
Note: Active Table of Contents – Click to follow link

Table of Contents
EXECUTIVE SUMMARY................................................................................................................3
SCOPE ........................................................................................................................................4
METHODOLOGY ..........................................................................................................................4
DEFINITIONS ..............................................................................................................................4
INTRODUCTION ..........................................................................................................................5
RECOMMENDATIONS ..................................................................................................................6
UW HEALTH IMPLEMENTATION .................................................................................................8
TABLE 1: MEDICATION RISKS AND CONSIDERATIONS ............................................................10
FIGURE 1: MANAGEMENT OF EXTRAVASATION ......................................................................19
REFERENCES ............................................................................................................................20
Executive Summary
Guideline Overview
Many medications have the potential to cause tissue damage if extravasation occurs. The severity of the extravasation and amount of tissue injury is dependent upon the dose of the medication, concentration, site of administration, and duration of medication exposure.

Prevention is the most effective tool in the management of extravasation. In the event that extravasation occurs, a clear, concise policy is important to ensure prompt management of extravasation and help minimize the amount of tissue damage that results from extravasation. The most frequently encountered non-chemotherapeutic extravasation wounds are caused by hyperosmolar solutions and vasopressor agents. Vasopressors and hyperosmolar drugs both have an antidote, (phentolamine and hyaluronidase, respectively) that can help prevent tissue damage due to extravasation, and timely management and administration is important.

Key Practice Recommendations
1. Prevention is the most effective tool in the management of extravasation.
2. Vasopressors and hyperosmolar drugs have antidotes, (phentolamine and hyaluronidase, respectively) that may help to prevent tissue damage due to extravasation.
3. Timely management and administration of antidotes, if available, is key in the management of extravasation.

Companion Documents
1. Guidelines for the Management of Extravasation of Antineoplastic Agents

Pertinent UW Health Policies & Procedures
1. 7.08 Management of STAT Medications for Inpatient Units
2. Administrative Policy 8.20 – Adverse Drug Event Documentation
Scope
This guideline is to be used by nurses for the prevention and treatment of chemical phlebitis and extravasation of peripherally administered non-chemotherapeutic agents in both adult and pediatric patients in the inpatient setting. This guideline does not include management of the extravasation of contrast agents. For management of the extravasation of chemotherapeutic agents, please refer to the Guidelines for the Management of Extravasation of Antineoplastic Agents on U-Connect.

Methodology
A modified Grading of Recommendations Assessment, Development and Evaluation (GRADE) developed by the American Heart Association and American College of Cardiology (Figure 2) was used to assess the quality and strength of the evidence. Prescribing information was reviewed and supplemented with recommendations from Micromedex, Lexicomp, and Facts and Comparisons. Trissel’s™ 2 Clinical Pharmaceutics Database (parenteral compatibility) was used for all pH information unless otherwise specified. Primary literature is cited when tertiary sources did not provide recommendations.

Definitions
1. Extravasation - the unintentional administration of a potentially vesicant medication or solution into tissue surrounding the intended vascular channel
   1.1. Patients at an increased risk of extravasation include:
       1.1.1. Geriatric, pediatric and neonatal populations, as they have fragile skin and vascular structures and may be unable to report pain.
       1.1.2. Ventilated, sedated, or confused patients who may not be able to report signs and symptoms of extravasation.
       1.1.3. Individuals with small veins.
       1.1.4. Patients with poor circulation or decreased sensation (peripheral neuropathy, diabetes, peripheral vascular disease, Raynaud’s syndrome).
       1.1.5. Patients who have undergone multiple venipuncture attempts.
   1.2. Signs and symptoms of extravasation:
       1.2.1. Patient complains of burning, stinging, or pain at the injection site.
       1.2.2. Increased resistance when administering medications intravenously.
       1.2.3. Induration, erythema, or swelling at the injection site. Subsequent symptoms include blister formation, ulceration, skin necrosis, compartment syndrome and complex regional pain syndrome.
   1.3. Medication properties associated with an increased risk of soft tissue damage with extravasation:
       1.3.1. High concentration
       1.3.2. Low or high pH
       1.3.3. High osmolarity
       1.3.4. Size of vein
       1.3.5. Rate of flow
       1.3.6. Amount of diluents
1.3.7. Molecular weight

2. Vesicant - an agent that causes blistering and can result in tissue necrosis.\(^4\)

3. Irritant - an agent that causes local sensitivity reactions, resulting in pain and inflammation at the injection site. Irritants do not cause necrosis. Solutions with a pH of <5 or >9 commonly exhibit irritant properties. These solutions have a greater propensity to cause symptoms of phlebitis.\(^5\) Hypertonic solutions with an osmolality >600 mOsm/L can also cause phlebitis. Infiltration of hypertonic solutions can result in nerve damage or compartment syndrome.

4. Chemical Phlebitis - a chemical irritation affecting the innermost layer of the vein, called the tunica intima. Chemical phlebitis can result in cell destruction, infiltration and inflammation. Damage caused by chemical phlebitis can occur proximally or distally to the tip of the catheter.

