Extravasation[1] Management (Vesicant and Contrast Agents)

Disclaimer: *This algorithm has been developed for MD Anderson using a multidisciplinary approach considering circumstances particular to MD Anderson's specific patient population, services and structure, and clinical information. This is not intended to replace the independent medical or professional judgment of physicians or other health care providers in the context of individual clinical circumstances to determine a patient's care. This algorithm should not be used to treat pregnant women.*

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[1]Unintentional instillation, leakage, passage or escape of a vesicant out of a blood vessel into surrounding tissue. This may result in varying degrees of impairment including pain, necrosis, and tissue sloughing.

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ADMINISTRATION OF VESICANT AGENT

Patient to be administered vesicant[1] agent

Is the infusion ≥ 60 minutes?

A

Yes

Prior to starting infusion:
- CVAD required. If no CVAD, then nurse to contact ordering provider.
- Nurse to conduct pre-administration prevention strategies and line assessment (see Appendix B)
  - If any of the criteria are not met, do not start infusion and contact ordering provider and VA&P Team

During infusion, monitor:
- Infusion flow rate
- Infusion site for signs and symptoms of extravasation[2] after the first 15 minutes of infusion, then at least every 4 hours[3] until completion
- Document as indicated[4]

No

- Infusion via CVAD preferred, see Box A above
- If only peripheral intravenous (PIV) access available, prior to starting PIV infusion:
  - Nurse to conduct pre-administration prevention strategies and line assessment (see Appendix B)
    -Avoid using established PIV access that is more than 24 hours old
    -Administer via new, non-traumatic adequately secured venipuncture site
  - If any of the criteria are not met, do not start infusion and contact ordering provider

If infusion through PIV:
- Nurse to remain in room for entire infusion, monitor for signs and symptoms of extravasation[2,3]
- Check for blood return and line patency[5]:
  - IVPB every 5-10 minutes
  - IVP every 2-5 mLs
- Document as indicated[4]

Signs and symptoms of extravasation[2] during infusion?

Yes

See Page 3 for management of extravasation during infusion

No

After infusion:
- Document all assessment, interventions, evaluation, and patient education[6]
- If patient experiences signs and symptoms of extravasation[2] see Page 3 for management

CVAD = central venous access device
IVPB = intravenous piggyback
IVP = intravenous push
VA&P = Vascular Access and Proceduress

[1] Vesicant is any agent that has the potential to cause tissue destruction, blistering, severe tissue injury, or tissue necrosis when extravasated. Refer to current institutional list of vesicant agents.
[2] See Appendix C for signs and symptoms of extravasation
[3] This does not apply to patients who are going home with a CVAD other than an implanted venous port. Refer to Vascular Vesicant/Irritant Administration and Extravasation Policy (#CLN0986).
[4] Refer to Medication Administration Record (MAR) Policy (#CLN0648)
[5] If blood return and/or line patency cannot be established and there is no sign of infiltration, the infusion must be stopped and a PIV access must be restarted using a new site. Refer to Vascular Vesicant/Irritant Administration and Extravasation Policy (#CLN0986).
[6] Refer to patient education Chemotherapy Vesicant Administration Special Instructions

