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Evidence-Based Series #12-12-2 Version 2

A Quality Initiative of the Program in Evidence-Based Care (PEBC), Cancer Care Ontario (CCO) and CCO's Systemic Treatment and Nursing Programs

Safe Administration of Systemic Cancer Therapy Part 2: Administration of Systemic Treatment and Management of Preventable Adverse Events

M. Leung, R. Bland, F. Baldassarre, E. Green, L. Kaizer, S. Hertz, J. Craven, M. Trudeau, A. Boudreau, M. Cheung, S. Singh, V. Kukreti, R. Raha, and the Safe Administration of Systemic Cancer Treatment Expert Panel

Report Date: November 30, 2018

An assessment conducted in December 2017 deferred the review of Evidence-based Series (EBS) 12-2-2. This means that the document remains current until it is assessed again next year. The PEBC has a formal and standardized process to ensure the currency of each document (PEBC Assessment & Review Protocol)

Modifications were made in 2018 pertaining to infusion of low-volume high-concentration monotherapies and safe administration

Evidence-Based Series #12-2 Part 2 is comprised of 3 sections:

Section 1:	**Guideline Recommendations**
Section 2:	**Evidentiary Base**
Section 3:	**EBS Development Methods and External Review Process**

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Evidence-Based Series #12-12-2

A Quality Initiative of the Program in Evidence-Based Care (PEBC), Cancer Care Ontario (CCO) and CCO's Systemic Treatment and Nursing Programs

Safe Administration of Systemic Cancer Therapy. Part 2: Administration of Systemic Treatment and Management of Preventable Adverse Events

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Guideline Report History

Systematic Review			Publications	Notes and Key changes
Guideline Version	Search dates	Data		
Original Version March 10, 2014	January 1980 to October 2005	Full Report	Web publication	N/A
Current Version 2 November 30, 2018	Grey literature search November 2018	Modifications pertaining to medication infusions were made by the Oncology Nursing Program	Updated Web publication	N/A

Evidence-Based Series #12-12-2: Section 1

A Quality Initiative of the Program in Evidence-Based Care (PEBC), Cancer Care Ontario (CCO) and CCO's Systemic Treatment and Nursing Programs

Safe Administration of Systemic Cancer Therapy Part 2: Administration of Systemic Treatment and Management of Preventable Adverse Events: Guideline Recommendations

M. Leung, R. Bland, F. Baldassarre, E. Green, L. Kaizer, S. Hertz, J. Craven, M. Trudeau, A. Boudreau, M. Cheung, S. Singh, V. Kukreti, R. Raha, and the Safe Administration of Systemic Cancer Treatment Expert Panel

Report Date: November 30, 2018

PURPOSE

The purpose of Part 2 of Evidence-Based Series #12-12 is to provide guidance on processes, technologies and devices for the prevention and control of adverse effects that can happen during or following the administration of systemic treatment to adult cancer patients.

TARGET POPULATIONS

- Adult patients who are going to receive chemotherapy treatment or are already receiving chemotherapy treatment for cancer.

INTENDED USERS

- Organizations that provide systemic cancer treatment, including chemotherapy, targeted therapy, and biologics to patients.
- Clinicians and health care providers (e.g., nurses, pharmacists, physicians, administrative support) involved with the administration of systemic cancer treatment, and hospital administrators.

DEVELOPMENT OF THIS REPORT

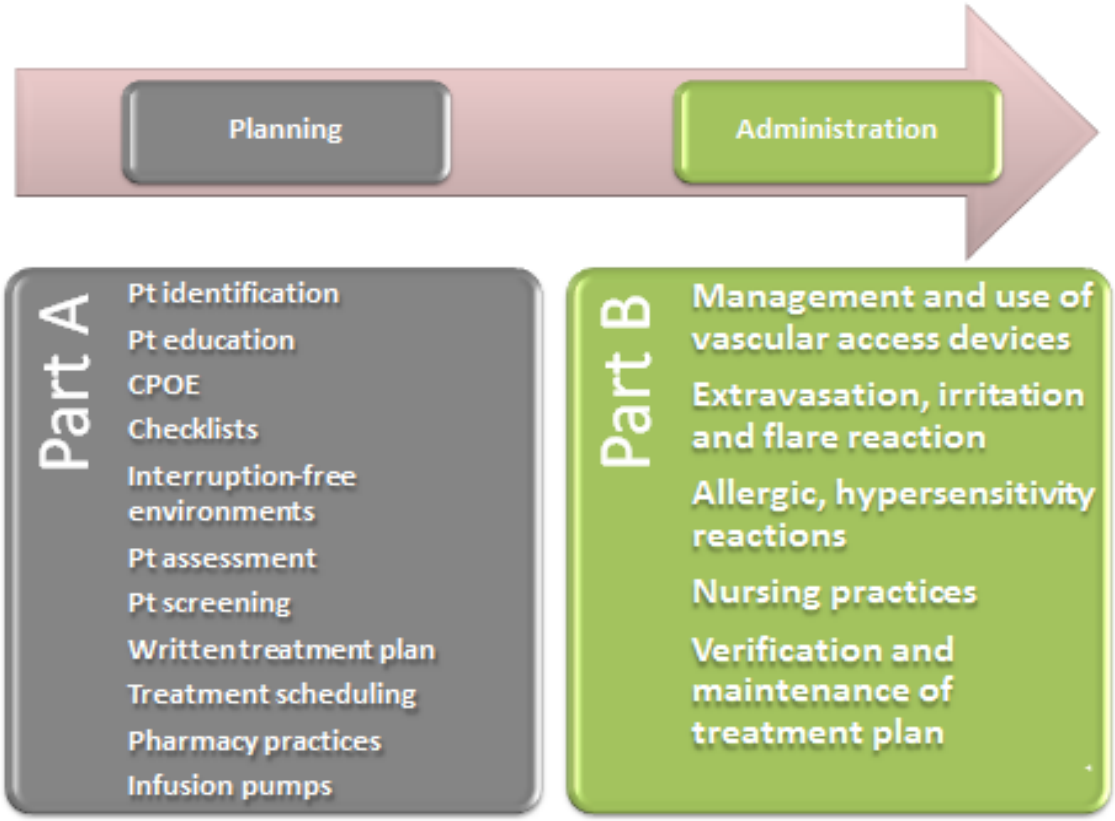
The goal of the Safe Administration of Systemic Cancer Treatment series is to provide recommendations that enable safe administration of chemotherapy with consideration for the "correct patient," "correct drug," "correct route," "correct dose," "correct time," "correct schedule" as well as adequate documentation.

