

Prevention, recognition and treatment of Infiltration and Extravasation

Key Points

- **Prevention**
Safe IV therapy administration and vascular access practice is essential to preventing infiltration and extravasation occurring in the first instance. All healthcare professionals involved in the delivery of intravenous therapies and the use of vascular access devices should be aware of the preventative measures associated with infiltration and extravasation, vessel health and preservation and the principles of vascular access.
- **Recognition**
Recognising the early stages of extravasation is vital. Early diagnosis can reduce the amount of damage sustained by the patient's tissue.
- **Treatment**
Early intervention and treatment to reduce or stop tissue damage. Hot or cold compress, injectable antidotes, tissue wash out and referral to Plastic surgeons should be considered as part of the treatment pathway for extravasation.
- **Follow-up**
Ensure the patient is followed up the appropriate department, either IVAS, Plastics or tissue viability and supported by the clinical team. Clinical photography should be used to continuously document the extravasation injury. The patient may need psychological support depending on the extent of the injury. Social support may also be necessary on discharge.
- **Reporting**
Standardised local incident reporting of the infiltration and extravasation should be undertaken.

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1. Introduction

The purpose of this document is to set out the guidelines for the management of infiltration and extravasation incidents associated with vascular access and intravenous therapy within Frimley Health NHS Foundation Trust. For extravasation injuries associated with chemotherapy agents, this guideline should be used in conjunction within the Trust chemotherapy and cancer networks guidance on cytotoxic extravasation (available on the Trust intranet site).

- **Prevention**

Safe IV therapy administration and vascular access practice is essential to preventing infiltration and extravasation injury occurring in the first instance. All healthcare professionals involved in the delivery of intravenous therapies and the use of vascular access devices should be aware of the preventative measures associated with infiltration and extravasation, vessel health and preservation and the principles of vascular access ⁽⁴⁵⁾.

- **Recognition**

Recognising the early stages of extravasation is vital. Early diagnosis can reduce the amount of damage sustained by the patient's tissue ⁽⁴⁵⁾.

- **Treatment**

Early intervention and treatment to reduce or stop tissue damage. Hot or cold compress, injectable antidotes, tissue wash out and referral to plastic surgeons should be considered as part of the treatment pathway for extravasation ⁽⁴⁵⁾.

- **Follow-up**

Ensure the patient is followed up the appropriate department, either IVAS, Plastics or tissue viability and supported by the clinical team. Clinical photography should be used to continuously document the extravasation injury. The patient may need psychological support depending on the extent of the injury. Social support may also be necessary on discharge ⁽⁴⁵⁾.

- **Reporting**

Standardised local incident reporting of the infiltration and extravasation should be undertaken ⁽⁴⁵⁾.

2. Definition of Infiltration and Extravasation

- Infiltration is the leaking of fluid or medication into extravascular tissue from an intravenous device, this injury is classed as an extravasation if the fluid or medication was a vesicant ⁽⁴⁵⁾.
- Infiltration of large volumes of fluid can cause nerve compression and compartment syndrome ⁽⁴⁵⁾.
- Infiltration of some intravenous therapy can cause psychological harm due to permanent staining of the skin if infiltration occurs. IV Iron is an example of this type of injury ⁽⁴⁵⁾.
- Extravasation injury results from a vesicant leaking into the extravascular space, where the medication or fluid itself causes damage to the tissues. The damage increases the longer the vesicant is within the tissues. Extravasation by vesicants can cause blistering, tissue necrosis and loss of parts of the tissue ⁽⁴⁵⁾.
- Risk factors for extravasation injuries include using small or fragile veins, insertion sites across joints, sedated patients who cannot express pain, poorly secured vascular access devices (VAD), devices placed in difficult IV access patients and bariatric or oedematous limbs ⁽⁴⁵⁾.
- Extravasation can occur in peripheral and central vascular access devices ⁽⁴⁵⁾.
- Prompt recognition and management can prevent the need for surgical intervention, permanent scarring, loss of function or loss of parts ⁽⁴⁵⁾.
- Appropriate management can vary depending on volume, pH, osmolality and pharmacological action of the vesicant ⁽⁴⁵⁾.

3. Types of Vesicants

Vesicants are drugs or solutions (cytotoxic or non-cytotoxic) with the potential to cause blistering and ulceration and if left untreated, tissue necrosis ⁽⁴⁵⁾.

- Chemotherapy
- Non-physiological pH – (high or low pH)
- Vasopressors
- Hyperosmolar solutions

4. Chemotherapy

Many chemotherapy agents can cause direct cellular toxicity upon extravasation ⁽⁴⁾.

Chemotherapy extravasation injuries can be separated into two categories on the basis of their mechanisms of cellular damage:

- Non-binding vesicants (agents that do not bind to tissue nucleic acids).
- DNA-binding vesicants (agents that bind to tissue nucleic acid) ⁽²⁾.

The most destructive extravasation injuries are caused by the DNA-binding agents (e.g., anthracyclines, antitumor antibiotics, and some alkylating agents) ⁽³⁾, which cause immediate tissue injury which can be prolonged and evolve over time because the agents remain in the tissues ⁽²⁾.

Non-binding vesicant agents (egg, vinca alkaloids and taxanes) ⁽³⁾, cause immediate tissue damage, but because they do not bind to DNA, these drugs are more easily metabolized resulting in a less destructive tissue damage and quicker tissue healing ⁽²⁾.

Even agents that are not antineoplastics— such as antibiotics—can cause depletion of intracellular ADP and ATP levels and other enzymes that sustain cell function, leading to cell death. The impact appears to depend on drug concentration and time of exposure.

At Frimley Health the oncology departments and chemotherapy day units follow the cancer alliance network protocols and procedures when a chemotherapy extravasation occurs and can be found on the Trust intranet. These protocols should be used in conjunction with this guideline.

5. Non-physiological pH – (high or low pH)

Solutions that irritate the venous endothelium and vessel wall ultimately raise the risk of venous rupture, allowing the solutions to escape into the surrounding tissue ⁽⁵⁾. To minimize venous irritation, infused solutions should be close to physiologic pH 7.35 to 7.45 ⁽¹⁹⁾ and osmolarity 28 to 282 mOsm/L ^(20,21), anything outside of these ranges should be considered to have the potential to cause tissue damage ⁽⁴⁵⁾.

Extreme pH (both alkaline and acidic) can reduce peripheral vein tolerance ⁽⁹⁾ by damaging cell proteins and eventually causing cell death, leading to venous endothelial damage and making it susceptible to rupture ^(8, 45).

The pH of infusion solutions should generally be **between 5 and 9** ⁽⁸⁾. Drug pH values: the pH of blood is 7.35 to 7.45 and considered neutral within the body. Any drug or infusion solution with a pH outside of a neutral range has the potential to cause irritation to a vein and tissues. The further away from a neutral pH the drug is, the more damaging the extravasation injury can be to the tissue ⁽⁴⁵⁾.

The pH and osmolarity of IV drugs can be found on the monographs within the Medusa online injectable medicines guide ⁽⁴⁵⁾.

6. Hyperosmolar solutions

Hyperosmolar drugs and fluids with a high osmolarity, generally above 600 mOsm/L are also classed as vesicants because they also have the potential to cause significant tissue damage. For solutions that escape the vein, osmolarity can also influence the degree of tissue injury. For example, extravasation of hypertonic fluids such as 10% dextrose or parenteral nutrition solutions can cause skin necrosis and serious tissue damage ^(5, 10, 45).

