

British Columbia Cancer Agency | POLICY

Title: PREVENTION AND MANAGEMENT OF EXTRAVASATION OF CHEMOTHERAPY	Number: III-20
Effective Date: September 1, 1997 Revised Date: January 2016	Approved By: Provincial Systemic Program Committee

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Reason for Directive

A number of agents used in cancer chemotherapy are extremely irritating if they extravasate or infiltrate into the tissues rather than remaining within the vasculature.¹⁻¹³ The BCCA Cancer Drug Manual divides the extravasation hazard of these agents into the following categories:

1. Vesicant
2. Nonvesicant
 - a. Irritant
 - b. None

See the list of drugs in the Extravasation Hazard Table in the Cancer Drug Manual.

The agents listed as vesicants can cause extensive necrosis. Doxorubicin, daunorubicin, epirubicin and mitomycin bind to DNA, recycle locally and may cause a progressive slough of tissue over several weeks, requiring excision and skin grafting.

In order to avoid problems of this kind, great care must be taken to assure that these agents are given into an intact vein with a good free flow of blood. Drug may leak from sites of previous recent punctures or from veins which are occluded from any cause such as tight clothing, obstructing masses or clotting. Therefore, the insertion site should not be distal to a recent venipuncture or in an arm with compromised circulation. It is preferable to select, if possible, a large vein which is not adjacent to a joint or structures which may be particularly troublesome should a tissue slough occur (such as the wrist or hand). A large vein in the mid-forearm would be ideal, if available.

These guidelines are used in conjunction with :

[BCCA Systemic Therapy Policy III-80 Algorithm for Patency Assessment of Needle Placement / Catheter Patency in CVC Devices](#)

[BCCA Nursing Practice Reference C-252 Administration of Chemotherapeutic Agents](#)

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Definitions

<i>Extravasation</i>	escape of drug from a vessel into the subcutaneous tissues
<i>Vesicant</i>	blistering, local or extensive tissue necrosis with or without ulceration ^{10,14-16}
<i>Irritant</i>	<ul style="list-style-type: none"> - no tissue necrosis or ulceration¹⁰ - burning sensation, pain, tightness, with or without inflammation, at <u>extravasated</u> injection site or along the vein^{10,14-17} <p>If no extravasation data available:</p> <ul style="list-style-type: none"> - classify a drug as irritant if it causes phlebitis and/or sclerosis of veins at <u>intact</u> injection site or along the vein¹⁵⁻¹⁷ - phlebitis is the local inflammation of the vein due to irritation of endothelium with or without vasospasm - flare reactions¹⁵ alone are insufficient for irritant classification
<i>None</i>	a drug that can be given by subcutaneous, intradermal, or intramuscular, <u>and/or</u> no reported evidence of any reactions as seen with vesicant or irritant
<i>Flare</i>	<p>painless local reaction along the vein or near the intact injection site characterised by:</p> <ul style="list-style-type: none"> - immediate, red blotches or streaks (histamine release phenomenon), or local wheals¹⁵; edema may sometimes occur¹⁵ - with or without pruritus or irritation¹⁵ - symptoms usually subside with or without treatment 30 min after the infusion is stopped, although they may last for 1-2 hours and rarely more than 24 hours⁴

Precautions

Via a Peripheral Intravenous (PIV) line:

1. Select a large vein away from joints or tendons, if possible, e.g., in forearm. (Warming with water may help to dilate veins). Hand veins may be used and may be easier to observe in some patients, however extravasation in this area may cause severe damage.
2. Establish a new PIV site, rather than using a pre-existing PIV.
3. Make a clean venipuncture. Leave the needle entry site visible so that it can be watched during injection.
4. Have IV flowing freely at all times with normal saline.
5. The majority of vesicants are injected into the medication injection port of IV tubing slowly enough that the IV drip does not stop or reverse. Watch needle tip for evidence of extravasation and check for blood return every 2-3 mL during injection.
6. The following vesicants: mechlorethamine, streptozocin and vinorelbine are mixed in a minibag and infused by intermittent infusion due to irritation caused by IV push. Vincristine is

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mixed in minibag to prevent inadvertent intrathecal administration.¹⁹ Watch needle tip for evidence of extravasation and check for blood return every 1-2 minutes.