4.1. Medication properties associated with an increased risk of phlebitis
   4.1.1. High concentration
   4.1.2. Low or high pH
   4.1.3. High osmolarity
   4.1.4. Size of vein
   4.1.5. Rate of flow
   4.1.6. Amount of diluents
   4.1.7. Molecular weight

5. Hyaluronidase - an antidote used for treating hyperosmolar drug extravasations.\(^6\)

   5.1. Mechanism of action: Increases the distribution and absorption of injected substances by modifying the permeability of connective tissue through the hydrolysis of hyaluronic acid. The increased permeability caused by hyaluronidase is transient and lasts for only 24-48 hours.

6. Phentolamine - an effective antidote for vasopressor extravasation.\(^7\)

   6.1. Mechanism of Action: Phentolamine is a nonspecific alpha-adrenergic blocking agent. It is a competitive antagonist of alpha-adrenergic agonists. By acting on both arterial and venous sites, vasoconstriction is reversed improving blood circulation.\(^8\)

7. Neonate – less than 30 days old
8. Infant – between one and 12 months old
9. Children – greater than one year old

B. Introduction

1. Many medications have the potential to cause tissue damage if extravasation occurs.\(^9\)

   The severity of the extravasation and amount of tissue injury is dependent upon the dose of the medication, concentration, site of administration, and duration of medication exposure.\(^5\) Prevention is the most effective tool in the management of extravasation. In the event that extravasation occurs, a clear, concise policy is important to ensure prompt management of extravasation and help minimize the amount of tissue damage that results from extravasation. The most frequently encountered non-chemotherapeutic extravasation wounds are caused by hyperosmolar solutions and vasopressor agents. Vasopressors and hyperosmolar drugs both have an antidote, (phentolamine and hyaluronidase, respectively) that can help prevent tissue damage due to extravasation, and timely management and administration is important.
C. Recommendations

1. **Prevention of Extravasation**

   1.1. Become familiar with medications that are likely to cause soft tissue damage if extravasation occurs and precautions to take with medications (Table 1). If unsure of the risk of an extravasated medication, consult a reputable drug information reference or pharmacist.

   1.2. When administering an IV push medication, use a large peripheral vein with appropriately diluted medication. Avoid foot veins for irritant or vesicant medications. Avoid placing the intravenous catheter in areas of flexion. (Class III, Level C)

   1.3. Use the smallest gauge and shortest catheter to accommodate the prescribed therapy. (Class I, Level C)

   1.4. Stabilize the catheter to minimize movement at the insertion site. (Class I, Level C)

   1.5. Flush the patient’s line and establish patency before administering medication. (Class I, Level C)

   1.6. Administer medications at appropriate rates and ensure dilution to appropriate concentrations. (Class I, Level C)

   1.7. Continuous administration of vesicant medication should not be given in a peripheral vein. (Class I, Level C)

   1.8. Medications with a high potential for soft tissue damage if extravasation occurs should be administered in the largest vein possible. (Class I, Level C)

   1.9. If therapy with an irritant medication is expected to last longer than six days, the placement of a central vascular access device line should be considered. (Class I, Level C)

   1.10. Ask patients to report burning, pain or stinging. (Class I, Level C)

   1.11. Observe the site during the administration of medications checking for swelling, discoloration or inflammation. (Class I, Level C)

   1.12. Do not rely on alarms from electronic infusion devices to detect infiltration or extravasation. These same devices are used to administer medications subcutaneously, and the pump cannot distinguish if it is in the vessel or if the vessel has been damaged. (Class I, Level C)

   1.13. In the event that extravasation occurs and vascular access is needed, use an alternate extremity or site remote from the extravasation. (Class I, Level C)

2. **Prevention of Chemical Phlebitis**

   2.1. Use large veins to increase hemodilution. (Class I, Level C)

   2.2. Consider the use of a 10mL syringe over a 3mL syringe when administering medications known to cause tissues damage if extravasation occurs. (Class I, Level C)

   2.3. Rotate infusion sites often. (Class I, Level C)

   2.4. The first sign of phlebitis is usually pain on palpation; change IV site often to prevent the progression of phlebitis. (Class I, Level C)

   2.5. If therapy will last longer than six days, the need for a central vascular access line should be discussed with the patient’s physician. (Class I, Level C)

   2.6. See Table 1 for considerations regarding specific IV medications.

3. **Management of Extravasation**

   11, 12
3.1. See Figure 1 for general measures for the management of extravasation.

3.2. It is not known if application of physical modalities to extravasations is helpful and in fact may have untoward consequences and worsen the outcome (Class III, Level C). Prior to applying physical modalities, and specifically heat, seek knowledgeable medical and pharmacy advice.