Dextrose solutions are often administered with other products premixed such as potassium, which can increase osmolarity even further. Extravasation of hypertonic solutions (e.g., osmolarity 350 mOsm/L) causes a fluid shift from inside cells to the interstitial space ⁽¹⁾, which disrupts cell function ^(5, 11). The shift from subcutaneous cells to interstitial tissues leads to swelling and increased local pressure, which can cause Acute Limb Compartment Syndrome and other injuries ^(5, 45).

While hyperosmolar solutions can shrink cells and collapse the internal structures, hyposmolar solutions can swell cells and lead to cell rupture ⁽¹⁷⁾.

7. Vasopressor

Vasopressors are a powerful class of drugs that induce vasoconstriction and thereby elevate mean arterial pressure (MAP). Vasopressors differ from inotropes, which increase cardiac contractility; however, many drugs have both vasopressor and inotropic effects. Vasopressors are classed as vesicants because they can cause tissue necrosis and ultimately the loss of a limb due to local vasoconstriction ^(12, 45).

7.1 Peripheral Administration of Noradrenaline

Peripheral Administration of Noradrenaline is only for the use in adult patients on ICU and those accepted to ICU with an outreach nurse prior to transfer. The decision to commence peripheral noradrenaline can only be made by an ICU doctor.

The Protocol for peripheral noradrenaline can be accessed via the critical care team.

8. Reducing the risk of Extravasation

- Dislodgement of the distal tip of the cannula into the tissues surrounding the vein. In order to avoid dislodgment 80% of the catheter should be cited in the vessel ^(20, 45). The use of ultrasound for placing peripheral canula should be considered for patients with difficult IV access in order to achieve this ^(21, 45). Cannula for mild vesicant administration should not be cited above the antecubital fossa to avoid dislodgment and aid early visualisation of extravasation (with the exception of CT contrast administration) ^(20, 45).
- Constriction of the blood flow distal to the cannula tip can increase venous pressure which can cause fluid to leak from the perforation in the vein made by the cannula ⁽⁴⁵⁾.
- Avoid inflating blood pressure cuffs on arms which have IV therapy running into ⁽⁴⁵⁾.
- Avoid points of flexion when placing peripheral cannula as these can constrict blood flow and cause mechanical phlebitis when the joint is closed ⁽⁴⁵⁾.
- Inappropriate selection of the position and size of cannula and the length of time which the cannula is left in situ. Do not cannulate feet or other bony areas. If the patient needs ongoing vesicant IV therapy treatment, consider referral for a PICC or another central device; refer to the IVAS team ⁽⁴⁵⁾.
- Where possible vesicants should be administered via a central vein into the SVC or IVC ⁽⁴⁵⁾.
- If vesicants are being administered in peripheral veins this should be completed in the safest way possible and be justifiable. The reason for peripheral vesicant administration should be documented in the clinical notes. The smallest cannula gauge should be used in the lowest available vessel in the arm or hand to ensure blood flow around the indwelling cannula and localise any extravasation damage to the furthers part of the arm ^(18, 22, 45).
- The cannula position, the cannula calibre and time in-situ are the factors that have the greatest bearing on the likelihood of problems occurring. If difficulties were experienced or multiple attempts at venepuncture were required prior to the intravenous device is established the risk of extravasation is increased ^(18, 45).
- The use of steel needles (butterfly needles) placed into the vessel for IV administration should be avoided as they are associated with increased risk of extravasation and other complications. These steel needles usually come in the form of a butterfly and are designed for taking blood samples (venepuncture) not for indwelling devices that can be used for drug administration ^(19, 45).
- An Infusion pump should always be used to administer infusions of vesicant IV therapy ^(23, 45). Care should be taken to check the infusion and pump hourly, and observations documented on an infusion pump check list. An extravasation may cause an infusion pump to turn off and begin to alarm, alarms should not be ignored. Alarms should be investigated, and actions documented ⁽⁴⁵⁾.
- The infusion pump pressure should be set at between 2 and 4 to ensure pump is sensitive to pressure changes to indicate early infusion problems ^(23, 45).
- Extravasations occurring during the night may not be noticed immediately. Infusion pumps must be used, and the alarm settings activated to allow audible alarms to be heard if occlusions or pressure changes occur during the infusion ⁽⁴⁵⁾.
- A pump check list should be used to ensure the infusion site is checked hourly and two nurses should confirm and document the starting rate has been correctly set on the pump before starting the infusion ⁽⁴⁵⁾.
- The administration of a vesicant intravenous medicine by inexperienced staff can increase the risk of extravasation. All staff should be supervised until they are signed off as competent to administer IV therapy and should be encouraged to seek help if they are unfamiliar with a specific drug administration protocol ⁽⁴⁵⁾.
- Chemotherapy MUST only be administered by an IV competent nurse who has undergone additional chemotherapy qualifications and competencies ⁽⁴⁵⁾.
- Central Venous Catheter device tip location should always be in the lower 3rd of the SVC. If the catheter has migrated outwards, the CVC should not be used and replaced as soon as possible by referral to the IVAS team ^(24, 45).

- Practitioners' unfamiliarity with the drug and the manufacturer's recommendations for administration. The online injectable medicines guide (MEDUSA) should be consulted prior to intravenous therapy administration ⁽⁴⁵⁾.

9. Risks Related to Patient and medical history

- Difficult IV access patients (DIVA)
- Paediatrics and neonates
- Cancer patients have additional risk due to: These patients should be offered long term central IV access devices such as PICC, PORT or Tunnelled catheters if their IV therapy treatment is long term. For IV therapy regimes, ultrasound guided midline or peripheral cannula should be offered if appropriate ⁽⁴⁵⁾. A referral to the IVAS team should be made.
- Peripheral vascular access device associated risks include ⁽⁴⁵⁾:
 - Fragile, mobile veins that are difficult to cannulate.
 - 'Recall' phenomenon, in patients previously given radiotherapy.
 - A previous extravasation injury where tissue is at risk of further damage when subsequent chemotherapy is given even if administered at a different site.
 - Limbs with lymphoedema due to poor venous flow.
- Intravenous drug user (recreational drugs). This group of patients is high risk for extravasation but also high risk for abusing central vascular access devices such as PICC by injecting illegal substances into the lumen of the catheter. This can have catastrophic consequences. In light of this, this group of patients should be managed with either peripheral cannula/midline or for vesicant therapies or a neck CVC. This is outlined in the Frimley Health Vascular Access Guideline's part 1.
- Peripheral vascular disease.
- Raynaud's Phenomenon.
- Diabetes.
- Superior Vena Cava Syndrome.
- History of a previous Cardiovascular Accidents.
- Patients receiving care post Cerebrovascular Accident.
- Dark pigmentation skin tone – visual symptoms of extravasation can be harder to determine if the skin pigmentation is dark. The patient may still have pain, swelling blistering etc..

Advice should be sought from the IVAS team for support with vascular access for these types of patients.

Peripheral cannula should not be covered with bandages, the site surrounding the device should be observable for signs of phlebitis and extravasation.

10. Paediatric considerations.

- In paediatrics, vesicants should not be administered via feet cannula ⁽⁴⁵⁾. If a foot cannula is used in paediatrics it should not be bandaged and should be observed hourly during the infusion. An infusion pump should always be used with the pressure setting low to enable alarming if pressure changes occur. Life changing injuries can occur due to extravasation injuries in children's feet ^(31, 45).
- A risk assessment should be documented to weigh up the risk versus benefit of administering a vesicant drug via a peripheral cannula, especially a cannula that is not placed in the forearm or hand.
- For DIVA paediatric patients call the IVAS team to assist with device placement.