7. Flush thoroughly with normal saline.
8. Elevate limb and maintain gentle pressure over the venipuncture site for five minutes after needle withdrawn.

Via a [Central Venous Access Device \(CVAD\)](#):

1. Prior to administration of chemotherapy, brisk blood flash back should first be visible upon aspiration to ensure location in the vein and proper function of the central venous access device.
2. A 25-mL bolus of normal saline should then be infused via gravity to ensure free flow without local discomfort or swelling. The medication can then be administered.
3. Following infusion of the medication, the IV line should be flushed with at least 25 mL of Normal Saline.

[Note](#)⁴²:

1. Patients with Implanted Venous Access Devices (IVADs) placed deep within subcutaneous tissue may need to have their IVAD accessed with longer needles to avoid needle dislodgement and risk of extravasation.
2. PIVs and IVAD needles must be stabilized securely, easily observable and IV tubing anchored to allow flexibility without disturbing connections.
3. Patients and staff members must take care to avoid dislodging IV devices during transfers, transports and clothing changes.
4. Reassess venous access site, to ensure needle remains in situ following patient ambulation.

Patient Education⁴²:

1. Explain the risks of dislodgement that can occur should the access site be disturbed.
2. Teach patient to inform the RN immediately if discomfort, swelling, redness, pain (at site, chest or pleuritic), burning, fever, or cough is experienced.

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Assessment of Extravasation Versus Other Reactions *

Assessment Parameter	Extravasation		Spasm/Irritation of the Vein	Flare Reaction
	Immediate Manifestations of Extravasation	Delayed Manifestations of Extravasation		
Pain	Severe pain or burning at the needle site and / or anywhere along the vein or catheter in the case of a CVAD that lasts minutes or hours and eventually subsides; usually occurs while the drug is being given.	Hours - 48	Aching and tightness along the vein	No pain
Redness	Blotchy redness around the needle site; it is not always present at time of extravasation	Hours - months	The full length of the vein may be reddened or darkened	Immediate blotches or streaks along the vein, which usually subside within 30 minutes with or without treatment
Ulceration	Develops insidiously; usually occurs 48-96 hours later	Hours - months	Not usually	Not usually
Swelling	Severe swelling or "bleb" formation at the needle site and / or anywhere along the vein or catheter in the case of a CVAD; usually occurs immediately	Hours - 48	Not likely	Not likely; wheals may appear along the vein line
Blood return	Inability to obtain blood return	Good blood return during drug administration	Usually	Usually
Other	Change in the quality of infusion	Local tingling and sensory deficits	Possibly resistance felt on injection	Urticaria

* Adapted from ONS Cancer Chemotherapy Guidelines

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If there is aching or red streaking along the vein or resistance is felt on injection, inflammation and **spasm of the vein** may have occurred. The injection should be discontinued and the saline infusion allowed to flush the vein until the pain, redness or spasm has subsided. Doxorubicin and epirubicin are particularly likely to cause a local wheal or red streaking (a histamine release phenomenon) which will subside but may take thirty minutes or more after the injection is stopped. Hydrocortisone injected into the IV line may hasten clearing of the reaction, and requires a physician's order. The injection may then be cautiously resumed.

Thrombosis or sclerosis of veins may occur due to the local effect of chemotherapeutic agents on the endothelium. These can be managed conservatively with warm or cold compresses to the area plus an analgesic for pain, if required.

Directive

- An extravasation tray will be kept in each patient care area where chemotherapy is administered.
- Each area will establish a procedure for monthly checking of the tray contents (see below)
- Despite every precaution, extravasations occasionally do occur. **If leakage is noted or suspected during the injection,⁴³ the following procedure describing the management, documentation and follow-up of the event will be followed.**

Extravasation Tray will contain:

- Pain Ease® spray
- dimethylsulfoxide (DMSO) 99% topical solution*
- hyaluronidase 1500 units /mL injection (HYALASE®) ampoule**
- hydrocortisone 1% cream
- sodium thiosulfate 25% injection, 10 mL vial***
- 10 mL syringe (for preparing sodium thiosulfate)***
- 25 gauge needles
- 3 mL syringes
- black indelible ink marker
- ice pack - in freezer
- sterile gauze dressings and tape
- sling

* Available from Xenex (Sel-Win) in B.C., tel: 1-800-663-1002, as 99.7% solution.