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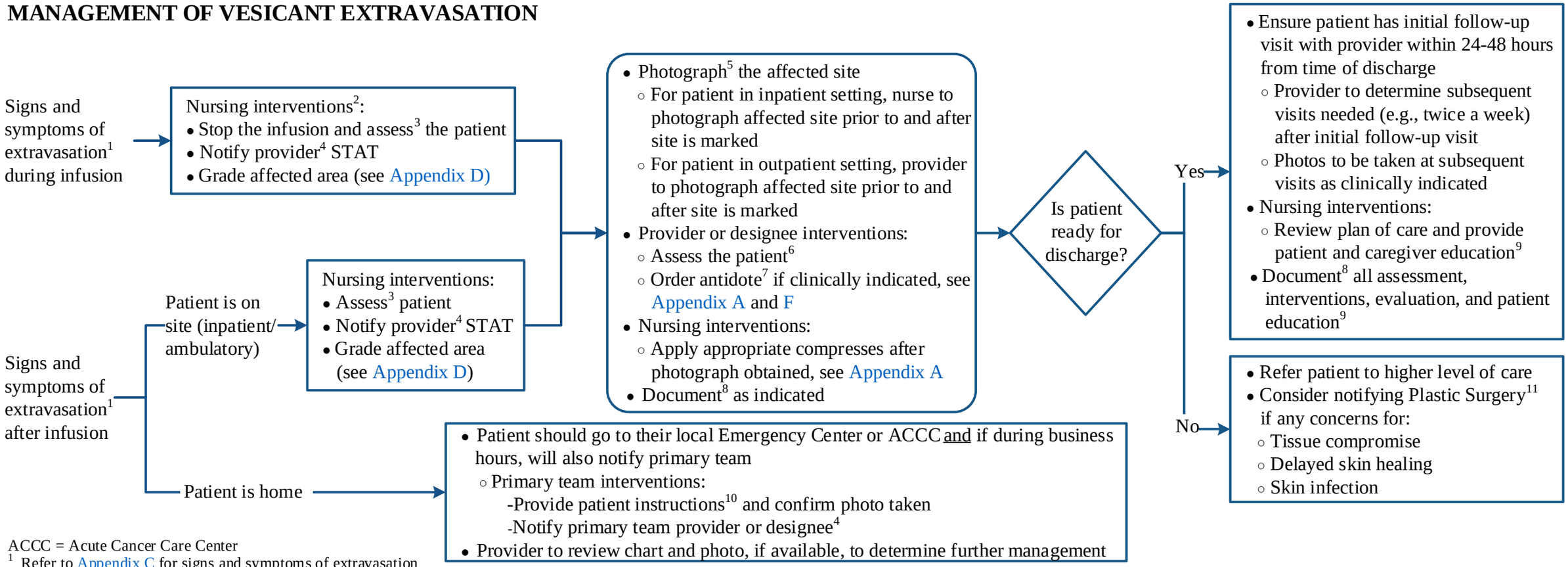
MANAGEMENT OF VESICANT EXTRAVASATION



ACCC = Acute Cancer Care Center

[1] Refer to Appendix C for signs and symptoms of extravasation

[2] **SLAPP** – **S**top infusion. Do not flush. **L**eave IV in place. **A**ssess and aspirate with 1-3 mL syringe (document description and volume aspirated). **P**ull IV/implanted port needle. **P**rovider notification.

[3] Nursing assessment to include checking capillary refill, motor function and sensation

[4] For the main campus, the primary team/ordering provider is notified first. For after hours, holidays or weekends, contact the on-call advanced practice provider (APP), nocturnal team or the on-call provider for the ordering physician. For Houston Area Locations (HALs), contact site-specific on-call provider or the primary team. For after hours and the weekend, contact the appropriate covering provider.

[5] Subsequent photos to be obtained as clinically indicated. For medical photography, refer to Photographs – HIPAA Authorizations General Reference Tool (ATT1597)

[6] Consider transfer of patient to ACCC based on clinical assessment and medical history. For patient at a HAL, consider calling 911 if appropriate.

[7] Antidote to be ordered by provider after assessment and evaluation are completed

[8] For additional documentation, see Appendix E

[9] Refer to patient education Chemotherapy Vesicant Administration Special Instructions