11. Signs and Symptoms of Extravasation

- Pain, stinging, burning or any other acute change at the injection site. Adults or children who are frightened of needing a new cannula may deny pain or discomfort ⁽⁴⁵⁾.
- Induration, erythema, venous discolouration or swelling at the injection site ⁽⁴⁵⁾.
- Delayed capillary refill surrounding the device insertion site ⁽⁴⁵⁾.
- There is increased resistance to administration despite positional changes of the limb ⁽⁴⁵⁾.
- Blistering of the skin which can occur after the injury, up to 2 weeks after in some cases ⁽⁴⁵⁾.

Signs and symptoms of infiltration and extravasation from CVADs ^(32, 45)				
Event	Related Device	Causative factors	Potential objective manifestations	Potential subjective manifestations
Needle dislodgement	IVAP	Needle not in port, needle not stable/secured, incorrect needle length	Sudden swelling about port pocket or chest area; no or loss of blood return; palpable subcutaneous tissue; fluid leaking around needle	Pain, stinging, burning at port pocket or chest area
CVC damage	IVAP, tunnelled CVC	Separation of port from catheter; nicked catheter at insertion	Swelling and erythema in port pocket or catheter tunnel with infusion; no or loss of blood return	Pain or burning around port or CVC tunnel with infusion
CVC pinch off	IVAP, tunnelled CVC	Subclavian insertion medial to midclavicular line	Loss of blood return; swelling and erythema in clavicular area with infusion	Clavicular pain or burning with infusion
CVC tip displacement through SVC	IVAP, tunnelled CVC, PICC	Early: difficult insertion; Late: unknown; thrombosis of SVC or great veins may increase risk	Intractable cough with infusion, pleural effusions, abnormal CXR/CT	Substernal chest pain, dyspnoea, fatigue
CVC tip displacement from SVC	IVAP, tunnelled CVC, PICC	Unknown, possible increased risk with severe coughing	Loss of blood return, erythema in neck (if CVC in IJV)	Discomfort in chest about CVC or tip with infusion of irritants or vesicants
Fibrin sleeve and back-tracking	IVAP, tunnelled CVC, PICC	Fibrin sleeves are nearly universal; thrombosis is uncommon	Erythema at venous insertion site during infusion; backtracking can be confirmed by lineogram	Discomfort at CVC insertion site

12. Compartment syndrome

Compartment syndrome is a painful and potentially serious condition caused by bleeding or swelling within an enclosed bundle of muscles – known as a muscle compartment. This can occur when injectable infusions are inadvertently administered either rapidly or over a period of time when the vascular access device is not situated in a vessel correctly. Compartment syndrome is an emergency and should be dealt with as such. An urgent surgical review should be sought for any patient who may have a compartment syndrome as they may require an emergency fasciotomy ^(33, 45).

Causes and risks

- Uncontrolled infusion of large amounts of solution into a limb due to a dislodged cannula/device where a pump pressure has been increased and so does not alarm.
- Inadvertent administration of CT scanning contrast due to a dislodged cannula/device because the pressure of the contrast injection pushes the cannula out of the vessel but still remains in the limb tissue. Cannula used for CT contrast administration should be newly inserted where possible and have 80% of the indwelling cannula situated in the vessel. Where possible a BD Diffusics cannula can be used to reduce the risk of catheter dislodgment.
- Bleeding into a limb due to inadvertent arterial or venous puncture during vascular access insertion.

Symptoms can include:

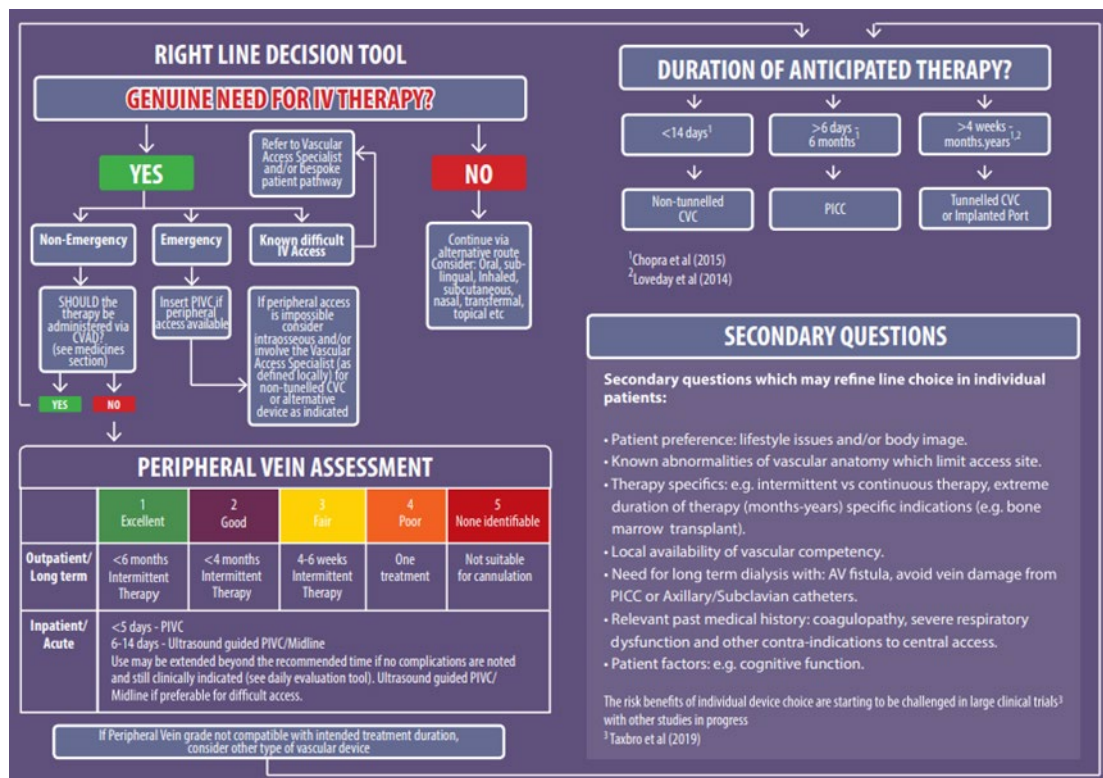
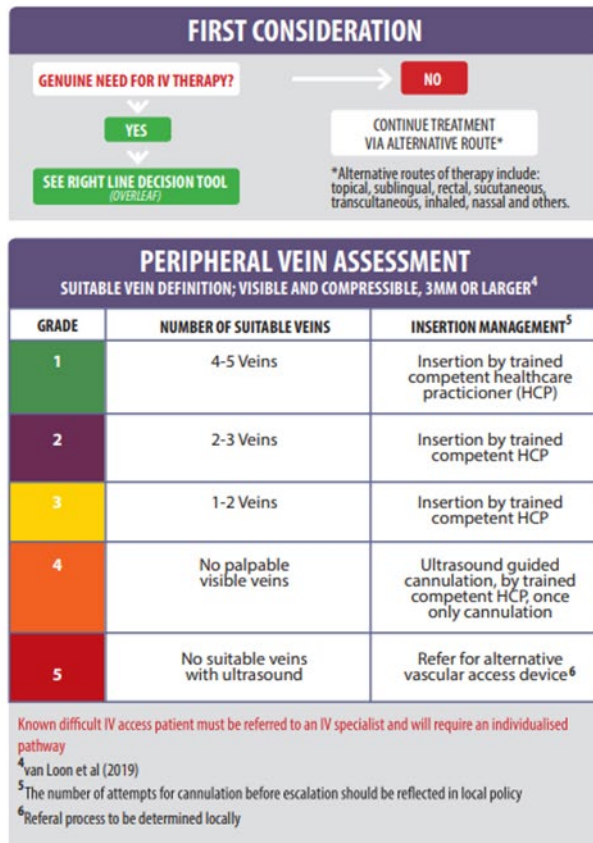
- Intense pain, especially when the muscle is stretched, which seems much worse than would normally be expected for the injury.
- Tenderness in the affected area
- Tightness in the muscle
- A tingling or burning sensation.
- In severe cases, numbness or weakness (these are signs of permanent damage)

Treat a suspected compartment syndrome as an emergency and contact the on call orthopaedic team via switch board, the on-call plastics team and vascular team can be contacted for advice. The IVAS team can also be contacted for advice and support.