** Available through Health Canada Special Access Programme

*** Only if intravenous mechlorethamine is available for use

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Procedure for the extravasation of a VESICANT

At the time of extravasation:

1. STOP INJECTING IMMEDIATELY.
2. STOP the IV Infusion. [Do not remove the venipuncture catheter/ needle.](#)^{40,43}
3. Disconnect the IV tubing from the Venous Access Device (PIV or CVAD) and attempt to aspirate as much drug as possible with a new (minimum 10ml) syringe.
4. Notify the attending oncologist or medical resident. If neither is available, page the medical oncologist or medical resident on call.
5. Refer to type of extravasation (see list below) for recommended actions:

Rationale

Prompt action to minimize the effect is important.
To prevent additional drug from being injected into the area.

Type of Extravasation	Actions	Rationale
a) Daunorubicin, doxorubicin, epirubicin, mitomycin	<ol style="list-style-type: none"> 1. Remove venipuncture catheter/ needle. 2. Apply DMSO 99% topical solution to an area twice that affected by extravasation (4 drops per 10 cm² of skin surface area).¹ 3. Allow DMSO to air dry, do not cover and repeat qid for at least 7 days. 4. Elevate limb and apply gentle pressure to site. 5. Apply ice pack wrapped in towel or cold compresses to the extravasation site for 1 hour. Care must be taken to avoid tissue injury from excessive cold. 6. Proceed to #6 of procedure. 	<p>DMSO speeds up removal of the drug from the tissue and is a free-radical scavenger.</p> <p>Air-drying is required as DMSO may cause blisters with occlusions.</p> <p>Causes local vasoconstriction and decreases fluid absorption.</p>

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Type of Extravasation	Actions	Rationale
b) Vinblastine, vincristine, vindesine, vinorelbine	<ol style="list-style-type: none"> 1. Remove venipuncture catheter/needle. 2. Elevate limb and apply gentle pressure to site. 3. Apply warm compresses to extravasation site for 1 hour. Care must be taken to avoid tissue injury from excessive heat. 4. See "Guidelines for the use of an antidote" in this policy if ordered by physician. 5. Proceed to #6 of procedure 	Cooling may have adverse effect.
c) Mechlorethamine	<ol style="list-style-type: none"> 1. Do not remove venipuncture catheter/ needle until discussion with physician re: use of antidote. If used, see "Guidelines for the use of antidote" in this policy. 2. Remove venipuncture catheter/ needle. 3. Elevate limb and apply gentle pressure to site. 4. Apply ice packs wrapped in towel or cold compresses. Care must be taken to avoid tissue injury from excessive cold. 5. Proceed to #6 of procedure 	Causes local vasoconstriction and decreases fluid absorption.
d) Amsacrine Carmustine Dactinomycin Idarubicin Melphalan Mithramycin Paclitaxel Streptozocin	<ol style="list-style-type: none"> 1. Remove venipuncture catheter/needle 2. Elevate limb and apply gentle pressure to site 3. Apply ice packs wrapped in towel or cold compresses. Care must be taken to avoid tissue injury from excessive cold 4. Proceed to #6 of procedure 	
e) Oxaliplatin	<ol style="list-style-type: none"> 1. Remove venipuncture catheter/needle. 2. Elevate limb and apply gentle pressure to site. 3. Apply warm compresses to extravasation site for 1 hour. Care must be taken to avoid tissue injury from excessive heat. 	Cooling may have adverse effect.

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| <ol style="list-style-type: none"> 6. Initiate Part 1 (evaluation and interventions) of the Flowsheet for Suspected / Actual Chemotherapy Extravasation (Appendix 1) and file on patient's chart. 7. Trace affected area on a transparent dressing (Opsite) or paper and attach to the flowsheet 8. Report to Patient Safety Learning System (PSLS) 9. Complete Part II of flowsheet and send a copy to Systemic Therapy Process leaders after completed. Original is sent to PIM. 10. As necessary, arrange for prescriptions for use at home (e.g., analgesics, hydrocortisone cream, dimethylsulfoxide). 11. Give patient written patient information on Care of a Suspected Extravasation. (Appendix II). | <p>For comparison at subsequent visits.</p> <p>To reinforce verbal information on home management of the injection site.</p> |
|---|--|