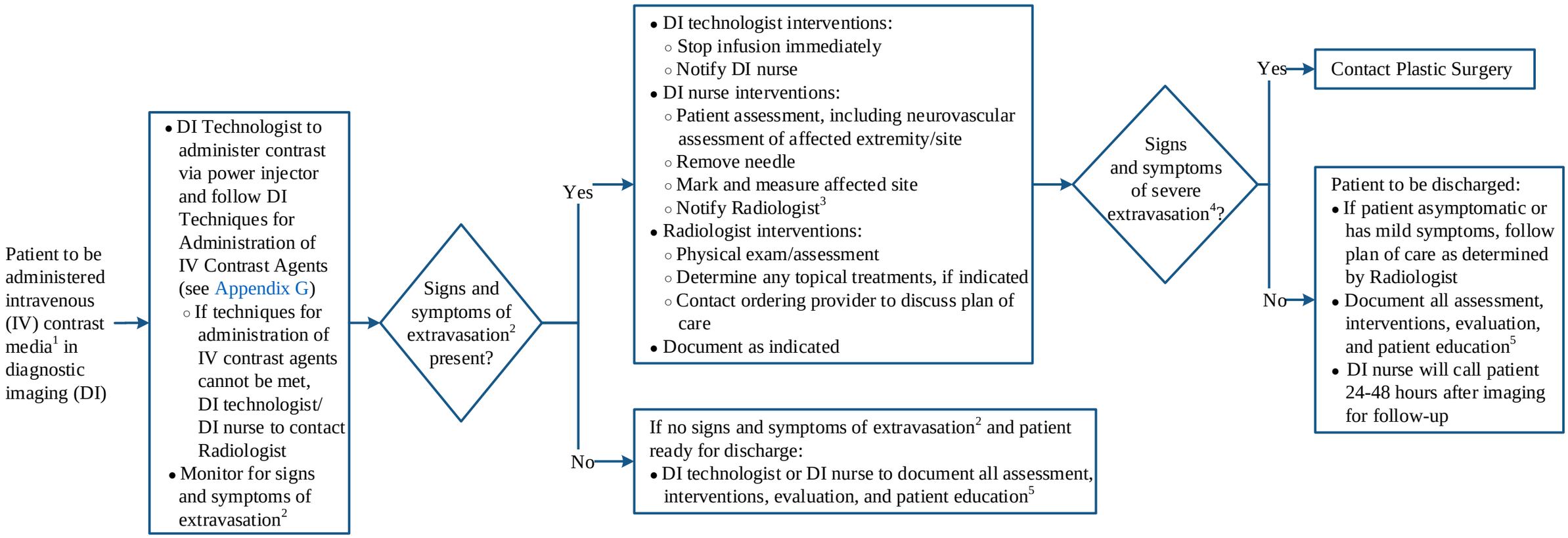
[10] Nurse to confirm patient is en route to ACCC or local Emergency Center. Recommend patient/caregiver to mark the boundary of the erythema with a pen and photograph the affected site, include time taken, and if photo taken using a mirror and upload via MyChart. Instruct patient to elevate affected extremity; do not apply any pressure on the affected area. If photo confirmed in MyChart, instruct patient to apply appropriate compress (see Appendix D).

[11] If notifying Plastic Surgery, consider ordering MRI of the affected area and if MRI is contraindicated, order CT scan with and without contrast; preferably prior to notifying Plastic Surgery

Department of Clinical Effectiveness V1
Approved by the Executive Committee of the Medical Staff on 07/20/2021

Extravasation Management (Vesicant and Contrast Agents)

DIAGNOSTIC IMAGING EXTRAVASATION MANAGEMENT



[1] Refer to Administration of Contrast Media in Diagnostic Imaging Policy (#CLN1268)
[2] Signs and symptoms of extravasation may include pain, tenderness, swelling, itching, skin tightness, redness
[3] If after hours, contact DI on-call resident
[4] Severe extravasation requires immediate surgical consult and includes one or more of the following signs or symptoms: progressive swelling or pain, altered tissue perfusion, change in sensation in the affected limb, worsening passive or active range of motion of the elbow, wrist, or fingers, and skin ulceration or blistering
[5] Refer to patient education

APPENDIX A: Extravasation Management of Vesicants

VESICANT	IMMEDIATE TOPICAL THERAPY	ANTIDOTE[1]
Anthracyclines: danorubicin, doxorubicin, epirubicin, idarubicin	Apply COLD compress (remove at least 15 minutes prior to dexrazoxane administration)	Dexrazoxane
Alkylating agent: mechlorethamine	Apply COLD compress for 6-12 hours **after** sodium thiosulfate injection	Sodium thiosulfate
Vinka alkaloids: vinblastine, vincristine, vinorelbine	Apply WARM compress for 15-20 minutes four times daily for the first 24 hours. Elevate extremity for peripheral extravasations.	Hyaluronidase[2]
Dactinomycin, mitomycin	Apply COLD compress for 15-20 minutes four times daily for the first 24 hours	No available antidote[3]
Vasopressors: dobutamine, dopamine, epinephrine, norepinephrine, phenylephrine	Apply WARM pack proximal to the cannulation site for 15-20 minutes four times daily for the first 24 hours. Elevate extremity for peripheral extravasations.	Phentolamine (preferred) or tertubaline if phentolamine not available

[1] Refer to Appendix F for Antidote Dosing and Administration
[2] Hyaluronidase should be avoided with vasopressor and taxane related extravasations as it may worsen outcomes
[3] For extravasated vesicants that do not have effective antidotes available, local non-pharmacologic measures and close monitoring are important. Non-cytotoxic vesicant extravasations typically are best managed with WARM packs (*e.g.*, vasopressors, hyperosmolar solutions).

