



## NONCYTOTOXIC VESICANT MEDICATIONS and SOLUTIONS

INS established a vesicant task force with the goal of developing an evidence-based list of noncytotoxic vesicant medications/solutions.

Outside of oncology practice, there is not a list of noncytotoxic vesicants as established by a professional organization. INS identified the need to address this gap based on the following premise: the first step in preventing extravasation is the identification and recognition of vesicant drugs and solutions.

The scope of work was limited to creating an **evidence-based list of noncytotoxic vesicant medications/solutions** and developing an **extravasation checklist** that outlines risk reduction strategies including early recognition of signs and symptoms of extravasation.

Both documents, along with a **summary of work** are available in the INS LEARNING CENTER.

# Development of an Evidence-Based List of Noncytotoxic Vesicant Medications and Solutions

## Summary of Work

**Vesicant Task Force:** Chair Lisa A. Gorski, MS, RN, HHCNS-BC, CRNI®, FAAN; Marc Stranz, PharmD; Lynda Cook, MSN, RN, CRNI®; James M. Joseph, MPH, BSN, RN, CRNI®, VA-BC; Kathy Kokotis, MBA, BS, RN; Pam Sabatino-Holmes, MSN, ARNP, CRNI®; Lori Van Gosen, MSN, RN, PCNS-BC, CRNI®, VA-BC

The Infusion Nurses Society (INS) established a task force with the goal of developing an evidence-based list of noncytotoxic vesicant medications and solutions. Infiltration of a vesicant drug, defined as extravasation, may result in patient injuries that range from prolonged length of stay, rehospitalization, and long-term treatment requirements to permanent functional impairment and even loss of limb. Outside of oncology practice, there is no list of noncytotoxic vesicants established by a professional organization. While some health care organizations provide such lists, many do not, and clinicians frequently are unaware of vesicant drugs and the risks and consequences of extravasation. As the global authority in infusion nursing, INS identified the need to address this gap based on the following premise: The first step in preventing extravasation is the identification and recognition of vesicant drugs and solutions.

The scope of work for the Vesicant Task Force (TF) was limited to creating an evidence-based list of noncytotoxic vesicant medications and solutions and developing a clinical practice tool that outlines risk-reduction strategies, including early recognition of signs and symptoms of extravasation. Treatment and interventions for extravasation were outside the TF's scope of work and were not addressed.

### Methodology: Development of a Noncytotoxic Vesicant List

The TF developed a list of all drugs and solutions as labeled by the U.S. Food and Drug Administration (FDA) for infusion, using the U.S. National Library of Medicine. Additional references included the American Society of Health-System Pharmacists' *Handbook on Injectable Drugs*<sup>1</sup> and an intravenous medication reference book.<sup>2</sup> This review isolated drugs having characteristics related to extravasation: tissue necrosis, sloughing, blistering, phlebitis, thrombophlebitis, and patient pain. Only noncytotoxic drugs were retained on this list. Four literature reviews served as the primary sources for further development of the list.<sup>3-6</sup> Data from these literature reviews were reviewed by the TF members; the review included analysis of the source citations. Drugs with limited citations or questionable or unsubstantiated extravasations were eliminated from the list based on discussions of the TF during conference call meetings. An additional literature search, using the search terms *extravasation*, *infiltration*, and *vesicants*, was completed before finalizing the TF's work.

The TF compiled the final list of vesicants using a red and yellow color scheme, as used by Clark and colleagues.<sup>4</sup> High-risk infusates were classified as "red"; this list includes well-recognized vesicants with multiple citations and reports of tissue damage on extravasation. Intermediate risk infusates, classified as "yellow," were associated with fewer reports of extravasation, but are recognized as vesicants. Published drug information and infusate characteristics indicate caution and potential for tissue damage. A simple list of the red and yellow vesicants can be found on the INS website. A comprehensive list of the vesicants, including infusate pH and osmolarity levels, will be published in an article in the *Journal of Infusion Nursing*. While some vesicant infusates possess extreme pH levels (eg, acyclovir, pentobarbital, phenobarbital, phenytoin) or are clearly hyperosmolar (eg, calcium chloride, high dextrose concentrations), many of the vesicants have neither property.

The TF also created a tool, based on a review of recommendations compiled from a variety of infusion references, outlining extravasation prevention interventions that could be implemented by organizations and clinicians who administer vesicants.

### Limitations

The noncytotoxic vesicant list was established based on literature reviews that primarily included case reports and drug literature of currently available infusates. Not all case reports are fully analyzed, and it is important to recognize that most often extravasation cases are not reported in the formal literature.