4. **Treatment of Extravasation**

4.1. See Table 1 for management and antidote information for specific IV medications.

4.2. Medications to treat extravasation should be entered and processed as STAT medications (see 7.08 Management of STAT Medications for Inpatient Units)

4.3. Phentolamine mesylate (Oraverse®)

4.3.1. Phentolamine mesylate may not be effective if more than 12 hours have elapsed since the onset of the extravasation event.\(^7,13\) (Class IIb, Level C)

4.3.2. Phentolamine mesylate (Oraverse®) administration\(^13,14\)

4.3.2.1. Remove IV catheter.

4.3.2.2. Clean site with chlorhexidine.

4.3.2.3. Obtain 1.18 mg (5 mL) syringe of phentolamine mesylate (OraVerse\(^\text{®}\)) from Central pharmacy (may request second syringe if necessary)

4.3.2.4. Using a new needle after each injection, inject 0.5 mL intradermally in a circular pattern around the perimeter of the extravasation.

4.3.3. For neonates, the maximum phentolamine dose is 0.1 mg/kg or 2.5 mg (10.6 mL) total dose\(^16\)

4.4. Alternatives to phentolamine (due to shortages):

4.4.1.1. Nitroglycerin topical 2% ointment (Class IIb, Level C):

4.4.1.1.1. Apply 4 mm/kg as a thin ribbon to the affected areas. May repeat after 8 hours if needed\(^13\)

4.4.1.2. Alternative- apply a 1-inch strip on the affected site\(^14\)

4.4.1.2.1. Terbutaline (Class IIb, Level C)\(^15\):

4.4.1.2.1.1. Administer subcutaneously throughout the extravasation area using a solution of terbutaline 1 mg diluted to 10 mL in normal saline

4.4.1.2.2. For a large extravasation site; administration volume may vary from 3-10 mL, or 1 mg diluted in 1 mL normal saline

4.4.1.2.3. For a small/distal extravasation site; administration volume may vary from 0.5-1 mL in normal saline

4.5. Hyaluronidase

4.5.1. Hyaluronidase is most effective when given within the first hour after extravasation, and should not be given after 3 hours.\(^16\) (Class I, Level C)

4.5.2. Hyaluronidase administration\(^16\)

4.5.2.1. Clean site with chlorhexidine.

4.5.2.2. Obtain a 1 mL hyaluronidase (150-200 units/mL, depending on stocked manufacturer) syringe from pharmacy.

4.5.2.3. Inject 0.2 mL through the IV catheter before removing it from the extravasation site.

4.5.2.4. Remove IV catheter.
4.5.2.5. Using sterile technique and a 25 gauge needle, inject 0.2 mL subcutaneously at the edge of the infiltrate.

4.5.2.6. Using a new needle after each injection, continue making 0.2 mL injections in a circular pattern around the perimeter of the extravasation until all hyaluronidase is used.

5. Management and Treatment of Chemical Phlebitis
   5.1. Remove peripheral venous catheter.
   5.2. It is not known if application of physical modalities to chemical phlebitis is helpful and in fact may have untoward consequences and worsen the outcome. (Class III, Level C)
      Prior to applying physical modalities, and specifically heat, seek knowledgeable medical and pharmacy advice.
   5.3. Consider treatment with an analgesic or anti-inflammatory medication. (Class IIb, Level C)

6. Documentation of Extravasation and Chemical Phlebitis
   6.2. Extravasation events should be reported as adverse drug events within Patient Safety Net and should be documented within the patient’s permanent medical record.
   6.3. Documentation of the incident within Patient Safety Net and within the patient’s permanent medical record should include the following information:
      6.3.1. Date and time of occurrence.
      6.3.2. Site of administration, condition of the vein, and age of the IV site.
      6.3.3. Method of administration and equipment used with administration.
      6.3.4. Patient dialogue including symptoms, complaints etc.
      6.3.5. Suspected agent and any other medications administered or procedures completed around the same time period.
      6.3.6. Treatment interventions.
      6.3.7. Plan for follow-up care.

D. UW Health Implementation

Potential Benefits:
This clinical practice guideline provides a standardized approach to the management and treatment of extravasation of peripherally administered non-chemotherapeutic agents. A decreased risk of adverse effects secondary to timely management of extravasation is possible through implementation of this clinical practice guideline.

Potential Harms:
Termination of intravenous medications in the event of extravasation may pose harm to patient. Phentolamine and hyaluronidase both carry risks for adverse events which may pose a potential harm to the patient.

Implementation Tools/Plan
1. Release of the guideline will be advertised in the Clinical Knowledge Management Corner within the Best Practice newsletter.
2. Pharmacy and nursing will be informed of changes to the guideline.
3. This guideline will be searchable on U-connect using the terms: extravasation, vesicant, irritant, phentolamine, hyaluronidase, terbutaline
4. Nursing educational services will be provided with the document to ensure adequate staff education.
5. Ongoing monitoring and assessment of Patient Safety Net reports of extravasation will occur.