Part 1 of this series focuses on processes occurring before chemotherapy is administered (e.g., patient assessment, education and identification, and chemotherapy ordering, transcribing and dispensing). Part 2 focuses on the safe administration of chemotherapy. The series was developed by considering existing practice guidelines from other jurisdictions, a systematic review of the published literature, and clinical and content expertise from the members of the Working Group (Appendix 1). The values of patient-

centred care and context-specific flexibility guided decisions. A summary of the series and the methods that were used to establish the series can be found at: (https://www.cancercare.on.ca/toolbox/qualityguidelines/clin-program/systemic-ebs/).

The evidence-based series (EBS) guidelines developed by Cancer Care Ontario's Program in Evidence-Based Care (PEBC) use the methods of the Practice Guidelines Development Cycle (1). The PEBC is supported by the Ontario Ministry of Health and Long-Term Care through Cancer Care Ontario. All work produced by the PEBC is editorially independent from its funding source.

Figure 1. Organization of EBS #12-12 Safe Administration of Systemic Cancer Treatment series according to the process of chemotherapy administration.



CPOE = Computerized Prescriber Order Entry; Pt = patient

Scope of this guideline

The scope of this guideline is to provide guidance to institutions on areas for which policies and procedures should be provided, and to healthcare professionals on flags for safety risks in this specific area of practice. The guidance is based on a review of the content of available practice guidelines, primary literature when necessary, and the Working Group's clinical expertise.

Selected guidelines from other jurisdictions were systematically selected, examined and assessed. It was realized by the Working Group that many of the recommendations were representative of procedures and beyond the scope of this provincial guideline. Thus, for readers seeking more specific procedural details, resources are provided throughout the document: references to relevant, evidence-based guidelines, links to examples of procedures or practical tools to facilitate implementation (see "Useful Resources" boxes at the end of

topic sections) and examples of procedures in Appendix 1a to 1c. For the purpose of this document, "chemotherapy" is defined as any agent active against cancer.

In 2018 some modifications pertaining to medication infusions were made to the guideline by the Oncology Nursing Program (Appendix 1d). The evidence used to formulate the modifications is summarized in Appendix 1e.

Areas of Interest and Summary Recommendations

To optimize the level of professional practice to ensure the safety of chemotherapy administration, it is recommended that:

- **Institutions develop, implement and monitor specific policies and procedures for the safe administration of chemotherapy**

- **The development of policies and procedures be considered as a quality indicator (step 1) and the subsequent impact of these policies and procedures on patient-relevant outcomes be assessed (step 2)**

To help institutions implement these recommendations, this document describes key aspects of safe administration, key components that a policy would address, examples of protocols, lists of resources that could be used to inform policies and procedures as institutions develop their own, and recommended principles to enable successful implementation. Within the main objective, the Working Group addresses education and competencies as an overall safety issue underlying all areas, and then highlights three main areas of interest:

1) Selection, use and management of vascular access devices, including potential complications, during the administration of systemic cancer treatment
2) Extravasation, phlebitis, flare, allergy and hypersensitivity complications of chemotherapy administration
3) Nursing practices before, during and immediately after the administration of systemic cancer treatment, including verification and maintenance of the treatment plan

Recommendations are framed into boxes, and specific references and links to select practice guidelines are provided. Interested readers can refer to these additional resources when producing policies and procedures or resolving practice issues.

Education and competencies

The CCO Regional Models of Care for Systemic Treatment guideline (available at: https://www.cancercareontario.ca/en/guidelines-advice/types-of-cancer/1186%20) presents specific health professionals' education and competency requirements in different types of organizations in Ontario.

For the education and competencies of nursing staff, the Working Group endorses the principles contained in the Canadian Association of Nurses in Oncology Standards (CANO) (2) available at http://www.aqio.org/docs/normes_chimio_anglais.pdf and broadens its content to roles and responsibilities of health professionals participating in the care of persons with cancer who are receiving chemotherapy.

