

Appendix A

GUIDELINES for MANAGING EXTRAVASATION with VESICANT and IRRITANT DRUGS

| ANTINEOPLASTIC DRUGS [generic name (brand name)] | RISK CATEGORY VESICANT (V), IRRITANT (I), OR UNKNOWN (U) | ANTIDOTE / INTERVENTION and PREPARATION | LOCAL CARE | COMMENTS | REFERENCES |
|--|---|--|--|--|------------|
| actinomycin-D | | | | see "Dactinomycin" | |
| Adriamycin® | | | | see "Doxorubicin" | |
| BCNU | | | | see "Carmustine" | |
| Carboplatin (Paraplatin®) | U | none known | 1. No specific local therapy is indicated after extravasation with carboplatin. | | |
| Carmustine (BiCNU®) | I | none known | 1. Aspirate back through the VAD to remove any accessible extravasated drug. 2. No specific local therapy is indicated after extravasation with carmustine. | 1. Pts may complain of irritation and stinging pain during administration; a result of ethanol in the formulation used to reconstitute carmustine. 2. Carmustine should be diluted in at least 250 mL fluid (dilution volumes may be constrained by protocol specifications). 3. Topical sodium bicarbonate solution will inactivate carmustine spilled or splashed on the skin, but MUST NOT BE INJECTED locally in the event of carmustine extravasation. | 1 |
| Cosmegen® | | | | see "Dactinomycin" | |

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| Cisplatin (Platinol®) | I <i>(see comments)</i> | <i>(see comments #2-4)</i> | Treat as for mechlorethamine extravasation <i>(see comments #2-4)</i> | <ol style="list-style-type: none"> 1. Extravasation injury has been reported following extravasation of concentrated cisplatin solutions (>0.4 mg/mL). 2. No local therapy is indicated after extravasation with small volumes of dilute cisplatin solutions. 3. Extravasation with large volumes and/or highly concentrated cisplatin solutions may be treated as is an extravasation with mechlorethamine. 4. In this indication, neither effective nor optimal sodium thiosulfate doses have been identified. | 2-5 |
| Dacarbazine (DTIC-Dome®) | I | none known | <ol style="list-style-type: none"> 1. Aspirate back through the VAD to remove any accessible extravasated drug. 2. No local therapy is indicated after extravasation with dacarbazine. 3. Protect exposed tissues from light following extravasation. 4. Avoid applying pressure to the extravasation site. | <ol style="list-style-type: none"> 1. Increased skin toxicity was produced in some animal models when light exposure followed intradermal dacarbazine. | 6-8 |
| Dactinomycin (Cosmegen®) | V | none known | Treat as for doxorubicin extravasation. | <ol style="list-style-type: none"> 1. Topical cooling has been inconsistently effective in animal studies. | |
| Daunorubicin | V | none known | Treat as for doxorubicin extravasation. | | |
| Daunorubicin Citrate Liposomal (DaunoXome®) | I | none known | Treat as for doxorubicin extravasation. | | 9, 10 |
| DaunoXome® | | | see "Daunorubicin Citrate Liposomal" | | |
| Docetaxel (Taxotere®) | U | none known | Treat as for paclitaxel extravasation. | | |
| Doxil® | | | see "Doxorubicin, Liposomal" | | |

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| Doxorubicin (Adriamycin®) | V | none known | <ol style="list-style-type: none"> 1. Aspirate back through the VAD to remove any accessible extravasated drug. 2. Apply cold packs with circulating ice water, an ice pack, or other cold pack for 15–20 minutes at least four times daily for 24–48 hours after extravasation. 3. Avoid applying pressure to the extravasation site. 4. Elevate the extremity. | 1. Consider surgical consultation, especially if pt reports pain at the extravasation site 7–10 days after the event. Surgical excision may be required to remove non-viable tissues, release trapped drug, and prevent more extensive prolonged tissue injury. | 11-14 |
| Doxorubicin, Liposomal (Doxil®) | V | | Treat as for doxorubicin extravasation. | | 15, 16 |
| Ellence® | | | see "Epirubicin" | | |
| Epirubicin (Ellence®) | V | | | | 17 |
| Etoposide (VePesid®) | I <i>(see comments)</i> | | Treat as for vinblastine extravasation. | 1. Skin ulceration is unlikely when etoposide injection is diluted to concentrations used clinically. | 18 |
| Fluorouracil (Adrucil®) | I | | 1. No specific local therapy is indicated after extravasation with fluorouracil. | | |
| Idarubicin (Idamycin®) | V | none known | Treat as for doxorubicin extravasation. | | 19 |