13. Distinguishing Extravasation from other Conditions

Distinguishing extravasation from other conditions ⁽³²⁾				
Characteristic	Flare reaction	Vessel irritation	Venous shock	Extravasation
Presenting symptoms	Itchy blotches or hives; pain/burning uncommon	Aching & tightness	Muscular wall of blood vessel in shock (can be caused by very cold drugs or by rapid administration)	Pain/burning common at injection site; stinging may occur during infusion
Colouration	Raised red streak, blotches or hive like erythema along the vessel; diffuse or irregular pattern	Erythema or dark discolouration along vessel	n/a	Erythema around needle/venepuncture site
Timing	Usually appears suddenly and dissipates within 30-90 minutes	Usually appears within minutes after injection. Colouration may only appear later in the process.	Usually appears right after the injection.	Symptoms start to appear right after injection, symptoms endure
Swelling	Unlikely	Unlikely	n/a	Occurs often; does not dissipate for several days
Blood return	Usually, but not always intact	Usually, but not always intact	Often absent	Usually absent or sluggish

14. Vessel health and preservation (34)



15. Vascular Access Device Selection

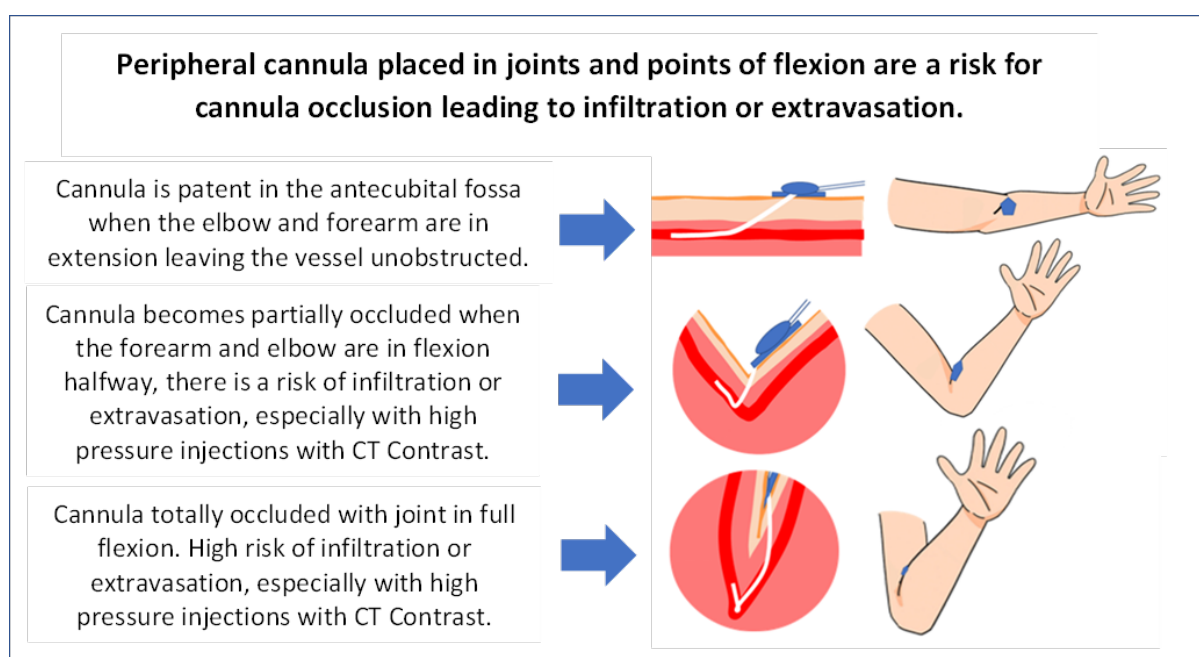
Prevention of infiltration and extravasation is heavily reliant on the vascular access device used to administer the intravenous therapy. Vascular access devices classification can be simply divided into peripheral and central sited devices. In order to classify a vascular access device as central, the tip of the catheter must pass the carina and sit in the lower 3rd of the SVC ⁽⁴⁵⁾.

Vascular Access Device Decision (VADD) Tool							
Indwell time	96 hours plus	Up to 10 days	Up to 29 days	Up to 6 weeks	Over 18 months	Permanent	Difficult Vein Access
Vascular Access Device	Peripheral Intravenous cannula	Short Term Acute CVC (neck or groin)	Short Midline (6cm to 8cm)	Midline (15cm to 25cm)	PICC	Long-term Tunnelled CVC	Implanted PORT
Suitable Treatment Option	Peripheral Ph 5-9 ONLY	Central Vesicants Multi-lumen	Peripheral Ph 5-9 ONLY	Peripheral Ph 5-9 ONLY	Central Vesicants Multi-lumen	Central Vesicants Multi-lumen	Central Vesicants
	IV Infusion IV Bolus	Blood draw IV Bolus	Blood draw IV Bolus	OPAT IV Infusion IV Bolus	Blood draw IV Infusion IV Bolus	Blood draw IV Infusion IV Bolus	IV Infusion IV Bolus
	Emergency	IV Infusion	IV Infusion	IV Bolus	IV Bolus	IV Bolus	Blood products
	High flow rates achievable	Emergency	Emergency	Blood products	High flow rates achievable	High flow rates achievable	Chemotherapy
	Blood products	High flow rates achievable	High flow rates achievable	Osmolarity Under 600	Blood products	Blood products	CT Contrast power injectable** (restrictions apply)
	CT Contrast power injectable** (restrictions apply)	Blood products	Blood products		Chemotherapy	Chemotherapy	Osmolarity ≥ 600
	Chemotherapy* (restrictions apply)	Chemotherapy	CT Contrast power injectable** (restrictions apply)		CT Contrast power injectable** (restrictions apply)	Osmolarity ≥ 600	
	Osmolarity Under 600	Osmolarity ≥ 600	OPAT Osmolarity Under 600		Osmolarity ≥ 600		
* For chemotherapy administration the peripheral cannula should be a 24g or 22g cannula sited in the biggest vein in the forearm or back of the hand with points of flexion avoided. (follow local guidelines) ** ENSURE CATHETER IS POWER INJECTABLE: For power injection specifications follow each individual manufacturers specifications and recommendations for device. (follow local guidelines)							

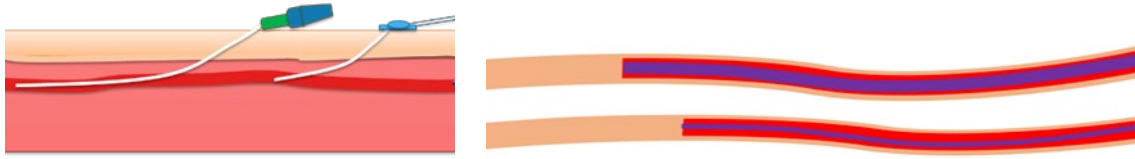
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It is not safe to leave the tip of any vascular access device catheter past the axilla or before the carina. Catheter tips in this location have a high risk of causing thrombosis and other associated complications³⁷.