The Working Group recommends that organizations have policies and procedures in place that address:

- Roles and responsibilities of health professionals participating in the care of persons with cancer who are receiving chemotherapy
- Education and skill development of professionals to establish competence in caring for persons receiving chemotherapy and in operating any equipment required to provide this care
- An ongoing and sustained competency program for all professionals caring for persons receiving chemotherapy that regularly (i.e., annually) evaluates maintenance of competency and adherence to policies and procedures
- Education of health professionals specifically regarding the prevention, management and reporting of side effects and adverse events

2018: This recommendation was modified by the CCO Oncology Nursing Program

- *Standards for all major processes involved in the prescribing, dispensing and administration of systemic treatment (chemotherapy, targeted therapies, and immunotherapy). For example: how systemic treatment is prescribed, the use of standardized systemic treatment protocols (with supporting references and documentation when there are protocol deviations), a process for order verification and independent double-checking, systemic treatment preparation and dispensing, administration set-up and equipment, pre-treatment assessment, catheter selection, maintenance and removal, post-administration management, monitoring, patient education, and discharge documentation*
- Proper dose of chemotherapy (not routinely capped for larger patients)
- Proper dose adjustment of chemotherapy based on adverse events and conditions (e.g., febrile neutropenia, neurotoxicity, nephrotoxicity)
- Safe labelling, and the timing and scheduling of chemotherapy drugs
- Prevention, early detection and management of complications related to the catheter/device use and to the drug administered
- Safe handling of hazardous drugs, including drug preparation, equipment for personal protection, drug administration, chemotherapy spill management and waste disposal, that meets provincial and national occupational health and safety standards
- Education and promotion of self-management in persons receiving chemotherapy (e.g., on prevention, management and reporting of side effects and adverse events)

Justification: The above recommendations are based on the standards published by CANO and integrated with the expertise from Working Group members.

Qualifying statement

A resource for the safe handling of hazardous drugs is the CCO special report "Safe Handling of Parenteral Cytotoxics" available at: https://www.cancercareontario.ca/en/guidelines-advice/types-of-cancer/2161.

Special consideration and precautions should be made to the labelling and scheduling of drugs that are to be administered intrathecally. Mistaken intrathecal administration of drugs prepared for IV administration (e.g., bortezomib and vincristine) have resulted in fatal outcomes. A resource for the safe labelling of chemotherapy drugs is in the CCO Evidence-Based Series #12-11 "Patient Safety Issues: Key Components of Chemotherapy Labelling" available at: https://www.cancercareontario.ca/en/guidelines-advice/types-of-cancer/1191.

AREA OF INTEREST 1: Selection, use and management of vascular access devices (VAD), including potential complications, during the administration of systemic cancer treatment

In this section, the Working Group reviews:

A. Selection and management of peripheral and central venous access devices and intra-peritoneal catheters
B. Prevention and detection of complications, (e.g., infection, occlusion and thrombosis)

Techniques for the insertion of VAD are beyond the scope of this document.

A. Selection and management of peripheral and central venous access devices and intra-peritoneal catheters

Many different devices and several models of the same device are available from vendors and are in use in various hospitals. Therefore, the Working Group makes general recommendations, and refers to individual institutions for protocols on the use of each specific device.

The devices used in the administration of systemic cancer therapy are peripheral intravenous catheters (i.e., intravenous [IVs], "midlines") and central venous access devices (CVAD) and other devices. Other devices such as implanted intraperitoneal, intravesicular, intrapleural, intraventricular devices and Ommaya reservoirs are used for local delivery of chemotherapeutic agents into anatomic compartments. Intra-arterial devices are used for regional delivery of chemotherapy but are restricted to non-ambulatory procedural settings, generally in tertiary centres. This guideline will discuss peripheral, central venous access devices and intraperitoneal catheters because they are most commonly used for systemic cancer therapy.

Definitions and device characteristics

Peripheral IV access devices are catheters placed into a peripheral vein (generally in the upper extremity), either superficial (i.e., hand or forearm) or deep (i.e., brachial or basilic) *but do not extend further central than the axillary vein.* The vast majority of these are short (i.e., 2.5-5.0 cm) catheters placed in a superficial vein by visual and/or palpation guidance, although longer (i.e., 7.5-20 cm) "midlines" fall in this category as well from a functional perspective.

Central venous access devices (CVADs) are catheters with their tip placed into the central venous circulation (ideally the lower third of the superior vena cava (SVC) or at the SVC-right atrial junction). For the purposes of this guideline, these are divided into four distinct categories:

Peripherally inserted central catheters (PICCs), which enter via a peripheral (usually deep) vein of the upper extremity, but the tip of which is in the central venous circulation.

Non-tunnelled central venous catheters (CVCs) are catheters that enter the venous system via a large vein in the neck, chest or groin and reside with their tip in the central venous circulation. These are restricted to the inpatient, usually monitored (i.e., ICU) setting.

Tunneled central venous catheters (i.e., Hickman catheters) most commonly enter the venous system via a large vein of the neck, chest or groin and reside with their tip in the central venous circulation. These are characterized by the presence of a subcutaneous tunnel between the vein entry site and skin exit site, containing a cuff of material (usually Dacron) bonded to the catheter, which incites local subcutaneous inflammatory response. This serves both to secure the catheter and resist infection.

Totally implanted/implantable ports also usually enter the venous system via a large vein in the neck, chest or arm and reside with their tip in the central venous circulation. As their name implies, these are characterized by implantation of the *entire* device under the skin. They are then accessed percutaneously when needed.

Peritoneal catheters are single-lumen catheters implanted in the peritoneum for the delivery of chemotherapy in the peritoneal cavity. These are also, generally, totally implanted.

Table 1 below shows the general characteristics of intravenous access devices and presents some principles that can serve as a reference when selecting the device. Table 2 summarizes the characteristics of the different devices and typically recommended dwell-duration times.

