# Beyond Irritant, Not Quite Vesicant? Irritant with Vesicant Properties: An Updated Approach to Extravasation Hazard Classification

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## Background

**Extravasation** is the inadvertent leakage of an intravenous drug into surrounding tissues. Although rare, extravasation of oncology drugs may cause tissue damage (e.g., necrosis) and serious complications.

Oncology drugs are traditionally classified as vesicant, irritant, none (non-irritant/non-vesicant) at BC Cancer, based on their ability to cause tissue damage. However, this classification does not capture **irritant drugs with rare reports of tissue damage,** leading to uncertainty and inconsistent guidance for extravasation prevention and management. Some guidelines have introduced an intermediate category between vesicant and irritant, such as "**irritant with vesicant properties**", but it is still poorly defined.

## Objectives

1. To clearly **define** an intermediate category between vesicant and irritant by developing classification criteria
2. To **refine** the definitions and classification criteria of existing extravasation hazard categories (vesicant, irritant, none) at BC Cancer

## Method

### Environmental scan

Definitions and classification from the existing BC Cancer extravasation guidelines[1] were compared with international oncology practice guidelines on extravasation: ONS/ASCO[2], EONS/ESMO[3], National Health Service (NHS)[4], and Cancer Institute of New South Wales (NSW)[5]. Drugs classified as "irritant with vesicant properties" (or equivalent) were identified. Their extravasation data was reviewed for the frequency and severity of reported tissue damage.

### Literature review

MEDLINE, CINAHL, PubMed and Google Scholar were searched using terms extravasation, vesicant, necrosis, and individual drug names. Additional data sources included product monographs and post-marketing reports from manufacturers. Pre-clinical studies were excluded, and language was limited to English. Clinical data was used to define an intermediate category between vesicant and irritant by developing classification criteria, as well as to refine the definitions and classification criteria of existing extravasation hazard categories.

## Results

### Extravasation Hazard Categories

Significant variability of extravasation classification was shown across the reviewed guidelines. Guidelines used between 3 to 5 extravasation hazard categories. (Table 1)

**Two intermediate categories** between vesicant and irritant were identified, and their definitions were compared. (Table 2)

- **Irritant with vesicant properties**
- **Exfoliant:** included drugs with low vesicant potential; properties were considered equivalent to "irritant with vesicant properties" by definition. Drugs classified as exfoliants were included in the extravasation data assessment.

In addition, the "**inflammitant"** category (between neutral and irritant) included drugs that may cause flare reactions or mild to moderate inflammation. This category was **considered equivalent to "none**" at BC Cancer, and its characteristics were used to refine the classification criteria for "none".

**Table 1. Comparison of Extravasation Hazard Categories**

| | Extravasation Hazard Categories | | | | |
|---|---|---|---|---|---|
| **BC Cancer**[1] | Vesicant | - | Irritant | - | None |
| **ONS/ASCO**[2] | Vesicant | **Irritant with vesicant properties** | Irritant | - | Nonvesicant |
| **NSW**[5] | | | | | |
| **EONS/ESMO**[3] | Vesicant | - | Irritant | - | Nonvesicant |
| **NHS**[4] | Vesicant | **Exfoliant** | Irritant | Inflammitant | Neutral |

**Table 2. Intermediate Categories Between Vesicant and Irritant**

| | Definitions |
|---|---|
| **ONS***[6] | **Irritant with vesicant properties:** agents that may inflame and irritate peripheral vein and can cause skin and tissue damage (e.g., blistering, sloughing) when higher concentration or specific amount of the drug inadvertently enter the tissue. |
| **NSW**[5] | **Irritant with vesicant properties:** drugs or solutions that are difficult to classify as either a vesicant or irritant. They are capable of causing tissue damage and ulceration which is proportional to the amount and concentration of the drug extravasated into the tissue. |
| **NHS**[4] | **Exfoliant:** can cause inflammation and shedding of the skin but are less likely to cause tissue death. They can cause pain and may have a low-level vesicant potential which can cause superficial tissue injury. |

No definition of "irritant with vesicant properties" was provided in the ONS/ASCO guidelines[2]; therefore, the definition from previous ONS guidelines[6] was used for this review.