Vesicants and other agents that can cause extravasation are usually administered via a central vascular access device.



Peripheral cannula should be sited below the antecubital fossa. The smallest catheter size possible should be used and placed in the biggest vein as far down the arm as possible with joints and points of flexion being a last resort for cannula placement ^(36, 45).



The smallest gauge possible should be considered to avoid venous congestion and mechanical phlebitis from damage to the tunica intima. The flow rates of 24g and 22g cannula are sufficient to administer maintenance fluids and general IV therapy etc. Care should be taken to ensure the cannula is long enough to indwell into the vessel so that 80% of the cannula is in the vessel itself ^(35, 45).

A Guide to Choosing the Correct Cannula for your Patient					
		Approximate Flow Rates (l/hr)			
Colour	Common Applications	Size Gauge	Crystalloid	Plasma	Blood
Orange	Used in theatres or emergency for rapid transfusion of blood or viscous fluids	14G	16.2	14.2	12.9
Grey	Used in theatres or emergency for rapid transfusion of blood or viscous fluids	16G	14.1	10.9	10.0
Green	Blood transfusions, parenteral nutrition, stem cell harvesting and cell separation, large volume of fluids	18G	6.1	5.2	3.8
Pink	Blood transfusions, large volumes of fluids	20G	4.0	2.7	2.5
Blue	Blood transfusions, most medications and fluids	22G	2.5	1.6	1.4
Yellow	Medications, short term infusions, fragile veins, children	24G	0.8	0.7	0.5

16. Extravasation clinical pathway ⁽⁴⁵⁾

Suspected Infiltration or Extravasation Action



Has a vascular access device been in situ in the affected limb in or around the area of current concern, now or in the past 2 weeks , which was used for IV therapy that would be classed as a vesicant?

How does the affected limb look?

Is the whole limb swollen and/or cold and dusky looking with reduced or absent capillary refill and poor or absent radial pulses?

If Yes: THINK EXTRAVASATION OR COMPARTMENT SYNDROME

If NO it could be: Exit site infection, Phlebitis, MARSI, Cellulitis, Oedema

ACTIONS - Reassure patient - Manage pain - call IVAS/plastics

- Stop administration - Leave vascular access device in situ and attempt aspiration.
- Identify Vesicant involved and check for antidote in guidelines.
- If available administer antidote following guidelines (EP2 and EP3) if no antidote remove vascular access device.
- Consider referral for wash out treatment (EP4).
- Chemotherapy extravasations—refer to chemotherapy network guidance .
- Mark outline of extravasation injury and document incident on Epic.
- Apply Hot or Cold compress if appropriate (see guideline (EP1).
- Complete referral to plastics - take medical photography and upload to Epic.
- Complete RL, inform IVAS and arrange follow up as per advice form IVAS.

Contact IVAS vascular access team 7 days a week—8am until 8pm for advice and support

Wexham and Heatherwood 07917070523 Frimley 07363243071

Infiltration/Extravasation SYMPTOMS



STOP THE INFUSION



Try to aspirate the device
Reassure patient
Call for Help
Manage pain

- Stop administration - Leave vascular access device in situ and attempt aspiration, contact IVAS vascular access for help and advice.
- **Chemotherapy extravasations - refer to network guidance.**
- Mark outline of extravasation injury and document incident in patient record.
- Medical photography to record injury.
- Identify vesicant involved and check for antidote for specific drug.
- Contact Plastics for urgent review.
- Complete incident report and arrange follow up.

Contact IVAS for advice - 8am until 8pm everyday:

Frimley Site 07393243071 Wexham and Heatherwood sites 07917070523

17. Extravasation Injury Staging (25, 26, 27, 28, 29, 30, 45)

Extravasation Staging		
Stage	Assessment	Treatment options
1	- Painful infusion site - No erythema - Localized swelling (1%-10% of extremity above or below site)	- Remove cannula - Elevate extremity - Warm/cold compresses
2	- Painful infusion site - Slight swelling at site (up to 25% of extremity above or below site) - Slight erythema (localized to the central area of extravasation) - Good pulse below site - Brisk (1-2 s) capillary refill below site	- Remove cannula - Elevate extremity - Warm/cold compresses - Consider antidote
3	- Painful infusion site - Moderate swelling at site (25%-50% of extremity above or below site) - Marked erythema (extends beyond central area of extravasation) - Blanching (for vasopressor extravasation only) - Good pulse below site - Brisk (1-2 s) capillary refill below site - Skin cool to touch	- Leave cannula in place; using a 1 mL syringe, aspirate as much fluid as possible - Remove cannula unless it is needed for antidote administration - Elevate extremity - Warm/cold compresses - Consider antidote
4	- Painful infusion site - Severe swelling at site (>50% of extremity above or below site) - Very marked erythema (extends beyond borders of swelling) - Blanching (nonvasopressor extravasation) - Decreased or absent pulse - Prolonged capillary refill >4 s - Skin cool to touch - Skin breakdown including blistering or necrosis	- Leave cannula in place; using a 1-mL syringe, aspirate as much fluid as possible - Remove cannula unless it is needed for antidote administration - Elevate extremity - Warm/cold compresses - Consider antidote - If swelling of the site is tense and skin is blanched, obtain surgical consult

18. Evolving injury timings (45)

During or up to 24hrs after administration	- Pain/burning sensation at injection site and during infusion. - Erythema around needle/venepuncture site. - Symptoms start to appear right after administration. - Swelling that does not dissipate for several days - Blood return absent from vascular access device
Up to 2 weeks after administration	- Erythema around device extending through the limb - Hot and painful to touch - Fluid filled blisters - Reduced or absent capillary refill
Up to 4 weeks after administration	- Dark skin discoloration - Absent capillary refill - Fluid filled blisters - Pain
4 weeks and over after administration	- Necrotic tissue - Pain - Reduced limb mobility

19. Extravasation injury follow up ⁽⁴⁵⁾.



Review and redress injury after 24hrs then after 3 days then weekly.

Document progress with clinical photography

Observe for signs of infection, non-blanching skin and skin necrosis.

Discuss with speciality wound care team if required to manage evolving wound.

Ensure patient has a point of contact to telephone and is given information to access help.

- Follow up by Plastics, clinical team or IV team post extravasation / infiltration injury should be for in-patients and outpatients.
- Discharge plan should include extravasation follow up.
- Tissue damage can become extensive and serious days or weeks after the injury occurred.

20. Infiltration and Extravasation treatment options ⁽⁴⁵⁾

CHEMOTHERAPY EXTRAVASATION – FOLLOW NETWORK GUIDELINES.

- For infiltration of non-vesicants with no risk of compartment syndrome, the affected limb can be rested in a Bradford sling to assist with absorption and drainage. Areas of broken skin should be covered with a silicone occlusive dressing.
- Pain relief should be part of the pathway for treating infiltration and extravasation. Starting with paracetamol; and working up to opiates depending on the pain level.

