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## Prevent Extravasation Injury With the Use of Antidotes

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Although vesicant extravasations are rare events, they have the potential to cause permanent damage to patient tissue. Developing or updating institutional policies on how to manage extravasations can be difficult because organizational guidelines and recommendations are published only periodically. In her article in the August 2009 issue of the *Clinical Journal of Oncology Nursing*, Lisa Schulmeister addressed the concerns surrounding institutional policies for extravasation management and offered recommendations for healthcare providers looking to develop such policies.

### Challenges With Policies

Because expert organizations publish guidelines and recommendations only periodically, they may not contain information about new antidotes or treatments that become available after publication. Healthcare providers may be unaware of new antidotes that have been approved by the U.S. Food and Drug Administration (FDA). In addition, many antidotes currently in use are empirical and controversial. Adding to the confusion are vague statements from pharmaceutical manufacturers about how to manage extravasation injuries from the drugs they manufacture.

### Current Recommendations

Several resources may be used for developing institutional policies on ex-



travasation. Manufacturers of vesicant chemotherapy may offer recommendations in the prescribing information for their drugs. See Figure 1 for a summary of those recommendations.

Healthcare providers should also look to the FDA to see what antidotes have been approved to treat extravasations.

Currently, the only drug approved specifically for extravasations is Totect® (TopoTarget USA). Totect is administered as an IV infusion in anthracycline extravasations. Two other drugs often used to manage extravasations, sodium thiosulfate and hyaluronidase, are not approved by the FDA for this use.

### Key Definitions

**Antidote:** an agent that neutralizes a poison or counteracts its effects

**Extravasation:** leakage of agents from the vein into surrounding tissue during IV administration

**Vesicant:** an agent that, when exposed to tissue, may cause tissue damage

Five-Minute In-Service is a monthly feature that offers readers a concise recap of full-length articles published in the *Clinical Journal of Oncology Nursing (CJON)* or *Oncology Nursing Forum*. This edition summarizes "Vesicant Chemotherapy Extravasation Antidotes and Treatments" by Lisa Schulmeister, RN, MN, APRN-BC, OCN®, FAAN, which was featured in the August 2009 issue of *CJON*. Questions regarding the information presented in this Five-Minute In-Service should be directed to the *CJON* editor at [CJONeditor@ons.org](mailto:CJONeditor@ons.org). Photocopying of this article for educational purposes and group discussion is permitted.

## Figure 1. Pharmaceutical Manufacturers' Recommendations for Managing Extravasation

- **Anthracyclines:** According to Bedford Laboratories, no local treatments for doxorubicin extravasation have been shown to be beneficial. Bedford Laboratories and Pfizer Inc. stated that daunorubicin, idarubicin, and epirubicin have the potential to cause tissue injury but do not recommend any antidotes.
- **Mechlorethamine:** According to Merck & Co., Inc., extravasation of mechlorethamine causes painful inflammation that progresses to induration and sloughing of tissue. The area should be infiltrated with sterile isotonic sodium thiosulfate (1/6 molar) solution, and ice compresses should be applied for 6–12 hours.
- **Vinblastine and vincristine:** Bedford Laboratories, Mayne Pharma, Inc., and SICOR Pharmaceuticals, Inc., recommend that if extravasation of these plant alkaloids occurs, infusions should be discontinued immediately. Any remaining portion of the dose should be infused into a different vein. Hyaluronidase injection and application of moderate heat to the site will help disperse the drug, minimizing discomfort and the possibility of cellulitis.
- **Vinorelbine:** According to Bedford Laboratories, extravasation of vinorelbine causes irritation, local tissue necrosis, and thrombophlebitis. If extravasation occurs, stop the injection immediately and administer any remaining dose into another vein. Institutional policies should be followed because no established guidelines exist.

Note. Based on information from Schulmeister, 2009.

Professional organizations such as ONS have released their own guidelines for extravasation management. ONS guidelines recommend that anthracycline extravasations be treated with Totect, mechlorethamine extravasations with sodium thiosulfate, and plant alkaloid extravasations with hyaluronidase.

The European ONS also recommends Savene<sup>®</sup> (TopoTarget A/S) (the European equivalent of Totect) for anthracycline extravasations but does not suggest using sodium thiosulfate for mechlorethamine extravasation because of a lack of evidence. The European ONS recommends that the use of hyaluronidase be studied further as an antidote

to plant alkaloids. The United Kingdom ONS has adopted similar guidelines.

Other national and international oncology organizations have not developed or published guidelines for managing vesicant chemotherapy extravasations.

### How the Antidotes Work

Understanding how the antidotes work, including route of administration, formulations, and mechanisms of action, may aid in the development of institutional policies.

**Sodium thiosulfate:** This antidote is believed to neutralize the reactive alkylating species of mechlorethamine and reduce tissue-injuring hydroxyl radicals. It is given by local, subcutaneous injection into the extravasation area after the peripheral IV device or noncoring needle has been removed. Many institutions no longer use mechlorethamine, but those that do should have policies in place to ensure that their stock of sodium thiosulfate is not expired.

**Hyaluronidase:** In the United States, four formulations of hyaluronidase are available, three of which are animal derived and one that is a recombinant human product. The recombinant human antidote may be less likely to cause local reactions. Like sodium thiosulfate, hyaluronidase is given by local, subcutaneous injection into the extravasation area. It works by helping to disperse plant alkaloid chemotherapy throughout the tissue and by promoting absorption.

**Totect:** This antidote is believed to prevent damage by removing iron from iron-anthracycline complexes that form in the tissue. The drug is supplied in an individual kit for each patient that contains the complete three-day treatment. Totect is administered by IV infusion in a large vein in the opposite arm, away from the area of extravasation.

For more information on extravasation antidotes and the development of policies regarding their use, refer to the full article by Schulmeister (2009). \*

Schulmeister, L. (2009). Vesicant chemotherapy extravasation antidotes and treatments. *Clinical Journal of Oncology Nursing*, 13(4), 395–398.

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