Treatment for Extravasation of Non-Chemo Drugs

Non-chemotherapy drugs are not generally considered to be vesicants. However, extravasation or infiltration of non-chemotherapy drugs can still cause harm to skin and soft tissue. This is especially true for drugs that are intrinsically irritating to tissue such as nafcillin; drugs with higher than physiologic osmolarity, such as parenteral nutrition and some electrolytes; and drugs with a high pH such as phenytoin. Some general advice in the case of extravasation includes immediately stopping the drug infusion and elevating the affected limb to minimize swelling. Cold compresses (dry not moist) may also reduce swelling and are generally preferred for most vesicant or irritant drugs. Warm compresses (dry not moist) can cause vasodilation and help distribute the drug, reducing local drug concentrations. Other treatments can depend on the drug. Hyaluronidase (Vitrase; U.S. only) given subcutaneously around the affected site can help distribute the drug away from the site. Phentolamine can counteract local vasoconstriction caused by extravasation of vasoconstrictors. Quicker treatment may result in better outcomes for patients, but surgical intervention may be required for severe cases of extravasation. Treatments for extravasation are generally based on case reports in the literature, as opposed to more solid evidence. The following chart includes non-chemotherapy drugs that are more likely to be harmful with extravasation, along with treatments for their extravasation and other relevant information. Follow your hospital’s policy for extravasation of chemotherapy agents.

<table>
<thead>
<tr>
<th>Drug or Drug Class</th>
<th>Treatmenta,b,c,d</th>
<th>Comments</th>
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<tbody>
<tr>
<td>Calcium salts</td>
<td>• Hyaluronidase4</td>
<td>• Mechanism: hyperosmolarity4</td>
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| Contrast media     | • Cold compress or warm compress for alleviation of symptoms6,7  
                       • Cold compress to alleviate ulceration4,7  
                       • Hyaluronidase4 | • Mechanism: hyperosmolarity3,6  
                       • Tissue damage is more likely with ionic than with nonionic contrast agents3,6,7 |
| Dextrose (≥10%)    | • Hyaluronidase4,8 | • Mechanism: hyperosmolarity4,8 |
| Mannitol           | • Hyaluronidase9  | • Mechanism: hyperosmolarity9 |
| Nafcillin (U.S. only) | • Hyaluronidase4,10 | • Mechanism: direct irritant10 |
| Parenteral nutrition | • Hyaluronidase1,4  
                       • Topical nitroglycerin1,5 | • Mechanism: hyperosmolarity1 |
| Phenytoin          | • Warm compress11  
                       • Topical nitroglycerin11  
                       • Hyaluronidase12 | • Mechanism: high pH11  
                       • Extravasation may result in “purple glove syndrome”11 |
<table>
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<tr>
<th>Drug or Drug Class</th>
<th>Treatment&lt;sup&gt;a,b,c,d&lt;/sup&gt;</th>
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<tr>
<td>Potassium salts</td>
<td>• Hyaluronidase&lt;sup&gt;4&lt;/sup&gt;</td>
<td>• Mechanism: hyperosmolarity&lt;sup&gt;4&lt;/sup&gt;</td>
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<tr>
<td>Promethazine</td>
<td>• No proven treatment. Sympathetic block and heparinization have been used to manage promethazine extravasation based on animal data. 19, 20</td>
<td>• Mechanism: direct irritant&lt;sup&gt;19,20&lt;/sup&gt;</td>
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| Vasoconstrictors   | • Dobutamine  
• Dopamine  
• Epinephrine  
• Norepinephrine  
• Phenylephrine  
• Vasopressin  
• Phentolamine<sup>4,5,13</sup>  
• Topical nitroglycerin<sup>14</sup>  | • Mechanism: restriction of local blood flow<sup>13</sup> |

a. **Cold or warm compresses** should generally be applied for 20 minutes, every six to eight hours, for up to three days.<sup>2,4</sup>
b. The **dose of hyaluronidase** (U.S. only) 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.<sup>4,8</sup> A concentration of 15 units/mL (same instructions as above) has also been used for non-chemo agents.<sup>4</sup> Hyaluronidase should be used within about one hour of extravasation.<sup>18</sup>
c. The **dose of phentolamine** for adults is generally 5 to 10 mg diluted in 10 to 15 mL of normal saline injected subcutaneously into the area of extravasation as ten 1 mL injections. It should be used within 12 hours of extravasation.<sup>4</sup>
d. Different formulations of **topical nitroglycerin** have been used (per case reports) for extravasation including 2% topical nitroglycerin ointment.<sup>14</sup>
References