### Extravasation Data

Fifteen drugs were classified as "irritant with vesicant properties" (or equivalent) from the reviewed guidelines: bendamustine, cabazitaxel, carboplatin, carmustine, cisplatin, daunorubicin liposomal, docetaxel, doxorubicin liposomal, etoposide, melphalan, mitoxantrone, oxaliplatin, paclitaxel, paclitaxel NAB, topotecan. Their **extravasation data** was assessed for the frequency of tissue necrosis and the severity of tissue damage.

**Key characteristics** of "irritant with vesicant properties" were identified from extravasation data and the reviewed guidelines.

- **Frequency** of tissue necrosis: rare and inconsistent reports suggested a low vesicant potential compared with vesicants
- **Severity** of tissue damage: ranged from superficial injury (e.g., blistering, exfoliation) to necrosis; superficial injuries usually resolved without complications

### Updated Extravasation Classification (Table 3)

**1. New category: Irritant with vesicant properties**

Based on the characteristics identified, a new intermediate category, "irritant with vesicant properties" has been developed at BC Cancer. Compared with vesicants, irritants with vesicant properties behave as irritants but have low potential to cause tissue necrosis and/or serious complications.

**2. Existing categories** were refined with updated classification criteria. Key updates include:

- **Vesicant**: the potential of tissue necrosis or serious complications is specified as **high,** to contrast with "irritant with vesicant properties"
- **Irritant**: expanded to include **absence of blistering**
- **None**: expanded to include **flare reactions** or **mild to moderate inflammation** that are not associated with burning sensation or pain

## Discussion

- "**Irritant with vesicant properties**" is now clearly defined with new classification criteria. Existing categories (vesicant, irritant, none) have been refined for clear distinction between categories.
- Updated extravasation classification **reduces uncertainty** and supports **consistent classification**.
- Updated criteria can guide both the reclassification of existing drugs and the evaluation of new oncology drugs. (Figure 1)
- Classification is based on **clinical data**. Drugs are re-evaluated when new evidence emerges to support reclassification.
- Limitation: the updated classification criteria have not yet been applied to all existing vesicants and irritants; validation at BC Cancer is ongoing.

References
1. BC Cancer Provincial Systemic Therapy Program. Provincial Systemic Therapy Program Policy III-20: Prevention and Management of Extravasation of Chemotherapy. Vancouver, British Columbia: BC Cancer; March 1 , 2021.
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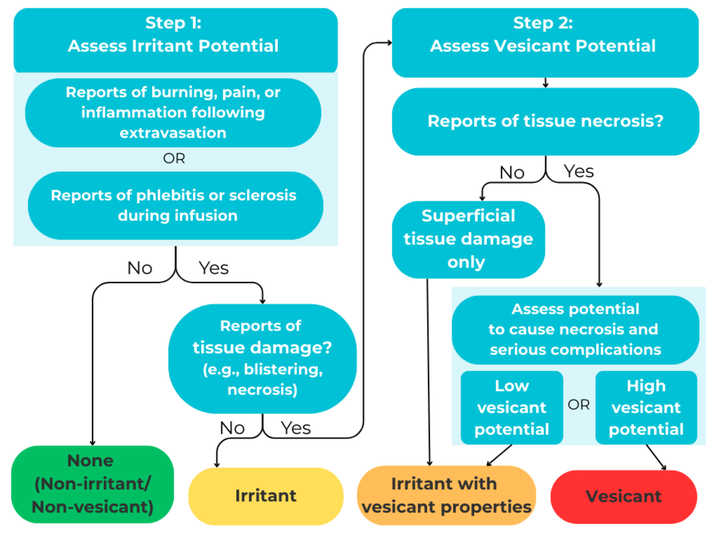
4. NHS Royal Cornwall Hospitals. Prevention and Management of the Extravasation of Systemic Anti-Cancer Therapy in Adults Clinical Guideline V7.0. England: National Health Service (NHS); March, 2025.
5. Cancer Institute of New South Wales (NSW) eviQ. Extravasation Management v.6. Cancer Institute NSW; Accessed November 4, 2025. Updated May 3, 2023. Available at: https://www.eviq.org.au/clinical-resources/extravasation/157-extravasation-management
6. Olsen M. Chemotherapy and Immunotherapy Guidelines and Recommendations for Practice. 2nd ed. Pittsburgh, United States: Oncology Nursing Society; 2023.