Extravasation procedure (EP) 1 – Warm and cold compress ^(13, 14, 45)

- Warm compresses are preferred for extravasation of specific drugs including vasopressors, vinca alkaloids, etoposide, and oxaliplatin to increase local blood flow and enhance drug removal.
- Generally cold compresses are recommended for extravasations of most irritants and some vesicant drugs (see table in Appendix 1 to know which drugs). Cold compresses cause vasoconstriction, limiting the spread of the extravasated drug. Additionally, the cold compress reduces local inflammation and pain.
- Apply compresses for 20 to 60 minutes 3 or 4 times daily for the first 24 to 72 hours after extravasation occurs.
- Where possible a temperature related, electric warmer should be considered with a disposable single use cover.
- Care should be taken to ensure warm compresses are not too hot and cold compresses are not too cold as to cause further tissue damage. Cold compresses from the freezer should not be directly applied to the skin.

Extravasation procedure (EP) 2 – Hyaluronidase subcutaneous injectable antidote ^(38, 39, 40, 45)

- Hyaluronidase is a family of enzymes that degrade hyaluronic acid (HA). It is found to increase vascular permeability and temporarily disrupt the extracellular matrix, promoting diffusion of substances through tissues. ⁽¹⁵⁾

- Hyaluronidase is often used in managing the extravasation of harmful agents such as chemotherapeutics (e.g., vinca alkaloids and taxanes), contrast media and total parenteral nutrition (TPN) solution. Hyaluronidase increases tissue permeability, rapidly dispersing extravasated chemicals, reducing the risk of skin necrosis and overall morbidity ⁽¹⁵⁾.
- Hyaluronidase should not be administered following extravasation of vesicant drugs unless it is either specifically indicated (see vesicant drug profiles in appendix) or used in the saline flush-out technique.

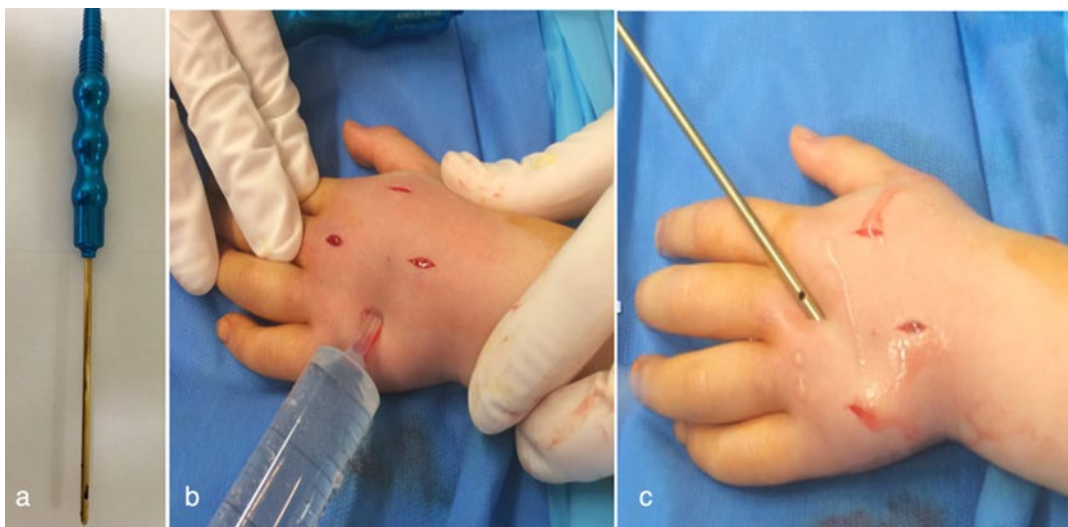
BNF indications and dose: Hyaluronidase for treatment of extravasation by local infiltration Adult:

1500 units, to be dissolved in 1 mL water for injections or 0.9% sodium chloride and infiltrated into affected area as soon as possible after extravasation.

- **Contra-Indications** for hyaluronidase
 - Not for intravenous administration,
 - not to be used to enhance the absorption and dispersion of vasopressors e.g, dopamine and/or alpha-adrenoceptor agonists,
 - not to be used to reduce swelling of bites,
 - not to be used to reduce swelling of stings.

Extravasation procedure (EP) 3 - Subcutaneous saline washout ^(43, 44, 45)

This procedure is performed by the Plastics team.



Saline washout technique: a) the 2-mm blunt cannula; b) saline solution introduction through the small skin incision; c) washout procedure with the lipo-aspiration cannula.

21. Incident reporting ⁽⁴⁵⁾

Report under the dedicated category of Intravenous Therapy Injury.

- Extravasation if vesicant involved.
- Infiltration if non vesicant involved.
- Chemotherapy extravasation
- Compartment Syndrome

Detail the:

- Site of the injury
- Drug/Intravenous fluid involved including its pH and osmolarity.
- Extravasation Stage / injury level.
- Vascular Access Device (VAD) involved – central or peripheral etc...
- Level of harm.
- Serious incident.
- Escalation and follow up plan.
- Duty of Candour

As the injury may evolve over time, the incident report may need to be updated at a future point, this includes the level of harm.

Ensure the patient safety team is made aware and that a referral for IVAS review is made on EPIC.

Appendix 1: Vesicant non-chemotherapy drugs commonly used in clinical practice



– this is not an exhaustive list, other vesicant drugs are available.

- The following list of non chemotherapy drugs are commonly used in clinical practice and have the potential to cause extravasation resulting in varying degrees of injury.
- These drugs can be classed as vesicants. It is important to know the pH and osmolality of the drug and recognise that large infiltrations of nonvesicant drug solutions may also be associated with severe tissue damage.
- pH and Osmolality values obtained from MEDUSA injectable medicines guide and cross referenced with the manufacturer drug profile and BNF.
- Cold or warm compresses should generally be applied for 20 minutes, every six to eight hours, for up to three days.
- The dose of hyaluronidase for adults for extravasations is generally 150 units/mL, 0.2 mL intradermally or subcutaneously at each of five sites of the edges surrounding the affected area. A concentration of 15 units/mL (same instructions as above) has also been used for non-chemo agents. Hyaluronidase should be used within about one hour of extravasation.

MEDICATION GENERIC/BRAND	pH	mOsmol/L	Hot/Cold Compress	Antidote	Comments
Acyclovir	10.5 - 11.6	316	Cold	Hyaluronidase (18)	Administration recommended via central vein
Amiodarone	3.5 – 4.5	157 – 283	Cold		Administration recommended via central vein
Aminophylline	8.6 - 9.6	300 to 327	Warm		Slow infusion reduces risk
Amoxicillin	8 - 10	245 – 548			Slow infusion reduces risk
Amikacin	3.5 – 5.5	319 – 500			Administration recommended via central vein
Ampicillin	9	~400			Slow infusion reduces risk
Calcium Chloride	5 - 8	2040 - 10% solution	Cold or warm if administering Hyaluronidase being used		Hypertonic solutions may cause prolonged depolarization and contraction of pre- and post-capillary smooth muscle sphincters, leading to tissue injury and ischaemia (2, 5, 10, 11, 13) Administration recommended via central vein
Calcium Gluconate	5.5 -8.2	Demo product osmolality: 290 to 310mOsmol/kg (In sodium chloride 0.9%) 310 to 320mOsmol/kg (in glucose 5%) B Braun product osmolality: 660mOsm/L	Warm		Soft tissue calcification (subcutaneous calcinosis) caused by extravasation.(4)