E. Disclaimer
1. This CPG provides an evidence-based approach for treatment of adult and pediatric extravasation of peripherally administered non-chemotherapeutic agents. It is understood that occasionally patients will not match the conditions considered in the guideline.
2. CPGs are described to assist clinicians by providing a framework for the evaluation and treatment of patients. This Clinical Practice Guideline outlines the preferred approach for most patients. It is not intended to replace a clinician’s judgment or to establish a protocol for all patients. It is understood that some patients will not fit the clinical condition contemplated by a guideline and that a guideline will rarely establish the only appropriate approach to a problem.
### F. Appendix A

**Table 1: Medication risks and considerations (Class I, Level C)**

<table>
<thead>
<tr>
<th>Intravenous Medication</th>
<th>pH[^17,18]</th>
<th>Potential Soft Tissue Damage with Extravasation or Chemical Phlebitis[^17,19-21]</th>
<th>Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acetazolamide (Diamox®)</td>
<td>9.6</td>
<td>Phlebitis</td>
<td>Use large veins</td>
</tr>
<tr>
<td>Acyclovir (Zovirax®)</td>
<td>10.85 - 11.5</td>
<td>Phlebitis</td>
<td>Rotate infusion sites often</td>
</tr>
<tr>
<td>Alprostadil (Prostin VR Pediatric®)</td>
<td>5.5</td>
<td>Phlebitis</td>
<td>Use large veins</td>
</tr>
<tr>
<td>Aminophylline (2:1 complex of theophylline and ethylenediamine)</td>
<td>8.6 - 9.0</td>
<td>Phlebitis</td>
<td>Rotate sites often; Antidote: Hyaluronidase</td>
</tr>
<tr>
<td>Amiodarone (Cordarone®)</td>
<td>3.5 - 4.5</td>
<td>Phlebitis</td>
<td>Phlebitis incidence increases with concentrations above 2.5 mg/mL. Central vascular administration preferred; Administration of continuous infusions using an in-line filter is recommended to reduce the incidence of phlebitis</td>
</tr>
</tbody>
</table>
| Amphotericin B Conventional (Fungizone®) | 5 - 6 | Phlebitis                                                                      | The addition of heparin 1,000 units per infusion can decrease the incidence of phlebitis. The use of a pediatric scalp-vein needle may lessen the incidence of thrombophlebitis.
<p>| Calcium Chloride 10%   | 5.5 - 7.5  | Severe necrosis and sloughing may occur if injected into tissues            | Push slowly through a small needle into a large veins; If extravasation occurs, stop infusion immediately and disconnect (leave needle/cannula in place); gently aspirate extravasated solution (do NOT flush the line); initiate hyaluronidase antidote; remove needle/cannula; apply dry cold compresses elevate extremity. |
| Calcium Gluconate 10%  | 6 - 8.2    | Local tissue necrosis occurs with extravasation                          | Inject through a small needle into a large vein to avoid possible necrosis; Antidote: Hyaluronidase |</p>
<table>
<thead>
<tr>
<th>Intravenous Medication</th>
<th>pH$^{17,18}$</th>
<th>Potential Soft Tissue Damage with Extravasation or Chemical Phlebitis$^{17,18-21}$</th>
<th>Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cefotaxime (Claforan&lt;sup&gt;®&lt;/sup&gt;)</td>
<td>5.0 - 7.5</td>
<td>Potential soft tissue damage with extravasation, phlebitis</td>
<td>Rotate infusion site.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Monitor infusion sites regularly.$^{23}$</td>
</tr>
<tr>
<td>Dextrose ≥10%</td>
<td>3.2 - 6.5</td>
<td>Potential soft tissue damage with extravasation</td>
<td>Stop infusion immediately and disconnect (leave needle/cannula in place); gently aspirate extravasated solution (do NOT flush the line); initiate hyaluronidase antidote; remove needle/cannula; apply dry cold compresses, elevate extremity. Use large veins and confirm vein patency. In patients with poor venous access consider IM glucagon to treat hypoglycemia.</td>
</tr>
<tr>
<td>Digoxin (Lanoxin&lt;sup&gt;®&lt;/sup&gt;)</td>
<td>6.8 - 7.2</td>
<td>Potential soft tissue damage with extravasation</td>
<td>If extravasation occurs, stop I.V. administration immediately and disconnect (leave cannula/needle in place); gently aspirate extravasated solution (do NOT flush the line); remove needle/cannula; elevate extremity.</td>
</tr>
<tr>
<td>Dobutamine (Dobutrex&lt;sup&gt;®&lt;/sup&gt;)</td>
<td>2.5 - 5.5</td>
<td>Phlebitis with infiltration</td>
<td>Use large veins</td>
</tr>
<tr>
<td>Dopamine (Intropin&lt;sup&gt;®&lt;/sup&gt;)</td>
<td>2.5 - 5.0</td>
<td>Necrosis with extravasation</td>
<td>Requires central vascular administration.</td>
</tr>
<tr>
<td>Doxycycline (Vibramycin&lt;sup&gt;®&lt;/sup&gt;, Doxy 100&lt;sup&gt;®&lt;/sup&gt;)</td>
<td>1.8 - 3.3</td>
<td>Prolonged IV administration may cause thrombophlebitis</td>
<td>Use of central line is preferred</td>
</tr>
<tr>
<td>Intravenous Medication</td>
<td>pH\textsuperscript{17,18}</td>
<td>Potential Soft Tissue Damage with Extravasation or Chemical Phlebitis\textsuperscript{17,18-21}</td>
<td>Considerations</td>
</tr>
<tr>
<td>------------------------</td>
<td>----------------</td>
<td>-------------------------------------------------</td>