Extravasation Management (Vesicant and Contrast Agents)

APPENDIX B: Pre-Administration Prevention Strategies

Vesicant Administration Strategies

CVAD Vesicant Administration:

- All medications classified as vascular vesicants will be dispensed from pharmacy with an extravasation warning label
- Verify patient has received education materials[1] regarding specific drug being infused
- Recommended to be infused through a central vascular access device
- If infused over 60 minutes or greater, vesicant must be administered through a CVAD
- Avoid continuous infusions of vesicants through a femoral-placed implanted venous ports
- Continuous infusions of vascular vesicant through implanted venous ports are permitted only on inpatient units
- Short term infusions of vesicant agents through implanted venous ports may be administered in the Ambulatory Treatment Center (ATC), Clinical Translation Research Center (CTRC), or Houston Area Locations (HALs). Continuous infusion of vascular vesicant agents, *e.g.*, home infusions, are prohibited for out-of-hospital/out of-clinic treatment.
- If an infusion pump is required for administration of a vesicant drug, it must be administered through a CVAD

Peripheral IV Vesicant Administration:

- All medications classified as vascular vesicants will be dispensed from pharmacy with an extravasation warning label
- Verify patient has received education materials[1] regarding specific drug being infused
- Must be infused in less than 60 minutes
- Will be administered via new, non-traumatic ("clean stick") adequately secured venipuncture site
- Avoid using an established PIV access that is more than 24 hours old
- Administration in the dorsum of the hand, any joint space or lower extremity require a physician order. Ensure adequate PIV securement and use joint stabilization device.
- Avoid using small, fragile veins, an extremity with previous multiple venipuncture sites, a vein below a recent (less than 24 hours) venipuncture site and/or venous access site
- Avoid using an extremity with altered sensation or recent/non-healed vesicant extravasation or infiltration site
- Administer with caution in patients with impaired cognition/mental status
- Must be administered via gravity drip or IV push (*e.g.*, no pump administration). If the medication is administered via a pump, it must be infused through a CVAD. Vasopressors during an emergent situation will be an allowed exception and may be infused via a PIV through a pump, if deemed medically necessary.

Line Assessment

CVAD and PIV Line Assessment Include:

A. Site assessment
B. Patency status *(i.e.*, no resistance and presence of blood return during the flushing procedure)
C. Placement verification
D. Dressing status
E. Needleless connector status
F. Line necessity
G. Any deviation in care
H. Hand hygiene
I. Care plan, as appropriate

Needle Length Selection for Implanted Venous Ports

- Needle length selection is dependent on nursing assessment of the depth of the reservoir (distance of the diaphragm from the skin)
- The needle length selected should allow for the non-coring needle tip to come in contact with the base of the port reservoir and to rest as closely to the skin as possible

[1] Refer to patient education Chemotherapy Vesicant Administration Special Instructions

APPENDIX C: Signs and Symptoms of Vesicant Extravasation

Signs and symptoms of extravasation include but are not limited to the following:

Immediate extravasation: Refers to those reactions typically occurring during or shortly after vesicant administration

- Pain, redness, or swelling on or around the injection/infusion site
- Resistance when performing IVP
- No blood return
- Leakage of infusion around injection/infusion site
- Infusion flow that slows or stops

Delayed extravasation: Depending on the vesicant drug, reactions can occur up to 1-2 weeks after vesicant administration

- Persistent, worsening pain, redness on or around the injection/infusion site
- Blistering, sloughing off, ulceration

APPENDIX D: Grading of Infusion Site for Extravasation and Injection Site Reaction CTCAE v5