Contrast medica – non-ionic		1,500 to over 2,000 mOsmol/kg	Cold	5 mL and 20 mL consider subcutaneous injection of Hyaluronidase (12) For ionic contrast media extravasation >20mL, consider surgical drainage within 6hrs (5)	Hypertonic solutions (e.g., radio contrast media) may cause prolonged depolarization and contraction of pre- and post-capillary smooth muscle sphincters, leading to tissue injury and ischemia. (5,10,11,13,14) Hyperosmolar solutions (e.g., conventional ionic contrast media) exert osmotic pressure, and may result in compartment syndrome if infiltration occurs (2,5,12)
Cefuroxime	4.5 - 7.3	335	Cold		Can cause phlebitis, pain, induration at injection site(4) Slow infusion reduces risk
Chlorphenamine	4 – 5.2	260 to 320			Small volume bolus over 5 mins
Chlorpromazine	5 – 6.5	329mOsm/L (50mg in 2mL). 308mOsm/L (chlorpromazine 50mg in sodium chloride 0.9% 1,000mL)			Small volume bolus over 5 mins
Ciprofloxacin	3.3 - 4.6	285			Slow infusion reduces risk
Clarithromycin	4 - 6	120 to 160	Cold		Slow infusion reduces risk
Cyclizine	3.3 – 3.7	285			Small volume bolus over 5 mins
Co-trimoxazole (Sulfamethoxazole-Trimethoprim)	9.5 - 11	600 – 700	Cold		Administration recommended via central vein
Daptomycin	4.7 – 6.8	323 to 364			Administration recommended via central vein
Dextrose 5%, 10%, 20%	3.5 – 6.5	278 to 320	Warm		Hypertonic solutions may cause prolonged depolarization and contraction of pre- and post-capillary smooth muscle sphincters, leading to tissue injury and ischemia. (2,5,10,11,13)
Diazepam	6.2 - 7		Cold		Administration may be associated with local reactions (thrombophlebitis and venous thrombosis) (16,17)
Digoxin	6.7 – 7.3	100micrograms in 1mL osmolarity: 7500mOsmol/L.			Slow infusion reduces risk

Dobutamine	3.5 (2.5 - 5.5)	280		Phentolamine (2,6,8,9) Terbutaline 2% Topical nitro-glycerine	Administration recommended via central vein
Dopamine	3.3 (2.5 - 4.5)	277	Warm	Phentolamine 2% Topical nitro-glycerine (2,6,8,9)	Ischaemic necrosis secondary to local vasoconstriction can result from extravasation of sympathomimetic agents including dobutamine, dopamine, epinephrine, metaraminol, and norepinephrine (2,10,11) Administration recommended via central vein
Doxycycline	5.1 – 6.1	1027mOsmol/L (undiluted 100mg/5mL) 380mOsmol/L (100mg diluted to 100mL with sodium chloride 0.9%) 322mOsmol/L (100mg diluted to 250mL with sodium chloride 0.9%) 353mOsmol/L (100mg diluted to 100mL with glucose 5%) 293mOsmol/L (100mg diluted to 250mL with glucose 5%)			Administration recommended via central vein
Epinephrine (adrenaline)	2.2 – 5.0	300	Warm	Phentolamine (2,6, 7, 9)	Ischemic necrosis secondary to local vasoconstriction can result from extravasation.(2, 10, 11) Administration recommended via central vein
Fentanyl	3.8 – 7.5	270 - 320			Administration recommended via central vein
Fluconazole	4 – 7	-300			Slow infusion reduces risk
Furosemide	8 – 9.3	250 – 315			Slow infusion reduces risk
Ganciclovir	11.0	320			Administration recommended via central vein
Gentamicin	3.0 – 5.5	160			Administration recommended via central vein
Glucagon	2.5 -3	300			
Glyceryl trinitrate (GTN)	3 – 6.5	314			Administration recommended via central vein

Intravenous Iron	5 – 7	Permeant skin staining can occur if infiltration occurs	Warm		Slow infusion reduces risk
Levofloxacin	3.8 - 5.8	270 – 340			Administration recommended via central vein
Linezolid	4.4 – 5.2	270 – 330			Administration recommended via central vein
Mannitol >20%	4.5 – 7	100mg in 1mL (10%): 549mOsmol/L 150mg in 1mL (15%): 823mOsmol/L 200mg in 1mL (20%): 1100mOsm/L	Cold		Administration recommended via central vein
Metoclopramide	3 - 5	270 – 310			Small volume bolus over 5mins
Metronidazole	5.5	308 - 310			Slow infusion reduces risk
Midazolam	2.9 – 3.7	170 - 230			Small volume bolus over 5 mins
Morphine Sulphate	2.5 - 6	270 – 310			Small volume bolus over 5 mins
Noradrenaline	3 – 4.5	250 – 350	Warm	Phentolamine (2,6,7, 9)	Administration recommended via central vein
Ondansetron	3.3 - 4	270 – 400			Small volume bolus over 5 mins
Parenteral Nutrition	5.5	>900	Warm	Hyaluronidase (15)	Hyperosmolar solutions (e.g., parenteral nutrition and conventional ionic contrast media) exert osmotic pressure, and may result in compartment syndrome if infiltration occurs (2,5,12) Administration recommended via central vein
Pantoprazole	9 - 11.5	270 – 382			Administration recommended via central vein
Pentamidine	4 - 4.4	455			Administration recommended via central vein
Penicillin V	3-4				Slow infusion reduces risk
Phenytoin	12	312	Warm	Hyaluronidase (15)	Administration recommended via central vein
Phenylephrine	4.5 - 6.5	270 – 300			Administration recommended via central vein

Phenobarbital Sodium	10 - 11	10,800mOsmol/kg (200mg in 1mL undiluted) 289-296mOsmol/kg (100mg in 50mL or 100mL glucose 5%) 317-325mOsmol/kg (100mg in 50mL or 100mL sodium chloride 0.9%)	Cold		Administration recommended via central vein
Potassium chloride (over 40mmol/L)	4 - 7	800	Warm		Hypertonic solutions may cause prolonged depolarization and contraction of pre- and post-capillary smooth muscle sphincters, leading to tissue injury and ischaemia. (2,5,10,13) Administration recommended via central vein
Piperacillin (Tazocin)	4.5 – 7	4.5g recon with 20ml water 927mOsm/L 4.5g/20ml recon with water added to 50ml 0.9% sodium chloride 440mOsm/L 4.5g/20ml reconstituted with water added to 100ml 0.9% sodium chloride 386mOsm/L			Slow infusion reduces risk
Propofol	5 – 8.5	250-390			Slow infusion reduces risk
Rifampicin	7.8 – 8.8	259 – 303			Slow infusion reduces risk
Sodium Bicarbonate	7 – 8.5	8.4% = 2000mOsmol/L 4.2% = 1000mOsmol/L 1.4% = 333mOsmol/L 1.26% = 300mOsmol/L	Warm		Slow infusion reduces risk

Sodium chloride >3%	4.5 – 7	Sodium chloride 0.45% w/v:154mOsm/L Sodium chloride 0.9% w/v: 308mOsm/L Sodium chloride 1.8% w/v:616mOsm/L Sodium chloride 2.7% w/v: 924mOsm/L Sodium chloride 5% w/v: 1711mOsm/L	Warm		Slow infusion reduces risk
Tobramycin	3 – 6.5	285 – 320			Administration recommended via central vein
Vancomycin	2.5 -4.5	290	Cold		Administration recommended via central vein
Vasopressin	2.5 – 4.5	200 – 400			Administration recommended via central vein
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Vesicant Drugs that cause serious tissue damage and necrosis.