<td>----------------</td>
</tr>
</tbody>
</table>
| Epinephrine (Adrenalin\textsuperscript{®}) | 2.2 - 5 | Potential soft tissue damage with extravasation | Central line preferred.  
If extravasation occurs, stop infusion immediately and disconnect (leave cannula/needle in place); gently aspirate extravasated solution (do NOT flush the line); remove needle/cannula; elevate extremity.  
Apply dry warm compress  
Antidote: Phentolamine |
| Erythromycin lactobionate (Erythrocin Lactobionate\textsuperscript{®}) | 6.5 - 7.5 | Phlebitis  
The severity of venous irritation may be reduced by use of in-line filtration. | If phlebitis/pain occurs, consider diluting further (eg, 1:5) if fluid status of the patient will tolerate, or consider administering in larger available vein  
Cold compress |
| Esmolol (Brevibloc\textsuperscript{®}) | 4.5 - 5.5 | Injection site pain  
Thrombophlebitis, necrosis, blistering | Use large veins. Avoid small veins or butterfly catheters.\textsuperscript{26}  
If local infusion site reaction develops, use an alternative site.  
If extravasation occurs, stop infusion immediately and disconnect (leave cannula/needle in place); gently aspirate extravasated solution (do not flush the line); remove needle/cannula; elevate extremity.  
Central line preferred |
| Foscarnet (Foscavir\textsuperscript{®}) | 7.4 | Phlebitis | Administer only into vein with adequate blood flow to prevent phlebitis.\textsuperscript{27}  
Peripherally administered foscarnet must be diluted to 12mg/mL |
<table>
<thead>
<tr>
<th>Intravenous Medication</th>
<th>pH&lt;sup&gt;17,18&lt;/sup&gt;</th>
<th>Potential Soft Tissue Damage with Extravasation or Chemical Phlebitis&lt;sup&gt;17,19-21&lt;/sup&gt;</th>
<th>Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fosphenytoin (Cerebyx&lt;sup&gt;®&lt;/sup&gt;)</td>
<td>8.6 - 9.0</td>
<td>Thrombophlebitis Edema, discoloration, and pain distal to the site of injection (described as &quot;purple glove syndrome&quot;) have also been reported following peripheral intravenous fosphenytoin injection. This may or may not be associated with extravasation. The syndrome may not develop for several days after injection.</td>
<td>Confirm vein patency</td>
</tr>
<tr>
<td>Immune Globulin (GAMMAGARD&lt;sup&gt;®&lt;/sup&gt;)</td>
<td>4.0 - 7.2</td>
<td>Phlebitis</td>
<td>Use large veins. Risk increases with higher concentration (&gt;10%).</td>
</tr>
<tr>
<td>Lorazepam (Ativan&lt;sup&gt;®&lt;/sup&gt;)</td>
<td>5.7</td>
<td>Potential soft tissue damage with extravasation/phlebitis</td>
<td>IV injection should be made slowly. If a patient complains of pain during administration, stop immediately to determine correct placement.</td>
</tr>
<tr>
<td>Mannitol</td>
<td>4.5 - 7.0</td>
<td>Potential soft tissue damage with extravasation, thrombophlebitis, phlebitis</td>
<td>If extravasation occurs, stop infusion immediately and disconnect (leave needle/cannula in place); gently aspirate extravasated solution (do NOT flush the line); initiate hyaluronidase antidote; remove needle/cannula; apply dry cold; elevate extremity. Antidote: Hyaluronidase</td>
</tr>
<tr>
<td>Nicardipine hydrochloride (Cardene&lt;sup&gt;®&lt;/sup&gt;)</td>
<td>3.7 - 4.7 (premixed solutions)</td>
<td>Phlebitis Thrombophlebitis</td>
<td>Do not use small veins, such as those on the dorsum of the hand or wrist. Use large peripheral veins or central veins. Change peripheral infusion site every 12 hours to minimize the risk of venous irritation.</td>
</tr>
<tr>
<td>Nitroprusside (Nitropress&lt;sup&gt;®&lt;/sup&gt;)</td>
<td>3.5 - 6.0</td>
<td>Irritation at infusion site Extravasation</td>
<td></td>
</tr>
<tr>
<td>Intravenous Medication</td>
<td>pH(^{17,18})</td>
<td>Potential Soft Tissue Damage with Extravasation or Chemical Phlebitis(^{17,18-21})</td>
<td>Considerations</td>
</tr>
<tr>
<td>----------------------------------------</td>
<td>----------------</td>
<td>----------------------------------------------------------------------------------</td>
<td>--------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Norepinephrine (Levophed(^{®}))</td>
<td>3.0 - 4.5</td>
<td>Potential soft tissue damage with extravasation.(^{31})</td>
<td>Requires central line administration</td>
</tr>
<tr>
<td></td>
<td></td>
<td>The infusion site should be checked frequently for free flow. Local necrosis might ensue due to the vasoconstrictive action of the drug.</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Check infusion site frequently for free flow, blanching along infused vein.</td>
<td></td>
</tr>
<tr>
<td>Partial Parenteral Nutrition (PPN)</td>
<td>N/A</td>
<td>Potential soft tissue damage with extravasation</td>
<td>Use large veins and rotate sites frequently</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Antidote: Hyaluronidase</td>
</tr>
<tr>
<td>Pentamidine isethionate (Pentam(^{®}))</td>
<td>4.3 - 5.4</td>
<td>Phlebitis</td>
<td>Use large veins</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Extravasations may cause ulceration, tissue necrosis and/or sloughing at the injection site.(^{32})</td>
