How is DMSO liquid applied?

1. After washing your hands, put on a pair of disposable gloves.
2. Moisten a cotton wool ball or cotton bud with DMSO.
3. Apply a thin layer to dry skin by dabbing the skin inside the affected area, avoiding contact with good skin.
4. You may experience some stinging on application.
5. Allow to dry in the air, do not cover.
6. Apply every six hours as directed.
7. Stop applying if blistering occurs and contact the oncology / haematology telephone helpline.
8. You may experience a garlic like taste / breath odour. This is quite normal.
9. If DMSO is splashed into the eyes, wash immediately with cold water. Seek medical advice if you experience pain or discomfort.

How is hydrocortisone 1% cream applied?

1. Wash your hands before and after applying hydrocortisone 1% cream.
2. Apply a thin layer to the affected area. Do not cover.
3. Use up to four times daily for maximum 7 days. Apply 3 hours after applying DMSO.

Store all medicines out of the reach and sight of children

Appendix 3- documentation

Extravasation record

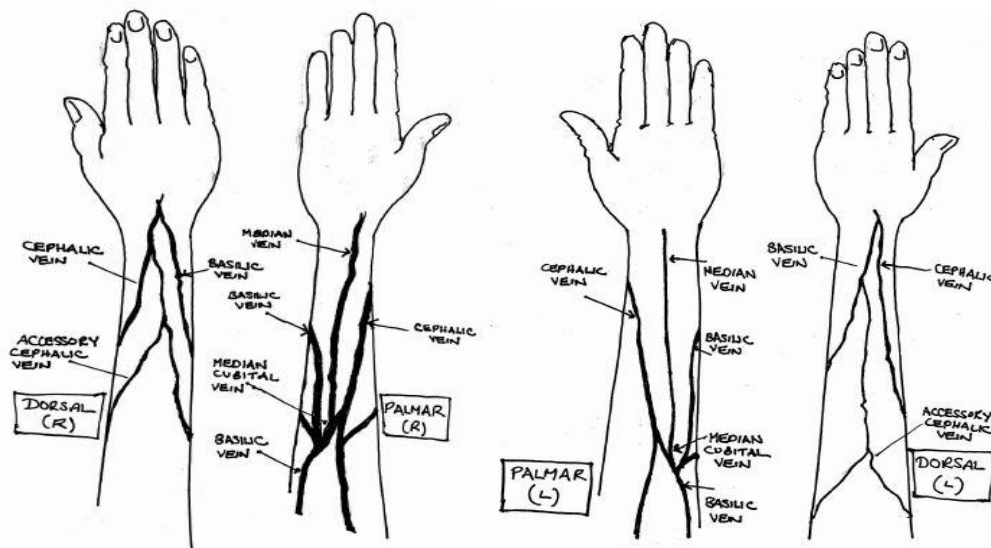
Patient's name:		Hospital No:	
Date of Birth:	Sex: Male / Female	Date:	Time:
Clinical area		Consultant	
SACT Regimen:	Course no:	Cannula type & size:	CVAD type:
Name of drug/s extravasated:		Dose/s:	
Drug/s classification:			
Type of administration Bolus <input type="checkbox"/> Infusion <input type="checkbox"/>			
(1) Was the intravenous chemotherapy administered via a fast running drip?			Yes / No
Fluid type? <input type="checkbox"/> Sodium chloride 0.9% <input type="checkbox"/> Glucose			
(2) Was the SACT administered via a pump? If YES please indicate model used:			Yes / No
Estimated volume of drug extravasated			mLs
Diameter of extravasation (length X width)			
Peripheral Venous Observation (PVO) chart completed			Yes / No

Signs and symptoms experienced by the patient

Signs and symptoms	Burning Yes/No	Stinging Yes/No	Leaking cannula site Yes/No	Swollen cannula site Yes/No
Cannula site status	Indurated Yes/No	Swollen Yes/No	Red Yes/No	Blistered Yes/No
Infusion related indicators	Blood return Yes/No	Resistance on syringe plunger Yes/No	Absence of free flow of infusion Yes/No/NA	
Any other comments				

Extravasation site

Please draw on the diagram(s) below, indicating the position of the cannula, infiltration/extravasation area and measurements of the length and width of the affected areas