Follow-up:

Patients should be closely followed after suspected extravasation so that appropriate further action can be taken. Some extravasations, although painful, may heal without surgical intervention. This is particularly true of vinca alkaloids. Others, particularly those due to doxorubicin, other DNA binders and mechlorethamine, may recycle locally and produce progressive necrosis and slough requiring surgical intervention. Areas of extensive blistering or ulceration, progressive induration and erythema, or persistent severe pain, are indications for surgical assessment and possible excision of the injured tissue. Surgical intervention should not be delayed for long in the presence of progressive local injury. Analgesics should be given, as required, for pain.

Procedure

1. Part II of the Flowsheet (Appendix I) will be completed on follow-up phone calls or visits.
2. For a suspected extravasation, the nurse will telephone the patient within 1-3 days. Based on the patient's report of the status of the site, the patient may be requested to return to the clinic for assessment.

Rationale

To determine if further interventions are necessary.

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Procedure

3. For a known extravasation, make arrangements for the patient to return to the clinic for assessment in 48 hours. Arrange follow-up assessments on day 5, 7 and 14. Continue weekly follow-up if necessary.
4. When the patient returns to the clinic for assessment, they will be seen by the nurse, and by the physician if necessary, based on the nurse's assessment.
5. If assessment is required on a weekend, this will be arranged with the on-call medical oncologist.
6. Areas of extensive blistering or ulceration, progressive induration and erythema, or persistent severe pain, are indications for surgical assessment and possible excision of the injured tissue. The attending oncologist should refer the patient for surgical intervention in the presence of progressive local injury.

Rationale

To determine if further interventions are necessary. Continual observation over a period of several weeks is important.

Procedure for the extravasation of porfimer (Photofrin®)

Extravasation hazard associated with porfimer is due to irritation caused by its local photodynamic effect. Area of extravasation should be protected from light for a minimum of 30 days.¹⁸

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Guidelines for the use of an ANTIDOTE

It is difficult to be certain that injection of antidotes into the area of extravasation is of benefit and reports are conflicting. Most small extravasations do not result in serious problems without injection of antidotes, so that injection of specific antidotes should likely be restricted to larger extravasations (>1-2 mL).

The use of an antidote other than DMSO requires a physician's order.

Extravasated Drug	Suggested Antidote
daunorubicin doxorubicin epirubicin mitomycin	<p>dimethylsulfoxide (DMSO) 99% topical solution, apply to an area twice that affected by the extravasation, allow to air dry, do not cover, repeat qid for at least 7 days.</p> <p>After extensive review it has been determined that the superiority of dexrazoxane over DMSO has not been established.^{1,7,20-37} It is the position of the BCCA that dexrazoxane not be included in this policy, and that DMSO remain the standard of care. The decision will be reviewed when new literature becomes available.</p>
mechlorethamine	2.5 mL of sodium thiosulfate 1/6 molar, given through the existing IV line (to prepare: mix 1.6 mL sodium thiosulfate 25% solution with 8.4 mL sterile water for injection to give 10 mL of 1/6 molar solution). If this is to be helpful it must be done immediately after the extravasation and preferably through the same needle to insure injection into the same tissue plane as the extravasation.
vinblastine vincristine vindesine vinorelbine	hyaluronidase 1500 units dissolved in 1 mL water for injections or 0.9% sodium chloride injection, infiltrated into affected area (as soon as possible after extravasation) subcutaneously (25 g needle) in a clockwise fashion in divided doses around the site. Anesthetize the skin surface with Pain Ease® spray if the patient cannot tolerate the subcutaneous injections. Hyaluronidase (Hyalase®) is available through Health Canada Special Access Programme.