Table 1. Vascular and Non-Vascular Access Devices. Adapted from O'Grady (3) and Camp-Sorrell (4).

Catheter Type	Entry Site	Length; dwell time	Comments
VASCULAR DEVICES			
Peripheral intravenous catheters	Usually inserted into veins of forearm or hand	<15 cm; Short duration (days)	Phlebitis with prolonged use; rarely associated with bloodstream infection
Midline catheters	Inserted via the antecubital fossa into the proximal basilic or cephalic veins; does not enter central veins, peripheral catheters	7 to 20 cm; Short duration	Anaphylactoid reactions have been reported with catheters made of elastomeric hydrogel; lower rates of phlebitis than short peripheral catheters
Non-tunneled central venous catheters	Percutaneously inserted into central veins (subclavian, internal jugular, or femoral)	≥8 cm depending on patient size; Approximately 6 weeks	Account for majority of catheter-related blood stream infections (CRBSI)
Peripherally inserted central venous catheters (PICCs)	Inserted into basilic, cephalic or brachial veins and enters the superior vena cava	≥20 cm depending on patient size; Approximately 12 months.	Lower rate of infection than with non-tunneled CVCs
Tunneled central venous catheters	Implanted into subclavian, internal jugular or femoral veins	≥8 cm depending on patient size; Several years	Cuff inhibits migration of organisms into catheter tract; lower rate of infection than with non-tunneled CVC
Totally implantable ports	Tunneled beneath skin and have subcutaneous port accessed with a needle; implanted in subclavian or internal jugular vein	≥8 cm depending on patient size; Indefinite	Lowest risk for CRBSI; improved patient self-image; no need for local catheter-site care; surgery required for catheter removal
NON-VASCULAR DEVICES			
Intraperitoneal catheters and ports	Inserted through the anterior abdominal wall at the level of the umbilicus.	External segment 20 cm Sub-cutaneous segment 2-10 cm Intra-abdominal segment 31-48 cm; Indefinite	*Implanted peritoneal ports:* Low risk of displacement, more expensive, does not allow for high-pressure forced irrigation

Selection of catheters

The Working Group recognizes that the decision to use a peripheral versus a central vascular device and the selection of a particular catheter is a complex decision. Routine insertion of catheters is not recommended. Many variables have to be integrated and balanced by clinical judgement to reach the best solution for each individual patient with the goal to increase comfort and decrease the risk of complications. Table 2 presents important factors to consider for the appropriate selection and insertion of a device.

Table 2. Factors That Impact Catheter Selection.

Related Factors	Specific Examples To Consider
Treatment: • Drug properties • Drug osmolarity/pH • Scheduling, route, duration and frequency of administration • Other treatments characteristics	• Patient's treatment contains vesicant drugs • Patient's treatment involves long-term continuous infusions • Patient is subjected to prolonged immunosuppression e.g., stem cell transplant • Chemotherapy solutions to be administered have pH <5 or >9 or osmolality >600 mOsm/L • Treatment protocol is associated with requirement for frequent blood samples
Patient: • Vein status • History • Physical status • Preferences • Age	• Failure to access veins peripherally • Patient has overlying skin changes due to radiation or surgery • Patient is on dialysis • Lymphedema, obesity • Patient has a very active lifestyle
Resources: • Patient/caregiver capabilities • Access to home care • Availability of expertise • Availability of device	• Patient/caregiver unable to care for external line • Geographically remote location of patient limits access

The Working Group recommends that:

Treatment factors are the primary consideration in the selection of an access device, as they may dictate the need for a particular device or class of devices. Clinical factors, patient informed decision making and resource concerns may further direct or guide selection.

The access to expertise or device availability should not be a barrier for the patient to receive the most appropriate device. For specific procedures such as the insertion of a port, network connections with other institutions should be in place so that the patient can receive the service if an institution does not have the expertise available.

Justification

The guidelines that informed our recommendations were the Centers for Disease Control and Prevention (CDC) (5), the European Oncology Nursing Society (EONS) Extravasation guidelines (6) and the Oncology Nursing Society (ONS) (4) documents. Concepts from these guidelines were integrated with the Working Group's expert consensus. The intent was to be as succinct as possible given that many factors often limit choices.

Examples of type of equipment include peripheral or central access devices, as well as size and type of cannula or catheter. It is important to choose cannulas that minimize the risk of being dislodged, that allow blood to flow around them (e.g., flexible cannula of 1.2-1.5 cm), and allow monitoring of the access point (e.g., using a clear dressing to secure the cannula, and not covered it with a bandage).

Qualifying statement

For more specific details on the selection and use of catheters, the Working Group refers the reader to the source guidelines by ONS (4) (book available for purchase), CDC (5) (available at http://www.cdc.gov/hicpac/pdf/guidelines/bsi-guidelines-2011.pdf) and EONS (6) (available at http://www.cancernurse.eu/documents/EONSClinicalGuidelinesSection6-en.pdf).

B. Prevention and detection of complications

The treatment of infections, occlusion and thrombosis is beyond the scope of this document. Patient-related factors (such as underlying hypercoagulable states) and thrombosis-provoking factors such as the type of chemotherapy given (i.e., immunomodulatory drugs, L-asparaginase) are also beyond the scope of this document.

Many complications can arise when access devices are used in cancer patients. The Working Group emphasizes the high morbidity, mortality and economic impact of preventable complications such as infections, thrombosis, occlusion, and extravasation.

The Working Group recognizes that the risk of experiencing complications with an access device is dependent upon a number of underlying contributing factors and the combination thereof.