Checklist for Immediate nursing management

Nursing actions and management	Action completed	Comments	Time, date and nurses signature
Stop the infusion, disconnect infusion set and cap infusion set	Yes/No/NA		
Mark affected area with a pen	Yes/No		
Aspirate drug from the cannula	Yes/No		
Administer antidote Drug _____ Dose _____	Yes/No		
Apply topical hydrocortisone 1% to the area	Yes/No		
Apply warm pack	Yes/No/NA		
Apply cold pack	Yes/No/NA		
Remove cannula following assessment	Yes/No		
Elevate limb	Yes/No/NA		
Inform appropriate medical staff	Yes/No		
Referral as appropriate to Medical Photography	Yes/No		
Refer patient to plastic surgery team	Yes/No/NA		
Implement any further medical treatment as prescribed	Yes/No/NA		
Complete incident form	Yes/No		
Provide patient with written information	Yes/No		
Replace extravasation kit contents	Yes/No/NA		

Continuing assessment

Insert grade in relevant box

Day post incident									
Skin colour									
Skin integrity									
Skin temperature									
Pain									
Oedema									
Pyrexia									
Mobility of area									

Grading scale

Scale	0	1	2	3	4
Skin colour	Normal	Pink	Red		Blackened
Skin integrity	Normal	Blistered	Skin loss	Tissue loss	Necrosis. Exposure of underlying structures
Skin temperature	Normal	Warm	Hot		
Pain	Normal	Tender	Sore to touch	Pain at rest	Pain requiring analgesia
Oedema	Normal	Minimal; non-pitting	Swollen; pitting		
Pyrexia	Normal	Present			
Mobility of area	Normal	Slightly limited	Very limited	Immobile	

Action taken:

Next review date (if required) _____

Staff Name _____ Designation _____

Clinical area _____ Signature _____

Appendix 4: References

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University Hospitals Bristol Prevention and management of extravasation V2.1 January 2015. (Accessed online at <https://www.bnssgformulary.nhs.uk/8-Malignant-disease-Guidelines/> September 2018)

Appendix 5: Version Control: Record of Changes

The following amendments have been made in Version 4:

Version 3 Section	Description or comment of changes made to produce version 4
Title	Changed to Management of Systemic Anti-Cancer Therapy (SACT) Extravasation
	Throughout document chemotherapy renamed SACT
	Inserted Section 1.4 Prevention of Extravasation
Table 1	Updated & reformatted, hot and cold compress identified
1.4	Now section 1.5 and inserted: Should an extravasation occur with CVAD please refer to Section 2.3
1.5	Now section 1.6 and removed reference superscript
Section 2.1	Reformatted as a flow chart. Named Flow Chart 1 Immediate Action Following an Extravasation
2.1 point 8: Attach a 20mL syringe and attempt to withdraw residual drug. Try to draw some blood back from the cannula.	Amended to: Attach a 10mL syringe and attempt to withdraw residual drug. Try to draw some blood back from the cannula.
Section 2.3	Reworded
Section 2.4	Reworded
Section 2.5	Removed Table 2 and inserted a flow chart. Flow chart 2: Drug specific management of SACT Extravasation. Removed Table 3. Inserted: Dexrazoxane (Savene®) has recently been licensed as a specific antidote for use with anthracyclines and is recommended by some authorities (Jackson et al 2006; Mouridsen, Lager et al 2007). There is some limited evidence from clinical trial to support its use. It has been considered by the Scottish Medicines Consortium and the All Wales Medicines Strategy Group, neither of which supported its use. Its use is not currently supported by Northern Ireland Cancer Network
Appendix 1 How to Report an Extravasation Injury to NEXIS	Removed
Appendix 2: Patient Information on Extravasation	Now Appendix 1. Reworded
Appendix 3: Use of Dimethylsulphoxide and Hydrocortisone 1% Cream for Treatment of a Suspected Extravasation Injury	Now Appendix 2. Reworded
	Inserted Appendix 3 inserted documentation
Appendix 4: Hospital check list for dealing with a suspected extravasation	Removed
Appendix 5	Updated. Now Appendix 4
Appendix 6	Updated. Now Appendix 5