Primary mechanism of injury	Drug	Other mechanism(s)	Toxicity	Compresses*	Potential antidote(s) for peripheral catheter extravasation
Hyperosmotic (osmolarity >290 mOsm/L) tissue damage may resemble compartment syndrome	Contrast media, radiographic	Pressure effect of large volume	Pressure necrosis	Cold or as per radiologist	None
	Calcium solutions	Vasoconstriction, calcinosis	Necrosis, calcinosis	Warm if hyaluronidase used; cold without hyaluronidase	Hyaluronidase [¶] Severe forms of cutaneous calcinosis have been treated with sodium thiosulfate infusions, eg, once weekly for 3 weeks
	Dextrose ≥10%	NI	Necrosis	Warm if hyaluronidase used; cold without hyaluronidase	
	Magnesium sulphate	NI	Necrosis	Warm if hyaluronidase used; cold without hyaluronidase	None
	Mannitol >5%	NI	Necrosis	Warm if hyaluronidase used; cold without hyaluronidase	Hyaluronidase [¶]
	Nafcillin	NI	Necrosis	Warm if hyaluronidase used; cold without hyaluronidase	Hyaluronidase [¶]
	Parenteral nutrition	Acidic	Necrosis	Warm if hyaluronidase used; cold without hyaluronidase	Hyaluronidase [¶]
	Potassium chloride >40 mEq/L	NI	Necrosis	Warm if hyaluronidase used; cold without hyaluronidase	Hyaluronidase [¶]
	Sodium bicarbonate	NI	Necrosis	Warm if hyaluronidase used; cold without hyaluronidase	Hyaluronidase [¶]
	Sodium chloride >1%	NI	Necrosis	Warm if hyaluronidase used; cold without hyaluronidase	None
	Valproate sodium	NI	Necrosis	Warm if hyaluronidase used; cold without hyaluronidase	None

Primary mechanism of injury	Drug	Other mechanism(s)	Toxicity	Compresses*	Potential antidote(s) for peripheral catheter extravasation
Acidic	Amiodarone	NI	Necrosis	Cold or warm	None
	Gentamicin	NI	Necrosis	Cold	None
	Metronidazole	NI	Necrosis, gangrene	Cold	None
	Nicardipine	NI	Necrosis	Cold	None
	Promethazine	NI	Necrosis	Cold or warm	None
	Vancomycin	NI	Necrosis	Warm if hyaluronidase used; cold may be used if hyaluronidase is not used	Hyaluronidase may be considered based on mechanism of injury [¶]
Primary mechanism of injury	Drug	Other mechanism(s)	Toxicity	Compresses*	Potential antidote(s) for peripheral catheter extravasation
Alkaline	Aminophylline	Hyperosmotic	Ischemia	Cold	None
	Furosemide	NI	Necrosis	Cold	None
	Ganciclovir	NI	Necrosis	Cold	None
	Phenobarbital	NI	Necrosis	Cold	None
	Phenytoin	Hyperosmotic, precipitation	Necrosis, purple glove syndrome	Warm	Hyaluronidase [¶] or topical nitroglycerin ^Δ may be considered based on mechanism of injury
Primary mechanism of injury	Drug	Other mechanism(s)	Toxicity	Compresses*	Potential antidote(s) for peripheral catheter extravasation
Chemical	Amphotericin	NI	Phlebitis	Cold	None
	Digoxin	NI	Inflammation, apoptosis	Cold	None
	Foscarnet	NI	Phlebitis, arteritis	Cold	None
	Propofol	NI	Necrosis	Cold	None

Primary mechanism of injury	Drug	Other mechanism(s)	Toxicity	Compresses*	Potential antidote(s) for peripheral catheter extravasation
Vasoconstriction (causing local ischemia)	Dobutamine	NI	Necrosis	Warm	2% topical nitro-glycerin ointment ^Δ and/or terbutaline administered subcutaneously may be considered
	Dopamine	Acidic	Necrosis	Warm	Preferred: Phentolamine [◇] Alternative: 2% topical nitro-glycerine ointment ^Δ Terbutaline administered subcutaneously has been used if phentolamine is unavailable
	Epinephrine	Acidic	Necrosis	Warm	
	Methylene blue	NI	Cellular toxicity	Warm	
	Norepinephrine	Acidic	Necrosis	Warm	
	Phenylephrine	Acidic	Necrosis	Warm	
	Vasopressin	Acidic	Necrosis	Warm	None documented; 2% topical nitro-glycerine ointment ^Δ followed by phentolamine [◇] may be considered based on mechanism of injury

Management of extravasation injury from non-neoplastic agents^[1-4]

• Recommendations are based on case descriptions, experience at some leading centers, or extrapolated according to mechanism of injury.

• Antidotes listed are potential adjuncts to general extravasation injury care

NI: none identified.

* Dry cold or warm compresses should be applied to affected area for 20 minutes once every 4 to 6 hours for 1 to 2 days after removal of the catheter/needle and limb elevation. Cold compresses reduce pain, inflammation, and localize the vesicant potentially facilitating administration of an antidote. Application of warmth causes vasodilation and may facilitate dispersion and absorption.

¶ Hyaluronidase, administered as multiple subcutaneous injections around affected area, enhances dispersion and absorption of extravasated medications. Ideally, administer within 1 hour of extravasation; some benefit may be derived within 12 hours. If hyaluronidase is used, avoid cold compresses as they oppose its action; warm compresses are preferred.

Δ Alternative, if phentolamine is unavailable, is topical nitroglycerin 2%, applied as 1 inch (2.5 cm) strip over affected area, should be applied within 1 hour of extravasation. Avoid use of warm compresses if topical nitroglycerin is used. Local injection of terbutaline has also been tried as an antidote for vasopressors if phentolamine is unavailable.

◇ Phentolamine, administered as multiple subcutaneous injections around affected area, antagonizes alpha-adrenergic receptors stimulated by catecholamine extravasation. Ideally administer as soon as possible; some benefit may be derived within 12 hours.

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45. NIVAS Board 2024 National Infiltration and Extravasation toolkit. NIVAS
<https://nivas.org.uk/contentimages/main/NIVAS-Infiltration-and-Extravasation-toolkit-version-1-Feb-2024.pdf>

Full version control record

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This guideline has been registered with the Trust. However, clinical guidelines are guidelines only. The interpretation and application of clinical guidelines will remain the responsibility of the individual clinician. If in doubt, contact a senior colleague or expert. Caution is advised when using guidelines after the review date.

This guideline is for use in Frimley Health NHS Foundation Trust hospitals only. Any use outside this location will not be supported by the Trust and will be at the risk of the individual using it.

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Related Documents

Type	Document Name
Guideline	Part 1 Principles of Clinical Practice
Guideline	Part 2 Vascular access LocSSIP
Guideline	Part 3 Peripheral Cannulation
Guideline	Part 4 Venepuncture
Guideline	Part 5 Midline IV Catheters
Guideline	Part 6 PICCs
Guideline	Part 7 Short Term Non-Tunnelled CVCs
Guideline	Part 8 Implanted Ports and Tunnelled Cuffed CVCs
Guideline	Part 9 Arterial Catheters and Blood Sampling
Guideline	Part 10 Injectable Medicines
Guideline	Part 12 Long-term CVC Complications
Guideline	Infection Prevention and Control guidelines at https://guidelines.fhft.nhs.uk/