Table 3 highlights preventable complications for each type of device and underlying factors and processes that influences these adverse events. Extravasation, infiltration and flare reactions are addressed in "Area of Interest 2: Extravasation, allergy and hypersensitivity complications of chemotherapy administration." Table 3 has been informed by several sources of evidence, shown in Table 1, Section 2 and by the expert opinion of the working group.

Table 3. Factors That Influence Development of Complications by Catheter Type.

Type of Catheter and Possible Complications	Factors Influencing Development of the Complication
Peripheral catheters:	
• Phlebitis • Infiltration • Infection • Occlusion • Catheter breakage	• Vein and catheter size; type of infusion; technique of insertion; patient characteristics; dwell time • Syringe size • Aseptic techniques • Patient and caregivers' education • Health care workers' education
Central catheters:	

• Catheter migration • Catheter failure • Pinch-off syndrome • Catheter fracture • Damage to the catheter • Infection • Occlusion • Thrombosis • Lack of wound closure/healing after insertion of port	• Ultrasound placement of the catheter • Fluoroscopic guidance and/or radiographic confirmation of catheter tip placement • Development of, and adherence to, regular flushing/locking protocol(s) • Level of awareness of manufacturers' warnings and labels • Consultation/communication among team members • Aseptic techniques • Patient and caregivers' education and follow-up support • Health care workers' education • Patient's level of activity • Use of vascular endothelial growth factor (VEGF) inhibitors (e.g., bevacizumab) after port insertion
Intraperitoneal catheters:	
• Leakage around the exit site of the external catheter • Tunnel or exit site infection • Catheter dislodgement • Catheter failure • Nonfunctioning catheter • Bleeding • Bowel obstruction, perforation or fistula • Infection	• Development of, and adherence to, regular flushing/locking protocol(s) • Level of awareness of manufacturers' warnings and labels • Consultation/communication among team members • Aseptic techniques (how well performed) • Patient and caregivers' education and follow-up support • Health care workers' education.
• Tunnel or exit site infection • Catheter dislodgement • Catheter failure • Nonfunctioning catheter • Bleeding • Bowel obstruction, perforation or fistula	• Development of, and adherence to, regular flushing/locking protocol(s) • Level of awareness of manufacturers' warnings and labels • Consultation/communication among team members • Aseptic techniques (how well performed) • Patient and carers' education and follow-up support

As a general, overarching recommendation on catheter-related complications, the Working Group advocates institutions where vascular access devices are inserted or maintained:

Promote a culture of safety, commit to best practice, patient-centred and standardized care, and provide education and resources to health care providers, patients and their caregivers.

Implement continuous monitoring and evaluation of the quality of provider performance and their adherence to organizational policy, procedures and relevant guidelines.

Have surveillance programs in place to monitor for device-related complications and conduct systematic error analyses on incident events.

Qualifying statement

For more specific details on the prevention, detection and management of complications, the Working Group refers the reader to the source guidelines highlighted in this document. The evidence base for many of the procedures needed in this area has been established, while several topics are still controversial and the evidence evolving (8).

The recommendations made in this document can assist health professionals to work with their organization and address gaps in policies and procedures. Institutions should facilitate this collaborative work.

In selecting, inserting and managing a VAD, health professionals should make their decisions with consideration of the multiple factors that may contribute to catheter-related complications.

Justification

The documents that informed the recommendations are the guidelines by ONS (4), National Institute for Clinical Excellence (NICE) (7) (available at http://www.nice.org.uk/nicemedia/live/13684/58656/58656.pdf), Mermel et al (9), Baskin et al (10), CDC (5) (available at http://www.cdc.gov/hicpac/pdf/guidelines/bsi-guidelines-2011.pdf) and the standards developed by Fung-Kee-Fung et al for intraperitoneal chemotherapy (11). Insertion techniques are beyond the scope of this document. For more details, interested readers can refer to the guidelines listed.

The Working Group recommends that:

Institutions have "care bundles" and standardized protocols at each point of care for preventing, diagnosing and treating infections, occlusions and thrombosis secondary to access devices. Specific instructions should be available for special populations such as patients who are immunosuppressed.

Evidence-based care bundles are structured ways of improving the processes of evidence-based care and patient outcomes. They are small, straightforward sets of evidence-based practices that, when performed collectively and reliably, have been proven to improve patient outcomes (12). An example of a care bundle for the prevention of catheter-related blood stream infections is presented in Appendix 1A.

Examples of topics included in such bundles are:

- Strict hand hygiene/decontamination
- Maximal barrier precautions
- Chlorexidine skin cleansing/decontamination
- Optimal insertion-site selection with avoidance of the femoral vein
- Frequency of assessment of VAD
- Removal of VAD when no longer needed
- Methods for surveillance of infection rates
- Patient and caregiver education
- Monitoring of patients when they may be more prone to infections
- Use of special precautions for patients who are immunosuppressed
- Documentation of procedures implemented to prevent infections
- Thrombolytic/heparin solution flush/lock

Justification

The guidelines used to inform the recommendations have been chosen through a rigorous and systematic review process (see Section 2 of this document). The guidelines used for infective complications are: ONS, CDC, NICE and Mermel et al (4,5,7,9); and for thrombotic/occlusive complications are: Baskin et al, ONS, Debourdeau et al, and ACCP (4,10,13,14).