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|--|---|--|--|--|------------|
| Mechlorethamine (Mustargen®, HN ₂) | V | Isotonic sodium thiosulfate (Na ₂ S ₂ O ₃ 1/6 Molar solution) To prepare a 1/6 M Na ₂ S ₂ O ₃ solution: <ul style="list-style-type: none"> starting with 10% Na₂S₂O₃ (1 g/10 mL) solution: in a syringe, mix 4 mL Na₂S₂O₃ with 6 mL Water for Injection, USP. starting with 25% Na₂S₂O₃ (2.5 g/10 mL) solution: in a syringe, mix 1.6 mL Na₂S₂O₃ with 8.4 mL Water for Injection, USP. | <ol style="list-style-type: none"> Aspirate back through the VAD to remove any accessible extravasated drug. Inject 1/6 molar Na₂S₂O₃ solution through IV access device: 2—5 mL for each milligram of mechlorethamine that was extravasated. Remove IV access device. With a 25-G needle, inject subcutaneously, 1/6 molar Na₂S₂O₃ solution circumferentially, into tissue surrounding the extravasation site. Avoid applying pressure to the extravasation site. | <ol style="list-style-type: none"> RAPID INTERVENTION IS ESSENTIAL in treating nitrogen mustard extravasation. Na₂S₂O₃ solution chemically neutralizes mechlorethamine. The intervention is clinically accepted, but reports confirming benefit are scant. | 20-22 |
| Mithramycin | | | see "Plicamycin" | | |
| Mitomycin (Mutamycin®, mitomycin-C) | V | none known | Treat as for doxorubicin extravasation. | <ol style="list-style-type: none"> Extravasation is typically accompanied by pain & swelling, but may be painless. Mitomycin is associated with ulceration at previous and subsequent venipuncture sites. Dermal injury after mitomycin may be delayed from 1—29 weeks after administration. Mitomycin extravasation injury may be exacerbated by subsequent sunlight exposure to the affected area. | 23-26 |
| Mitoxantrone (Novantrone®) | V | none known | Treat as for doxorubicin extravasation. | <ol style="list-style-type: none"> Causes blue discoloration in soft tissues where infiltration has occurred. Inconsistently produces tissue necrosis after extravasation. When ulceration occurs, lesions may spontaneously resolve with conservative treatment. | 5, 27 |
| Navelbine® | | | see "Vinorelbine" | | |

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| nitrogen mustard | | | see "Mechlorethamine" | | |
| Novantrone® | | | see "Mitoxantrone" | | |
| Oncovin® | | | see "Vincristine" | | |
| Paclitaxel (Taxol®) | V* | none known | <ol style="list-style-type: none"> 1. Aspirate back through the VAD to remove any accessible extravasated drug. 2. Apply warm compresses for 15–20 minutes at least four times daily for 24–48 hours after extravasation. 3. Avoid applying pressure to the extravasation site. | <ol style="list-style-type: none"> 1. Warmth increases local blood flow enhancing drug absorption and removal from the site. 2. Skin overlying the extravasation site may become inflamed (mimicking 1° thermal burn) and may breakdown and peel. | 28-31 |
| Paraplatin® | | | see "Carboplatin" | | |
| Platinol® | | | see "Cisplatin" | | |
| Plicamycin (Mithracin®) | I | none known | <ol style="list-style-type: none"> 1. Aspirate back through the VAD to remove any accessible extravasated drug. 2. No specific local therapy is indicated after extravasation with plicamycin. 3. Avoid applying pressure to the extravasation site. | | |
| Taxol® | | | see "Paclitaxel" | | |
| Taxotere® | | | see "Docetaxel" | | |
| Teniposide (Vumon®) | I | | Treat as for vinblastine extravasation. | | |
| Velban® | | | see "Vinblastine" | | |
| Vinblastine (Velban®) | V | none known | <ol style="list-style-type: none"> 1. Aspirate back through the VAD to remove any accessible extravasated drug. 2. Apply warm packs for 15–20 minutes at least four times daily for 24–48 hours after extravasation. 3. Avoid applying pressure to the extravasation site. | <ol style="list-style-type: none"> 1. Warmth increases local blood flow enhancing drug absorption and removal from the site. 2. Do not apply topical steroid products. Topical steroids have exacerbated extravasation injury in animal models. | 32-35 |

* Although paclitaxel produces microscopic cellular necrosis and is therefore categorized as a vesicant, its administration follows the standards developed for non-vesicant irritant hazardous drugs.

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| Vinblastine (Velban®) | V | none known | 1. Aspirate back through the VAD to remove any accessible extravasated drug. 2. Apply warm packs for 15–20 minutes at least four times daily for 24–48 hours after extravasation. 3. Avoid applying pressure to the extravasation site. | 1. Warmth increases local blood flow enhancing drug absorption and removal from the site. 2. Do not apply topical steroid products. Topical steroids have exacerbated extravasation injury in animal models. | 32-35 |
| Vincristine (Oncovin®) | V | none known | Treat as for vinblastine extravasation. | | 36 |
| Vindesine (Eldisine®) | V | none known | Treat as for vinblastine extravasation. | | 37 |
| Vinorelbine (Navelbine®) | V | none known | Treat as for vinblastine extravasation. | | |
| VM-26 | | | see "Teniposide" | | |
| VP-16, VP-16-213 | | | see "Etoposide" | | |

Caveats

When it is not known whether a drug is an irritant or vesicant, take the most conservative approach to intervention; *i.e.*, follow the recommendations for managing doxorubicin extravasation.

The **optimal frequency and duration for applying warm and cold compresses** over areas of extravasation injury are not known. Caregivers should instruct patients to apply heat or cold intermittently for as long as possible during each application, but not for durations that may adversely affect a patient's quality of life.

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