Adverse Event	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5
Infusion Site Extravasation	Painless edema	Erythema with associated symptoms (*e.g.*, edema, pain, induration, phlebitis)	Ulceration or necrosis; severe tissue damage; operative intervention indicated	Life-threatening consequences; urgent intervention indicated	Death

APPENDIX E: Suspected Extravasation Documentation

- Date and time event occurred
- Estimated amount of vesicant infused
- Signs/Symptoms observed or reported by patient
- Site assessment (range of motion, if applicable), include images of affected site, if available. Every attempt to obtain photographs should be taken in order to better assess extent and progression of tissue damage in the area.
- Physician/designee notification
- Nursing interventions implemented
- Description and volume aspirated
- Antidote administration, if ordered
- Discharge instructions (include consults, follow-up care, and wound management, if applicable)

APPENDIX F: Antidote Treatments[1]

Drug (antidote)	Use With	Dose	Administration	Comments
Dexrazoxane	Anthracyclines	Day 1: 1000 mg/m^2 (maximum dose 2000 mg) Day 2: 1000 mg/m^2 (maximum dose 2000 mg) Day 3: 500 mg/m^2 (maximum dose 1000 mg) • Reduce dose by 50% in patients with creatinine clearance < 40 mL/min	• Withhold cold pack 15 minutes prior to dexrazoxane infusion • Begin infusion as soon as possible and within 6 hours[2] of anthracycline extravasation • Administer over 1 to 2 hours in a large vein in an area remote from the extravasation • Treatment on day 2 and 3 should start at the same hour (± 3 hours) as on day 1	• Efficacy is optimal when administered within 6 hours of extravasation, although patients may still derive some benefit if received after this time[2] • Avoid other topical antidotes (*e.g.*, DMSO) as they may diminish dexrazoxane efficacy • Dexrazoxane may diminish antitumor response to anthracyclines. Clinical evaluation is required to fully assess the risk and determine whether re-dosing of the chemotherapy is warranted. • Use with other chemotherapy agents is untested
Hyaluronidase	Vinca alkaloids	150 units-250 units	• Dosing based on the size of the affected area and can be repeated up to a total dose of 250 units • Inject the total dose subcutaneously (SQ) with a 25-gauge (G) needle using the pentagon approach ○ Divide the total dose into 5 injections[3] ○ Administer across the affected area	Avoid use with taxanes and vasopressors due to potential for delayed healing
Phentolamine	Vasopressors	5-10 mg	• Administer as soon as possible and within 12 hours[2] of vasopressor extravasation • Inject total dose SQ with a 25G needle using the pentagon approach ○ Divide the total dose into 5 injections[3] ○ Administer across the affected area	• Efficacy is optimal when administered within 12 hours of extravasation, although patients may still derive some benefit if received after this time[2] • FDA-approved with norepinephrine; off-label use with phenylephrine, dopamine, and epinephrine

[1] Providers should contact pharmacy to coordinate therapy
[2] If more than the recommended time has passed for when to give the antidote, it is still recommended that it be administered, although efficacy may be compromised
[3] Change needle with each injection

Continued on next page

APPENDIX F: Antidote Treatments[1] – continued

Drug (antidote)	Use With	Dose	Administration	Comments
Sodium thiosulfate	Mechlorethamine	4 % solution (1/6 molar) solution	• Order 2 mL of 4% solution for each 1 mg of drug • Inject the total dose SQ with a 25G needle using the pentagon approach ◦ Divide the total dose into 5 injections[2] ◦ Administer across the affected area	Use with cisplatin and bendamustine are less substantiated
Terbutaline	Vasopressors, if phentolamine is not readily available	1 mg	• Volume administered will be 3-10 mL for large extravasations and 0.5-1 mL for small/distal extravasations • Inject the total dose SQ with a 25G needle or smaller using the pentagon approach ◦ Divide the total dose into 5 injections[2] ◦ Administer across the affected area	Used off-label with sympathomimetic vasoconstrictors

[1] Providers should contact pharmacy to coordinate therapy
[2] Change needle with each injection

Extravasation Management (Vesicant and Contrast Agents)