Infection, occlusion, thrombosis or extravasation can occur as a result of single or multiple events arising at different times during a course of treatment. Table 5 reviews events and conditions where patients may be placed at risk for infection, occlusion and thrombosis depending on the point of care. Recommendations made by the Working Group are presented after Table 4. Table 4 has been informed by several sources of evidence, shown in Table 1, Section 2 and by the expert opinion of the working group.

Table 4. Factors That May Lead to Catheter-Related Infection, Occlusion and Thrombosis Based on Point of Care.

Point of Care	A. Factors That May Lead To Infection	B. Factors That May Lead To Occlusion/Thrombosis

Point of care 1: catheter insertion	• Possible colonization/contamination of:
	  ○ the skin at VAD insertion site
	  ○ the catheter's exit site
	  ○ port pocket or tunnel
	• Patient's condition when VAD was inserted including the existence of a remote infection site
	• Patient's immune status and comorbidities
	• Material component of certain catheters such as polyurethane that may facilitate bacterial adherence
	• Other characteristics of catheters (e.g., multiple lumens)
		• Mechanical dysfunctions such as kinking of catheter, tight suture, or clamp closed
		• Catheter tip blocked by vein wall
		• Pinch-off syndrome

Point of care 2: during catheter access and use	• Possible contamination of the drug infused • Possible coring particle in the infusate • Possible contamination of other devices used during infusion (e.g., non-coring needles) • Type of infusion administered (e.g., chemotherapy agents that may cause irritation, extravasation and cutaneous infection, parenteral nutrition) • Inappropriate use of needleless connections • Lack of aseptic techniques • Patient's immune status and comorbidities	• Fibrin tail or sheath at the tip of the catheter or intraluminal clot • Mural thrombus or venous thrombosis • Port needle not in the proper position • Infusion of incompatible solutions • Infusion of solutions containing lipids • Drug crystallization • Inadequate flushing • Position of the catheter in the left subclavian vein • Malposition of the catheter
Point of care 3: de-access and maintenance (device not in use)	• Possible formation of a fibrin sheath • Methods for disconnecting an infusion: e.g., flush with sterile solution, cap when not in use • Patient's immune status and comorbidities	• Mechanical dysfunctions such as kinking of catheter, tight suture, or clamp closed • Material components of the catheter • Catheter tip blocked by vein wall • Pinch-off syndrome • Fibrin-sheath or intraluminal clot • Previous catheter-related infections • Mural thrombus or venous thrombosis • Port access needle dislodged or occluded in port • Patient's condition and life style • Fibrin tail or sheath or intraluminal clot at the tip of the catheter

For the prevention and early detection of infection, occlusion and thrombosis, the Working Group recommends:

Health professionals should be mindful of the catheter-related factors that may place patients with an access device at risk for catheter-related infection, catheter occlusion or thrombosis.

Health professionals should monitor for the appearance of signs and symptoms of local and systemic catheter-related infections on insertion, and during infusion and maintenance of the access device.

Health professionals should monitor for early signs and symptoms of access device-related partial or total occlusion as well as for signs and symptoms of venous thrombosis at all points of care.

Useful resources for implementation

The CUSP toolkit (15) may be a useful resource for the prevention of catheter-related blood stream infections, and it can be found at: http://www.ahrq.gov/cusptoolkit/index.html
The Safe Handling of Cytotoxics, PEBC EBS#16-3 is a resource for further information about issues of management of bodily fluids in the clinical and home settings, and it can be found at: (https://www.cancercareontario.ca/en/guidelines-advice/types-of-cancer/2161)

AREA OF INTEREST 2: Extravasation, phlebitis, flare, allergy and hypersensitivity complications of chemotherapy administration

Given the high tissue toxicity of many of the drugs administered for systemic treatment of cancer, extravasation (i.e., the leakage of the drug into tissues surrounding the vessel where it is being injected) is a serious condition that should be prevented and treated as soon as possible if it occurs. Extravasation has been reported to represent 0.5% to 0.6% of all adverse events associated with treatment. However, considering the high number of treatments administered, the number of events may be substantial (6). Extravasation should be considered both in the ambulatory or hospital setting and when chemotherapy is administered at home. Phlebitis is the inflammation of the vein and can be caused by chemical, mechanical or infectious stimuli. Drugs used for the systemic treatment of cancer may also cause allergic or hypersensitivity reactions. These are overactive responses of the immune system to the chemical substance injected and may cause tissue injury or changes in the entire body.

Table 5 shows the factors that may put patients at higher risk of extravasation, phlebitis, irritation, flare, hypersensitivity and allergic reactions when receiving systemic cancer treatment. Relevant recommendations are presented in the paragraphs below. Table 5 has been informed by several sources of evidence, shown in Table 1, Section 2 and by the expert opinion of the working group.

Table 5. Factors That May Put Cancer Patients at Risk of Complications at Different Points of Care.