<td>If extravasation occurs, stop infusion immediately and disconnect (leave cannula/needle in place); gently aspirate extravasated solution (do NOT flush the line); remove needle/cannula; elevate extremity. Apply dry warm compresses.(^{32})</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pentobarbital (Nembutal(^{®}))</td>
<td>9.0 - 10.5</td>
<td>Extravascular injection may cause local tissue damage with subsequent necrosis; consequences of intra-arterial injection may vary from transient pain to gangrene of the limb. Stop injection if any complaints of pain.(^{33})</td>
<td>Avoid intra-arterial administration.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Release of the tourniquet or restrictive garments to permit dilution of injected drug, brachial plexus block, prevention of thrombosis by early anticoagulant therapy, and supportive treatment.</td>
</tr>
<tr>
<td>Intravenous Medication</td>
<td>pH$^{17,18}$</td>
<td>Potential Soft Tissue Damage with Extravasation or Chemical Phlebitis$^{17,19-21}$</td>
<td>Considerations</td>
</tr>
<tr>
<td>------------------------------------------------------------</td>
<td>--------------</td>
<td>----------------------------------------------------------------------------------</td>
<td>--------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Phenobarbital sodium (Luminal®)</td>
<td>9.2 - 10.2</td>
<td>Potential soft tissue damage with extravasation, Phlebitis/thrombophlebitis</td>
<td>Treat with the application of moist heat on the affected area.$^{34}$</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Extravascular injection may cause local tissue damage with subsequent necrosis; consequences of intra-arterial injection may vary from transient pain to gangrene of the limb. Any complaint of pain in the limb warrants stopping the injection.$^{34}$</td>
<td></td>
</tr>
<tr>
<td>Phenylephrine hydrochloride (Neo-Synephrine®)</td>
<td>3.0 - 6.5</td>
<td>Extravasation associated with tissue slough or necrosis</td>
<td>Central line preferred</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Antidote: Phentolamine</td>
</tr>
<tr>
<td>Phenytoin (Dilantin®)</td>
<td>12</td>
<td>Potential soft tissue damage with extravasation and purple glove syndrome (may not develop for several days after the injection)$^{35}$</td>
<td>Use large veins (central line preferred) and confirm vein patency; Follow administration with a normal saline flush</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Avoid small hand, wrist or foot veins for administration. If extravasation occurs, discontinue the injection/infusion and elevate the limb.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>May consider hyaluronidase based on case report of its successful use in a 14 month old$^{36}$</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Antidote: Hyaluronidase</td>
</tr>
<tr>
<td>Potassium chloride, potassium acetate</td>
<td>4.0 - 8.0</td>
<td>Phlebitis</td>
<td>Confirm vein patency; extravasation will cause necrosis, have patient report burning or stinging</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Potential soft tissue damage with extravasation</td>
<td>Local infiltration of the affected area with hyaluronidase may often reduce venospasm and dilute the potassium remaining in the tissues locally. Local application of heat may also be helpful.$^{37}$</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Antidote: Hyaluronidase</td>
</tr>
<tr>
<td>Intravenous Medication</td>
<td>pH&lt;sup&gt;17,18&lt;/sup&gt;</td>
<td>Potential Soft Tissue Damage with Extravasation or Chemical Phlebitis&lt;sup&gt;17,19-21&lt;/sup&gt;</td>
<td>Considerations</td>
</tr>
<tr>
<td>------------------------</td>
<td>--------------------</td>
<td>-----------------------------------------------------------------</td>
<td>-----------------</td>
</tr>
<tr>
<td>Promethazine (Phenergan®)</td>
<td>4.0 - 5.5</td>
<td>Potential soft tissue damage with extravasation including burning, pain, erythema, swelling, sensory loss, palsies, paralysis, severe spasm of distal vessels, thrombophlebitis, venous thrombosis, phlebitis, abscesses, tissue necrosis, and gangrene. In some cases, surgical intervention, including fasciotomy, skin graft, and/or amputation.</td>
<td>If a patient complains of pain during intended intravenous injection, stop the injection immediately; suspect inadvertent intra-arterial injection or perivascular extravasation. If extravasation occurs, stop infusion immediately and disconnect (leave cannula/needle in place); gently aspirate extravasated solution (do NOT flush the line); remove needle/cannula; elevate extremity. Apply dry cold compresses. Use large veins and confirm vein patency. Consider IM administration in patients with poor IV access.</td>
</tr>
<tr>
<td>Propofol (Diprivan®)</td>
<td>7.0 - 8.5</td>
<td>Local pain, swelling, blisters, and/or tissue necrosis. Phlebitis</td>
<td>Causes local pain during injection. Minimize by using lidocaine prior to injection and use large veins.</td>
</tr>
<tr>