APPENDIX G: Techniques for Administration of IV Contrast Agents

CT Procedures with Power Injected IV contrast[1]:	**Additional Instructions for Administering Contrast Agents**
• 18G needle is the preferred catheter to utilize for PIV and not the 20G needle • 20G or 22G Diffusics™ may be used in routine protocols for difficult access patients • If utilizing power port and/or Power PICC line, ensure it is accessed with 19G Power Needle	• Placement of IV catheters should be at least above patients' wrist and if possible, utilize antecubital site when using power injection • Avoid placing the IV on the hand with power injection • If unable to get access in the arms and in need of a foot access, a Radiologist order is required and the rate should be 2 mL/sec or less to minimize risk of extravasation • If patient's primary cancer is breast cancer, utilize contra-lateral side of breast cancer • IV contrast media should be administered by power injector through a flexible plastic cannula ◦ Use of metal needles for power injection should be avoided whenever possible • Flow rate should be appropriate for the gauge of the catheter used ◦ Although 22G catheters may be able to tolerate flow rates up to 5 mL/sec, a 20G or larger catheter is preferable for flow rates of 3 mL/sec or greater • An antecubital or large forearm vein is the preferred venous access site for power injection. ◦ If a more peripheral (*e.g.*, hand or wrist) venipuncture site must be used, flow rates should be reduced if feasible (*e.g.*, 1-2 mL/sec)
MRI Procedures with Power Injected IV contrast[1]:	
• 20G is preferred catheter to utilize for PIV verses with power injection • 22G Diffusics™ may be used with power injection for difficult access patients • If utilizing power port and/or Power PICC line, ensure it is accessed with 19G Power Needle • Hand access is allowed when hand injecting only and/or using a 22G	

[1] Pediatric access may require a smaller gauge, along with a lower rate depending on age and protocol

SUGGESTED READINGS

ACR Committee on Drugs and Contrast Media. (2021). *ACR manual on contrast media*. American College of Radiology. https://www.acr.org/-/media/ACR/Files/Clinical-Resources/Contrast_Media.pdf

Goolsby, T.V. & Lombardo F.A. (2006). Extravasation of chemotherapeutic agents: prevention and treatment. *Seminars in Oncology, 33*(1),139-143. https://doi.org/10.1053/j.seminoncol.2005.11.007

Gorski, L. A., Hadaway, L., Hagle, M. E., Broadhurst, D., Clare, S., Kleidon, T., & Alexander, M. (2021). Infusion therapy standards of practice, (8th ed). *Journal of Infusion Nursing, 44*(1S), S1–S224. https://doi.org/10.1097/NAN.0000000000000396

Gorski, L. (2018). *Infusion Therapy: Essentials for Safe Practice*, (2nd ed). Brockton, MA: S.C. Publishing.

Jackson-Rose, J., Del Monte, J., Groman, A., Dial, L., Atwell, L., Graham, J., … Rice, R. (2017). Chemotherapy Extravasation: establishing a national benchmark for incidence among cancer centers. *Clinical Journal of Oncology Nursing, 21*(4), 438–445. https://doi.org/10.1188/17.CJON.438-445

Karius, D. L., & Colvin, C. M. (2021). Managing Chemotherapy Extravasation Across Transitions of Care: A Clinical Nurse Specialist Initiative. *Journal of Infusion Nursing, 44*(1), 14–20. https://doi.org/10.1097/NAN.0000000000000411

Kreidieh, F., Moukadem, H., & El Saghir, N. (2016). Overview, prevention and management of chemotherapy extravasation. *World Journal of Clinical Oncology, 7*(1), 87–97. https://doi.org/10.5306/wjco.v7.i1.87

Mackey, H. T. (2020). Antineoplastic drug administration: Vesicant and irritant agents (oncology) – CE. *Elsevier Performance Manager Clinical Skills*. Retrieved June 18, 2021, from https:/point-of-care.elsevierperformancemanager.com/skills/10739/extended-text?skillId=ON_033#scrollToTop

Nickel, B. (2019). Peripheral Intravenous Access: Applying Infusion Therapy Standards of Practice to Improve Patient Safety. *Critical Care Nurse, 39*(1), 61–71. https://doi.org/10.4037/ccn2019790

Olsen, M. M., LeFebvre, K.B., Brassil, K. J. (Eds.). (2019). *Chemotherapy and Immunotherapy Guidelines and Recommendations for Practice*. Pittsburgh, Pennsylvania : Oncology Nursing Society

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