A. Factors That Are Conducive To Extravasation	
Point of care 1: catheter insertion	• Peripheral vein-wall puncture • Failure of device eg. Hole in the catheter / hole in port
Point of care 2: during catheter access and use	• Administration of a drug with vesicant properties • Administration of a vesicant in a vein below a recent venipuncture • Inadequately secured IV catheter • Incomplete port needle insertion • Dislodged needle from port septum • Separation of catheter from port body • Deeply implanted port • Damaged long-term catheter in the subcutaneous tunnel • Catheter tip migration outside venous system and backtracking of drug along tunnel resulting from a fibrin sheath • Use of a needle that has inadequate length to pierce port septum • Inadequate securement of needle in port septum • Inadequate checks of the VAD exit site and of blood return during vesicant drugs administration • Inadequate involvement and participation of the patient in care • Inadequate patient education
B. Factors That Are Conducive To Phlebitis, Irritation, Flare Reaction	
Point of care 1: catheter insertion	• Mechanical irritation or injury to vein wall • Movement of the catheter in the vein • Chemical irritation when catheter is inserted before cleansing solution is dry
Point of care 2: during catheter access and use	• Chemical irritation by some high-acidity (e.g., vancomycin) or high-alkalinity (e.g., sodium bicarbonate) products, from drugs that are irritants (e.g., bleomycin, carboplatin), or from solutions with high osmolality
C. Factors That Are Conducive To Infiltration	
Point of care 2: during catheter access and use	• Leakage of a non-vesicant drug into tissue surrounding a VAD access • Inappropriate sequencing of medications
D. Factors That Are Conducive To Hypersensitivity	
Point of care 2: during catheter access and use	• Failure to give pre-medications or to identify whether patient has taken pre-meds appropriately • Infusion too fast • Inappropriate concentration of the drug being administered
E. Factors That Are Conducive To Allergic Reactions	
Point of care 2: during catheter access and use	• Factors are drug specific • Previous number of cycles Previous history of reactions to same drug or drugs in the same chemical class • Lack of patient education/disclosure • Lack of documentation of previous reactions

For the prevention of extravasation, phlebitis, infiltration, hypersensitivity, flare and allergic reactions, the Working Group recommends:

Health professionals be mindful of factors that can put patients at increased risk of extravasation, phlebitis, infiltration, flare, hypersensitivity reactions and allergic reactions. They should follow standardized procedures, including the use of checklists, for the administration of cancer systemic treatment.

Patients should be involved in the treatment process (see Part A of this document) and should be educated about the risk of vesicant extravasation and actions that they can take during the administration, in managing their care after administration, or after extravasation has been identified.

Health professionals working in chemotherapy administration settings should be specifically trained for these complications and, in collaboration with the patient, should monitor for early signs and symptoms of extravasation, phlebitis, infiltration, flare reaction, hypersensitivity and allergic reactions.

At the point of care of insertion of VADs, it is important that careful attention be paid to ensure optimal vein selection. In cases of failure of a first attempt to cannulation, it is recommended that the second insertion should be made above (closer to the heart) the original site. It is best to avoid administering cancer drugs below a previous venipuncture site.

Institutional policies and procedures may contain a complete description of other precautions that need to be taken when starting and when monitoring intravenous (IV) treatment including standardized procedures for managing hypersensitivity reactions, allergic reactions, and extravasation.

Justification

The guidelines by ONS were used for recommendations on extravasation, phlebitis, irritation, flare reaction and allergic reactions (4).

Training about cytotoxic handling with special attention to new agents and to techniques and devices of administration (16) should be maintained on an ongoing basis. Organizational policies should address venous access, venous assessment, administration of chemotherapy, management of extravasation, management of hypersensitivity, as well as training on how to meet the information needs of patients and their caregivers.

Health professionals involved in the administration of chemotherapy should be aware of their institution's extravasation policy and procedures, the location and contents of the extravasation kit and procedures for replacing used items within the kit. They should have an understanding of the precautionary steps to be taken to avoid extravasation.

Appendix 1B provides examples of a preventative protocol and an algorithm for managing extravasations, and Appendix 1C provides examples of antidotes that can be used for reacting to extravasation adapted from the EONS guideline (17,18).

Useful resources for implementation

- EviQ portal (16) may be a useful resource for chemotherapy administration and for the prevention of complications such as extravasation. It can be found at https://www.eviq.org.au/ and it is freely accessible upon registration.

- BC Cancer Agency provides policies and procedures online: http://www.bccancer.bc.ca/HPI/ChemotherapyProtocols/Policies.htm
- Avon Somerset and Wiltshire Cancer Services provides updated policies and procedures online: http://www.avon.nhs.uk/aswcs-chemo/NetworkPolicies/index.htm

Justification

Local protocols and policies represent the best tool for the prevention of extravasations. By standardizing procedures, safety is increased because reliance on memory is reduced and because new staff unfamiliar with procedures or devices can perform the procedure safely. The selected resources provide protocols that are institution specific and were developed with the input from all the members of the health care team. The protocols contain tools that are useful in the various phases of administration of chemotherapy and for reporting.

Patients play an important role as they can report the onset of symptoms that facilitate the early detection and management of extravasation. Patient participation in the care process has also been recommended in Part A of this series (19).

In addition to the existence of institutional policies and procedures, the clinical expertise of health professionals plays a key role in the prevention, early detection and management of complications. Strategies, implementable at each point of care, shown to be effective include checklists, and patient involvement in their care (see Part A of this series) (19).

Qualifying statement

Two selected guidelines represented by three publications were relevant for this topic area and applicable to Ontario: the EONS guideline (17,18) (available at http://www.cancernurse.eu/documents/EONSClinicalGuidelinesSection6-en.pdf) and the ONS guideline (4). Recommendations regarding patient education and their involvement in the detection and management of extravasation are from the EONS guidelines and endorsed by the Working Group (17,18).

AREA OF INTEREST 3: Nursing practices before, during, and immediately after the administration of systemic cancer treatment, including verification and maintenance of the treatment plan

This area of interest includes the use of volumetric and elastomeric pumps, independent checking of calculations and administration of treatment, removal and replacement of catheters and pre- and post-care.