<td>Rifampin (Rifadin®)</td>
<td>7.8 - 8.8</td>
<td>Potential soft tissue damage with extravasation</td>
<td>If irritation and inflammation observed, the infusion should be discontinued and restarted at another site.</td>
</tr>
<tr>
<td>Sodium Bicarbonate 8.4%</td>
<td>7.0 - 8.5</td>
<td>Chemical cellulitis, necrosis, ulceration and sloughing have been noted with extravasations</td>
<td>Confirm vein patency; promptly elevate the body part affected, provide warmth, and hyaluronidase. Antidote: Hyaluronidase.</td>
</tr>
<tr>
<td>Sodium Chloride 3% (Hypertonic Saline)</td>
<td>4.8</td>
<td>Potential soft tissue damage with extravasation</td>
<td>Causes severe tissue necrosis with extravasation. Central line preferred.</td>
</tr>
<tr>
<td>Sodium Tetradecyl Sulfate (Sotradecol®)</td>
<td>7.9</td>
<td>Potential soft tissue damage and necrosis with extravasation Phlebitis/thrombophlebitis</td>
<td>Monitor closely for extravasation.</td>
</tr>
<tr>
<td>Intravenous Medication</td>
<td>pH\textsuperscript{17,18}</td>
<td>Potential Soft Tissue Damage with Extravasation or Chemical Phlebitis\textsuperscript{17,18-21}</td>
<td>Considerations</td>
</tr>
<tr>
<td>--------------------------------------------</td>
<td>-----------------------------</td>
<td>-----------------------------------------------------------------------------------------------</td>
<td>-----------------------------------------------------------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Sulfamethoxazole/Trimethoprim (Bactrim\textsuperscript{®}, Septra\textsuperscript{®})</td>
<td>~10</td>
<td>Potential soft tissue damage with extravasation/phlebitis</td>
<td>Use large veins and confirm vein patency</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>If extravasation occurs, discontinue the infusion and restart at another site\textsuperscript{43}</td>
</tr>
<tr>
<td>Total Parenteral Nutrition (TPN)</td>
<td>N/A</td>
<td>Potential soft tissue damage with extravasation</td>
<td>Use large veins and rotate sites frequently</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Antidote: <strong>Hyaluronidase</strong></td>
</tr>
<tr>
<td>Tromethamine (Tham\textsuperscript{®})</td>
<td>8.4 - 8.7</td>
<td>Local tissue damage and sloughing may occur if extravasation occurs. Chemical phlebitis and venospasm also have been reported.</td>
<td>If extravasation occurs, stop I.V. administration immediately and disconnect (leave cannula/needle in place); gently aspirate extravasated solution (do NOT flush the line); remove needle/cannula; elevate extremity. Hyaluronidase infiltrated into the affected area dilutes the solution remaining in the tissues. Consider local infiltration of phentolamine\textsuperscript{44}</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Antidote: <strong>Hyaluronidase</strong></td>
</tr>
<tr>
<td>Vancomycin (Vancocin\textsuperscript{®})</td>
<td>2.5 - 4.5 (reconstituted)</td>
<td>Potential soft tissue damage with extravasation</td>
<td>Rotate infusion sites; use large veins, central vascular access device consult for prolonged therapy.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Phlebitis/thrombophlebitis</td>
<td>Consider further dilution and a slower infusion rate in patients with smaller veins.</td>
</tr>
<tr>
<td></td>
<td>3 - 5 (premix)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vasopressin (Pitressin\textsuperscript{®})</td>
<td>2.5 - 4.5</td>
<td>Potential soft tissue damage with extravasation</td>
<td>Confirm vein patency. Central line preferred</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>If extravasation occurs, stop infusion immediately and disconnect (leave cannula/needle in place); gently aspirate extravasated solution (do NOT flush the line); remove needle/cannula; elevate extremity. Initiate phentolamine (or alternative antidote).</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Antidote: <strong>Phentolamine</strong></td>
</tr>
<tr>
<td>Intravenous Medication</td>
<td>pH(^{17,18})</td>
<td>Potential Soft Tissue Damage with Extravasation or Chemical Phlebitis(^{17,18-21})</td>
<td>Considerations</td>
</tr>
<tr>
<td>------------------------</td>
<td>----------------</td>
<td>---------------------------------------------------------------------------------</td>
<td>----------------</td>
</tr>
<tr>
<td>Verteporfin (Visudyne(^{®}))</td>
<td>No information</td>
<td>Potential soft tissue damage and burns with extravasation</td>
<td>Use large veins, confirm vein patency</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>If extravasation occurs, the area must be thoroughly protected from direct light until the swelling and discoloration have faded in order to prevent the occurrence of a local burn which could be severe. Treat with cold compress.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>If emergency surgery is necessary within 48 hours after treatment, as much of the internal tissue as possible should be protected from intense light.(^{45})</td>
</tr>
</tbody>
</table>
Figure 1: Management of Extravasation\textsuperscript{11,12} (Class I, Level C)