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APPENDIX I

BC CANCER AGENCY

- Abbotsford Cancer Centre
- Fraser Valley Cancer Centre
- Vancouver Cancer Centre
- Vancouver Island Cancer Centre
- Cancer Centre for the Southern Interior
- Cancer Centre for the North

FLWSHEET FOR SUSPECTED / ACTUAL (circle one)
CHEMOTHERAPY EXTRAVASATION

PART I:

addressograph stamp

Date: _____

Date event occurred: _____

INITIAL EVALUATION (Day 0)

DESCRIPTION OF EXTRAVASATION

Name and volume of drug given: _____

IV site location: (indicate on diagram and describe):

Needle type, gauge, and length : _____

Patency: _____

Quality of blood return: _____

IV / CVAD site appearance: _____

Stabilizing dressing intact: Yes or No

Needle dislodged from IVAD : Yes or No

Infusion Pump used : Yes or No

Patient complaints: _____

Physician notified (name): _____

R.N. (name): _____

Diagram of Site

INITIAL INTERVENTIONS

Date _____ Antidote given *
(specify) _____
_____ Cold compresses
_____ Warm compresses
_____ 1% Hydrocortisone
cream applied
_____ Baseline photo

ADDITIONAL INTERVENTIONS

Date _____ Dermatology Consult*
_____ Plastic Surg. Consult*
_____ Wound Care (describe)

_____ Follow-up photo

PATIENT TEACHING

Date _____ Appendix II given and
reviewed
_____ Follow-up schedule
reviewed

PART II:

FOLLOW-UP FLOW CHART

Patient phone #: _____

(Refer to Grading Scale on reverse side)

	Day 1	Day 3	Day 5	Day 7	Day 14	Day 21**	Day 28**	Day 35**	Day 42**
Date									
Call/Visit									
Skin color									
Skin Temp.									
Edema									
Mobility									
Pain									
Fever									
RN initial***									

* Requires M.D. order for other than DMSO
** May omit if no signs of extravasation
*** Full signature required on reverse side

APPENDIX II

B C CANCER AGENCY:
Abbotsford Centre
Fraser Valley Centre
Vancouver Centre
Vancouver Island Centre
Centre for the Southern Interior
Centre for the North

FOR THE PATIENT: Care of a suspected extravasation

A rare but known complication of chemotherapy is extravasation, or the leaking of the chemotherapy out of the vein. There is a possibility that some of the chemotherapy you received today leaked out of your vein and under your skin. Some chemotherapy can cause skin irritation, sores, or deeper tissue injury where it was given. Your chemotherapy nurse will be calling you on a regular basis to monitor your condition.

Name of the chemotherapy drug, which may have extravasated: _____

Care of the Site:

To minimize the discomfort and irritation, it is important that you follow the instructions checked below.

	Procedure	Rationale
<input type="checkbox"/>	Apply a cold compress to injection site four to five times a day for 15-20 minutes over the next 24 to 48 hours.	This will decrease the swelling and discomfort and may reduce irritation to the tissue.
<input type="checkbox"/>	Apply a warm compress to injection site four to five times a day for 15-20 minutes over the next 24 to 48 hours.	This will decrease the swelling and discomfort and may reduce irritation to the tissue.
<input type="checkbox"/>	Elevate the affected arm on a pillow whenever possible.	This will help to reduce the swelling.
<input type="checkbox"/>	Apply a thin layer of hydrocortisone cream (1%) twice a day until the redness disappears. Discontinue if the area blisters. You may apply a dry gauze pad loosely over the cream to protect your clothing.	This will help to reduce the redness and inflammation.
<input type="checkbox"/>	After showering or bathing, gently pat with your towel to dry the site. Do not rub. If you take a tub bath or immerse the area in anything but rapidly running clean water, cover the site first with a protective watertight dressing or barrier.	This will help to protect the area while it heals.
<input type="checkbox"/>	Apply dimethylsulfoxide (DMSO) 99% solution to an area twice that is affected. Allow to air dry. Do not cover. Repeat four (4) times a day for at least 7 days.	This may help to reduce skin damage.

Call Your Doctor or Nurse if You:

- * Notice any changes at the site, including increased pain or redness, blisters, streaking along the arm, any signs of skin breakdown, or swelling.
- * Develop a fever of more than 100.5° F (38° C).
- * Have any questions, problems or concerns.

Special Points:

- * Do not apply any lotion, cream, or ointments unless instructed to do so by your doctor or nurse.
- * Do not expose the area to sunlight.
- * Avoid clothing that constricts the affected area.
- * Protect the area with an occlusive dressing if it is to be immersed in water.