## Conclusion

The first step in preventing extravasation is the recognition of vesicant infusates. Each organization should have a list of vesicant infusates and should address extravasation prevention, as well as management, in policies and procedures. This noncytotoxic vesicant list provides a sound reference for an organization. However, as stated in the *Infusion Therapy Standards of Practice*, each facility should reach consensus on which infusates are considered vesicants (and irritants) based on internal formularies.<sup>7(S98)</sup> Based on organizational experience and adverse events, the noncytotoxic vesicant list may be expanded to include additional infusates not on the INS list.

The knowledge and competency of clinicians who administer infusion therapy must be addressed. The pharmacist is a critical member of the health care team and should be consulted when questioning the characteristics of an infusate. This knowledge, along with a thorough patient assessment inclusive of comorbidities and mitigation of risk factors, will assist the clinician in advocating for the most appropriate vascular access device (VAD) given the prescribed therapy. Anticipated duration and frequency of the vesicant medication or solution is an important consideration. As stated in the *Policies and Procedures for Infusion Therapy*, VAD selection is a complex decision that requires critical thinking and analysis:

"...the decision is generally not based on a single factor, such as the drug or solution category of vesicant or irritant."<sup>8(p42)</sup> Peripheral administration of a short-term vesicant infusion in an emergency or a small number of intermittent doses may (or may not) be appropriate, given a patient's vascular assessment. For continuous vesicant infusion or frequent vesicant administration, clinicians must advocate for a central vascular access device (CVAD). While less common, it also must be recognized that there is a risk for extravasation with CVADs when infusing vesicants. Last, it must be recognized that any infusion drug can potentially cause harm; drugs must be carefully reviewed for extravasation risks. Organizations are encouraged to collect extravasation data and to report and publish findings in the interest of public safety. The TF recommends that this list be reevaluated on a regular basis as new data emerge and as new medications are introduced into the market.

## Acknowledgements

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## References

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## NONCYTOTOXIC VESICANT LIST

The first step in reducing the risk of extravasation is to identify and recognize medications and solutions that are associated with tissue damage when the solution escapes from the vascular pathway.

RED LIST	YELLOW LIST
Well-recognized vesicants with multiple citations and reports of tissue damage upon extravasation	Vesicants associated with fewer published reports of extravasation; published drug information and infusate characteristics indicate caution and potential for tissue damage
<b>Calcium chloride</b>	<b>Acyclovir</b>
<b>Calcium gluconate</b>	<b>Amiodarone</b>
<b>Contrast media - nonionic</b>	<b>Arginine</b>
<b>Dextrose concentration <math>\geq</math> 12.5%</b>	<b>Dextrose concentration <math>\geq</math> 10% to 12.5%</b>
<b>Dobutamine</b>	<b>Mannitol <math>\geq</math> 20%</b>
<b>Dopamine</b>	<b>Nafcillin</b>
<b>Epinephrine</b>	<b>Pentamidine</b>
<b>Norepinephrine</b>	<b>Pentobarbital sodium</b>
<b>Parenteral nutrition solutions exceeding 900 mOsm/L</b>	<b>Phenobarbital sodium</b>
<b>Phenylephrine</b>	<b>Potassium <math>\geq</math> 60 mEq/L</b>
<b>Phenytoin</b>	<b>Vancomycin hydrochloride</b>
<b>Promethazine</b>	
<b>Sodium bicarbonate</b>	
<b>Sodium chloride <math>\geq</math> 3%</b>	
<b>Vasopressin</b>	

It is important to recognize that large infiltrations of nonvesicant medications or solutions may also be associated with severe tissue damage.

# EXTRAVASATION CHECKLIST: PREVENTION AND IDENTIFICATION

## Health Care Organization:

- Presence of organizational policies/protocols for vesicant identification and extravasation prevention
- Written list of vesicant medications/solutions
- Initial and ongoing competency assessments established (venipuncture skill, extravasation prevention)

## Preadministration assessment:

- Identify anticipated duration for administration of vesicants
- Assess appropriateness of vascular access device (VAD) for vesicant administration
- Avoid peripheral infusion of vesicants when infusion time exceeds 30 to 60 minutes
- Advocate for early central vascular access device (CVAD) placement for continuous vesicant infusions, high-frequency intermittent vesicant drug infusions

