

Management of Non-Chemo Drug Extravasation

Some non-chemo drugs may be especially likely to harm soft tissue with infiltration or extravasation.²¹ **They can be classified as follows:**^{16,17,21,22,25}

- Hyperosmolar agents, which cause osmotic shifts leading to inflammation and cell death (e.g., hypertonic saline, parenteral nutrition, sodium bicarbonate).
 - Common preventive strategies: Infuse through a central line. In particular, ≥ 600 mOsm/L may not be well-tolerated by peripheral veins.^{21,22}
- Drugs with very high or low pH, which damage tissue and cause vasoconstriction (e.g., acyclovir, amiodarone, phenytoin, vancomycin).
 - Common preventive strategies: Dilute medication and infuse slowly. See detailed recommendations below.
- Vasopressors, which cause ischemia and necrosis (e.g., norepinephrine, vasopressin).
 - Common preventive strategies: Infuse through a central line, especially for longer durations and if a large peripheral vein is not available.²⁵

General treatment for non-chemo extravasations is as follows:^{1-3,15,17,18,21,22}

- Immediately stop the infusion
 - Aspirate residual drug through the needle or catheter
 - Elevate the affected limb to minimize swelling
 - Apply a cold compress to reduce swelling and localize the agent* OR
 - Apply a warm compress for vasodilation and to disperse the agent*
 - Administer an analgesic
- *Apply compresses, dry not moist, for 20 minutes every 6 to 8 hours for up to 3 days.^{2,22}

Drug treatments depend on the causative agent, and include the following, along with doses that have been cited in the literature:

- To distribute the causative agent away from the site (commonly used for hyperosmolar and pH-related extravasation injury):
 - Hyaluronidase (U.S. only) 150 units/mL, 0.2 mL intradermally or subcutaneously, into five sites around the area of extravasation.⁸ 15 units/mL has also been used (same instructions as above).²² Administer within about one hour of extravasation.^{18,22} Note that warm compresses may complement the action of hyaluronidase, while cold compresses may act in opposition.
- To counteract local vasoconstriction (commonly used for vasopressor extravasation):
 - Phentolamine (Canada only) 5 to 10 mg, in 10 to 20 mL normal saline, subcutaneously, into the area of extravasation as ten 1 mL injections. Administer within 12 hours of extravasation.²²
 - Terbutaline (U.S. only) 1 mg, in 10 mL normal saline for larger areas or 1 mL normal saline for localized ischemia, subcutaneously.²¹
 - Nitroglycerin topical formulations that have been used include 2% ointment, as a 1-inch strip, every 8 hours PRN.^{14,21,22}

Topical steroids and silver sulfadiazine reduce inflammation and prevent infection, respectively.²¹ Severe cases may require surgical intervention.^{16,17,22} **Note that treatments are often based on case reports and animal data.**

Continue to the next section for a list of non-chemo drugs that have some evidence for treatment of extravasation. Warm or cold compresses are included if data supporting use of one or the other is available. Some preventive strategies are also included. For drugs not listed, consider contacting the drug manufacturer or a poison control center for treatment strategies.

More . . .

Drug	Treatment Options	Comments
Calcium salts	Hyaluronidase²²	Mechanism: hyperosmolarity²²
Contrast media	- Cold compress or warm compress to alleviate symptoms^{6,7} - Cold compress to reduce the risk of ulceration^{7,22} - Hyaluronidase (data are conflicting)²²	Mechanism: hyperosmolarity^{3,6} - Tissue damage is most likely with ionic agents^{3,6,7} and with larger volumes²²
Dextrose (≥10%)	Hyaluronidase⁸	Mechanism: hyperosmolarity⁸
Mannitol	- Warm compress²² - Hyaluronidase^{9,22}	Mechanism: hyperosmolarity^{9,21}
Methylene blue	- Phentolamine²² - Topical nitroglycerin²²	Mechanism: vasoconstriction²²
Nafcillin (U.S. only)	Hyaluronidase^{10,21}	Mechanism: not clear; possibly hyperosmolarity²²
Parenteral nutrition	- Hyaluronidase¹ - Topical nitroglycerin^{1,22}	Mechanism: hyperosmolarity¹ - Formulations with up to 900 mOsm/L are considered safe for peripheral administration²³
Phenytoin	- Warm compress^{11,21,22} - Hyaluronidase^{12,21} - Topical nitroglycerin^{11,21}	Mechanism: high pH^{a,11} (vehicle composition and formation of precipitates may also contribute)²¹ - Extravasation may result in “purple glove syndrome”¹¹ - Suggested preventive strategies include:²² - Infuse at a rate of 20 mg/minute - Dilute doses to a concentration of 6.7 mg/mL
Potassium salts	Hyaluronidase²²	Mechanism: hyperosmolarity²²

Drug	Treatment Options	Comments
Promethazine	No proven treatment. Sympathetic blockade (i.e., nerve block) and systemic heparin therapy have been used to manage inadvertent intra-arterial administration and extravasation of promethazine based on animal data.^{19,20,22,24}	Mechanism: low pH,^a chemical irritant^{19,20,21} - Suggested preventive strategies include:^{5,21,22} - Dilute doses in normal saline to allow for slower administration - Start with smaller doses such as 6.25 to 12.5 mg - Infuse doses through a large bore vein over 10 to 15 minutes
Vasoconstrictors - Dobutamine - Dopamine - Epinephrine - Norepinephrine - Phenylephrine - Vasopressin	- Warm compress^{21,22} - Phentolamine¹³ - Terbutaline²¹ - Topical nitroglycerin^{14,22}	Mechanism: vasoconstriction, low pH^{a,13,21,22} - Infusing pressors through central lines is typically recommended, but some data suggest that the risk of extravasation injuries due to infusion of vasopressors through peripheral IV lines may be lower than once thought when patients are carefully monitored⁴

a. Do not attempt to neutralize acidic or basic extravasations due to the potential for gas formation and other reactions.²²

Users of this PL Detail-Document are cautioned to use their own professional judgment and consult any other necessary or appropriate sources prior to making clinical judgments based on the content of this document. Our editors have researched the information with input from experts, government agencies, and national organizations. Information and internet links in this article were current as of the date of publication.

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Cite this document as follows: PL Detail-Document, Management of Non-Chemo Drug Extravasation. Pharmacist's Letter/Prescriber's Letter. October 2015.



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