**Table 3. Updated Extravasation Classification at BC Cancer**

| Categories | Definitions and Classification Criteria |
|---|---|
| **Vesicant** | Drug causes **blistering,** local or extensive **tissue necrosis** or **ulceration** following extravasation. Extravasation would likely cause tissue necrosis if left untreated.<br><br>Drug meets one or more of the following criteria:<br>1) **High potential to cause tissue necrosis** following extravasation based on multiple consistent reports of tissue necrosis or ulceration (often preceded by blistering)<br>2) **High likelihood of serious complications** following extravasation based on reports of tissue necrosis extending into deeper structures (e.g., tendons or nerves) and/or resulting in permanent clinical sequelae (e.g., limited range of motion) |
| **Irritant with vesicant properties (NEW)** | Drug behaves as an **irritant** (causes burning sensation, pain, tightness, with or without inflammation) but **in rare cases** causes **tissue damage** following extravasation. Extravasation would potentially cause tissue necrosis if left untreated.<br><br>Drug meets criteria of irritant, and one of the following criteria:<br>1) **Low potential to cause tissue necrosis** following extravasation based on rare or inconsistent reports of tissue necrosis or ulceration<br>2) **Low likelihood of serious complications** following extravasation based on reports of damage limited to **superficial tissue only** (e.g., blistering or exfoliation[a]), but no reports of tissue necrosis |
| **Irritant** | Drug causes **burning sensation, pain, tightness,** with or without **inflammation** during infusion or following extravasation. Extravasation does not cause tissue damage[b] (e.g., blistering, necrosis, or ulceration).<br><br>Drug meets one or more of the following criteria:<br>1) Reports of burning sensation, pain, tightness, with or without inflammation along the intact vein or at the extravasated injection site, but no reports of tissue damage<br>2) Reports of phlebitis[c] and/or sclerosis along the intact vein or at the injection site, but no reports of tissue damage |
| **None** | Drug does **not cause reactions** (e.g., burning sensation, pain, or tightness etc.) during infusion or following extravasation.<br><br>Drug meets one or more of the following criteria**:**<br>1) No reports of reactions during infusion or following extravasation<br>2) No reports of burning sensation or pain during infusion, although flare reactions[d] or mild to moderate inflammation may have been reported<br>3) Recommended routes of administration include subcutaneous, intradermal, or intramuscular routes |

[a]Exfoliation reactions may include peeling, desquamation, shedding of skin with or without inflammation
[b]However, a large volume of a concentrated irritant solution can cause necrosis.
[c]Phlebitis: local inflammation of the vein due to irritation of endothelium with or without vasospasm
[d]Flare reactions: painless local reaction along the vein or near the intact injection site characterized by immediate, red blotches or streaks, or local wheals with or without edema, pruritus or irritation

**Figure 1. Classification Flow Chart**




## Conclusion

- A new intermediate extravasation hazard category, "irritant with vesicant properties," has been developed at BC Cancer, with clear delineation from the "vesicant" and "irritant" categories.
- Updated classification enhances safe drug administration by supporting the development of appropriate strategies for extravasation prevention and management.