## Identify potential risk factors:

Short Peripheral Catheter (SPC)	CVAD
<ul style="list-style-type: none"> <li><input type="checkbox"/> Small fragile veins</li> <li><input type="checkbox"/> Darker skin color (more difficult to assess for signs of extravasation)</li> <li><input type="checkbox"/> Diseases that produce changes in vasculature or impaired circulation (eg, diabetes, systemic lupus)</li> <li><input type="checkbox"/> Previous multiple venipunctures; difficulty with SPC access due to obesity</li> <li><input type="checkbox"/> Limited vein selection (axillary lymph node dissection/radiation therapy to affected extremity, affected extremity from stroke, arteriovenous fistula, lymphedema, amputation)</li> <li><input type="checkbox"/> Prior treatment with irritating/sclerosing drugs</li> <li><input type="checkbox"/> Probing during catheter insertion</li> <li><input type="checkbox"/> Venous spasms as result of body temperature changes, raised blood pressure, psychological factors</li> <li><input type="checkbox"/> Absence of blood return*</li> <li><input type="checkbox"/> Impaired cognition, altered mental status, somnolence, anesthetized, comatose (ie, unable to report symptoms)</li> </ul>	<ul style="list-style-type: none"> <li><input type="checkbox"/> Incomplete port needle insertion</li> <li><input type="checkbox"/> Needle dislodgment from port septum</li> <li><input type="checkbox"/> Separation of catheter from port body</li> <li><input type="checkbox"/> Deeply implanted port</li> <li><input type="checkbox"/> Loss of catheter integrity (eg, hole/crack in catheter)</li> <li><input type="checkbox"/> Catheter tip migration</li> <li><input type="checkbox"/> Backtracking of medication along the tunnel resulting from fibrin sheath development</li> <li><input type="checkbox"/> Pinch-off syndrome for VADs placed via subclavian vein</li> <li><input type="checkbox"/> Absence of blood return*</li> <li><input type="checkbox"/> Impaired cognition, altered mental status, somnolence, anesthetized, comatose (ie, unable to report symptoms)</li> </ul>

\*Blood return is defined as blood the color and consistency of whole blood. (Gorski LA, Hadaway L, Hagle M, McGoldrick M, Orr M, Doellman D. Infusion therapy standards of practice. *J Infus Nurs.* 2016;39(suppl 1):S40.)

**Reduce risk when planning for vesicant administration via an SPC:**

- Choose smooth, pliable veins, large veins
- Avoid areas of flexion
- Never place an SPC below (distal to) previously used site
- Avoid venipuncture sites on dorsal aspect of hand, all aspects of wrist, antecubital fossa and lower extremity, or in limb with impaired circulation or lymphatic drainage
- Do not use site more than 24 hours old
- Use smallest size, shortest length catheter (Exception: SPCs placed in deep veins via ultrasound. Use a longer catheter.)
- Do not use steel needles
- No more than 2 attempts at placement by any one nurse; no more than 4 attempts total; discuss alternative options with licensed independent practitioner
- Ensure presence of blood return before initiating infusion; thorough site assessment before using power injector including manual saline flush and check for blood return

**Reduce risk when planning for vesicant administration via a CVAD:**

- Select a needle length adequate to pierce implanted vascular access port septum and contact base of the port
- Stabilize noncoring needle of implanted vascular access port to reduce risk of dislodgment
- Before infusion initiation and during infusion, assess CVAD for a blood return and absence of resistance to flushing

**Administer vesicants safely via any VAD:**

- Instruct patient to immediately report swelling, skin tightness, pain, burning, discomfort
- Ensure integrity of infusion system (eg, absence of leakage, secure luer-lock connections)
- Ensure presence of blood return before, during, and after medication administration
- Use caution when using an infusion pump for peripheral vesicant infusion; continuous infusions should be converted to CVAD administration (eg, dopamine)
- Monitor closely for signs/symptoms of extravasation

**STOP and immediately discontinue infusion with evidence of extravasation**

- Complaints of pain, tightness, burning, discomfort at or around the insertion site, catheter tip, or entire venous pathway
- Cool skin temperature
- Swelling at or above insertion site or increase in size of extremity (SPC)
- Raised area on neck or chest (CVAD)
- Decreased mobility of extremity
- Change in infusion flow quality (gravity infusion)
- Absence of/inadequate (eg, pinkish) blood return
- Leakage of fluid at insertion site
- Resistance during fluid administration (eg, during VAD flushing, electronic infusion device occlusion alarms)
- Erythema is common but does not always occur
- Assess area, disconnect administration set, aspirate fluid from VAD using small syringe, estimate volume of extravasated fluid, and follow organizational protocols for actions following extravasation

# EXTRAVASATION CHECKLIST: PREVENTION AND IDENTIFICATION

## References:

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