1. **Stop infusion immediately**

2. **Assess pulses and circulation distal to the infusion site**

3. **Mark the affected area with a felt-tip pen**

4. **Elevate the extremity above the patient's heart. Avoid pressure or friction to the skin. **Avoid heat, cold and other physical modalities (massage, ultrasound, etc unless otherwise specified)**

5. **Check Table 1 for antidotes for certain medications**

   - **Is an antidote listed?**
     - **Yes**: Notify patient's physician and obtain order for antidote
     - **No**: Aspirate while removing IV catheter

6. **Administer antidote as outlined in E.4, and remove catheter as instructed**

7. **Consider the need for consultation with a plastic surgeon**

8. **Document occurrence in patient's clinical record and within Patient Safety Net**

9. **Observe the wound closely over the next several days**

10. **After 48 hours, encourage the patient to maintain elevation of the extremity, but also use the extremity normally to promote full recovery of the area**
G. References


41. Sodium bicarbonate 8.4% [package insert]. Lane Cove, Australia: Phebra Pty Ltd; 2011.
44. Tham (Tromethamine) injection [package insert]. Lake Forest, IL: Hospira Inc; 2005.
http://www.accessdata.fda.gov/drugsatfda_docs/label/2012/021119s022lbl.pdf.
Figure 2: Quality of Evidence and Strength of Recommendation Grading Matrix

<table>
<thead>
<tr>
<th>Level A</th>
<th>Level B</th>
<th>Level C</th>
</tr>
</thead>
<tbody>
<tr>
<td>Multiple populations evaluated*</td>
<td>Limited populations evaluated*</td>
<td>Very limited populations evaluated*</td>
</tr>
<tr>
<td>Data derived from multiple randomized clinical trials or meta-analyses</td>
<td>Data derived from a single randomized trial or nonrandomized studies</td>
<td>Only consensus opinion of experts, case studies, or standard of care</td>
</tr>
</tbody>
</table>

**Suggested phrases for writing recommendations**
- should
- is recommended
- is indicated
- is useful/effective/beneficial
- is probably recommended or indicated
- may/might be considered
- may/might be reasonable
- usefulness/effectiveness is unknown/unclear/uncertain or not well established
- is not recommended
- is not indicated
- should not
- is not useful/effective/beneficial
- may be harmful

**Size of Treatment Effect**

<table>
<thead>
<tr>
<th>Class I</th>
<th>Class IIA</th>
<th>Class IIB</th>
<th>Class III</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benefit &gt;&gt;&gt; Risk</td>
<td>Benefit &gt;&gt; Risk</td>
<td>Benefit ≥ Risk</td>
<td>Risk ≥ Benefit</td>
</tr>
<tr>
<td>Procedure/Treatment SHOULD be performed/administered</td>
<td>Additional studies with focused objectives needed</td>
<td>IT IS REASONABLE to perform procedure/administer treatment</td>
<td>Procedure/Treatment MAY BE CONSIDERED</td>
</tr>
<tr>
<td>Recommendation that procedure or treatment is useful/effective</td>
<td>Recommendation in favor of treatment or procedure being useful/effective</td>
<td>Recommendation’s usefulness/efficacy less well established</td>
<td>Recommendation that procedure or treatment is not useful/effective and may be harmful</td>
</tr>
<tr>
<td>Sufficient evidence from multiple randomized trials or meta-analyses</td>
<td>Some conflicting evidence from multiple randomized trials or meta-analyses</td>
<td>Greater conflicting evidence from multiple randomized trials or meta-analyses</td>
<td>Sufficient evidence from multiple randomized trials or meta-analyses</td>
</tr>
<tr>
<td>Recommendation that procedure or treatment is useful/effective</td>
<td>Evidence from single randomized trial or nonrandomized studies</td>
<td>Recommendation’s usefulness/efficacy less well established</td>
<td>Evidence from single randomized trial or nonrandomized studies</td>
</tr>
<tr>
<td>Recommendation in favor of treatment or procedure being useful/effective</td>
<td>Some conflicting evidence from single randomized trial or nonrandomized studies</td>
<td>Greater conflicting evidence from single randomized trial or nonrandomized studies</td>
<td></td>
</tr>
<tr>
<td>Recommendation that procedure or treatment is useful/effective</td>
<td></td>
<td>Recommendation’s usefulness/efficacy less well established</td>
<td></td>
</tr>
<tr>
<td>Only diverging expert opinion, case studies, or standard of care</td>
<td></td>
<td>Greater conflicting evidence from single randomized trial or nonrandomized studies</td>
<td></td>
</tr>
<tr>
<td>Only expert opinion, case studies, or standard of care</td>
<td></td>
<td>Only diverging expert opinion, case studies, or standard of care</td>
<td></td>
</tr>
<tr>
<td>Suggested phrases for writing recommendations*</td>
<td></td>
<td>Suggested phrases for writing recommendations*</td>
<td></td>
</tr>
</tbody>
</table>