A. Administration with volumetric and elastomeric pumps, including the importance of independent checking of calculations

- For elastomeric pumps, staff and patient education is required to ensure pumps are infusing at a rate as close to the nominal rate as possible. This includes:
  - User-specific education materials for pharmacy staff, nurses and patients
  - Ordering physician's awareness of the strengths and weaknesses of the technology, and of the importance of proper preparation and use
  - Instructions on how to identify a pump failure, and appropriate interventions in case of failure
  - Collaboration with the vendors to improve educational materials

- Administration of chemotherapy via volumetric or elastomeric pumps should only be performed by registered nurses trained and certified in their use
- There are physical and operational differences between volumetric pumps. The number of different brands or models of pumps in one institution should be minimized to reduce the risk for incorrect use or programming
- Pumps in a hospital should all be programmed using the same units that are included in the labeling of chemotherapy
- Refer to CCO guidelines for appropriate labeling of chemotherapy products.
- Pump programming should be independently checked by two RNs with the appropriate training for the particular brand and model of volumetric pump
- Prior to chemotherapy administration, a final check of patient and drug information should be performed independently by two RNs with the appropriate training and skills
- Administer continuous cytotoxic therapy via a central venous access device
- Only luer-lock fittings should be used with administration sets
- Devices should be checked for leakage or contamination prior to use and throughout the infusion period. If the infusion is occurring at home, the patient should be educated on periodically performing this check
- Where patients are receiving the infusion at home, they must be supplied with a spill kit and be educated on how to recognize and manage a spill
- Unused or remaining cytotoxic drug and its devices should be returned to the chemo suite for disposal
- Cytotoxic precautions (i.e., prevention of contact with cytotoxic drugs or bodily fluids of patients who received such drugs) should be taken according to the recommendations in EBS #16-3, available at https://www.cancercare.on.ca/common/pages/UserFile.aspx?fileId=293473

Qualifying statement

Factors that have been recognized as causes for variations in the flow rate of elastomeric pumps are (20):

- Fluid viscosity
- Head height
- Temperature
- Underfilling
- Diameter of access device
- Patient's blood pressure

Additional considerations and explanations and specific recommendations for the practical use of elastomeric pumps are reported in the resources for implementation reported in the box below.

Useful resources for implementation

- Easty and Fields report (20) available at: http://www.capca.ca/wp-content/uploads/IV-Ambulatory-Study-Final-Report-ENGLISH-Jan-14-2011_small.pdf
- EviQ portal (16) available at: https://www.eviq.org.au/
- Camp-Sorrell: "Access device guidelines: recommendations for nursing practice and education" (4)
- BC cancer agency policies and procedures available at: http://www.bccancer.bc.ca/HPI/ChemotherapyProtocols/Policies.htm

B. Nursing practices. Administration of treatment by nurse: Pre- and post-care

2018: The following statement was added by the Oncology Nursing Program
In preparation for the administration of systemic treatments (chemotherapy, targeted therapy, or immunotherapy), the nurse should ensure that the drug delivery to the patient is maximized through or by the administration set-up, while protecting staff as well as patient and family members. Among the nursing practices that may help protect patients' safety is communication with other healthcare providers, and pre- and post-care. Documentation is an essential tool for communication, and whether it occurs on paper files or electronically depends on the context of practice.

The Working Group recommends that healthcare practitioners:

- Document systemic treatment administration, including calculations and any relevant safety issues encountered in appropriate records
- Document any issues/concerns identified by the patient or his or her family, and subsequent interventions, including the response to these interventions
- Document any education provided to the patient and her or his family
- In case of errors, document the plan of care and expected outcomes

Before the administration of the drug, the Working Group recommends:

- Healthcare providers should follow organizational protocols and procedures for patient identification, administration of pre-medications, and patient education
- During the preparation and administration of systemic cancer treatment, multitasking should be avoided
- Prior to chemotherapy administration, a final check of patient and drug information should be performed independently by two RNs with the appropriate training and skills

2018: The following recommendations were added by the CCO Oncology Nursing Program

- *All intermittent systemic treatment infusions should be administered via a medication line connected to a main IV line. The main IV line, which is attached to the indwelling IV catheter, will be a non-medication containing solution and will be compatible with the prescribed therapy.*
- *When administration of intermittent systemic treatment from the medication line is complete, a flushing of the medication line should be done with a minimum volume equivalent to the tubing priming volume and occur before the next drug is administered and before disconnection from the patient unless special instructions are dictated in the orders. ** Please consult with your interprofessional team if flushing volume is unclear.*
    - *Some exceptions do occur and if the systemic treatment must be administered via the main line without priming with a non-medication containing solution (e.g., drugs known to cause hypersensitivity reactions that are titrated and clinical trial drugs that may involve pharmacokinetic sampling), then a minimum volume equivalent to the tubing priming volume should be used to flush afterwards. **Please consult with your interprofessional team if flushing volume is unclear.*
    - *A decision not to flush the medication line after administration of the systemic treatment should be made in consultation with the prescribing physician and/or pharmacist and be documented.*
- *A vesicant drug supplied in a minibag and given peripherally must be administered by gravity via a medication line connected to a free-flowing main IV line, not by an infusion*

pump. The RN will remain with the patient and will check blood return and assess the IV site as per local policy and procedure.

For post-care, the Working Group recommends:

- Patients who are going to be sent home with an ambulatory pump should be observed until the proper functioning of the pump can be verified, and possible allergic or hypersensitivity reactions can be excluded
- Protocols and procedures are to be followed for the safe handling and disposal of used equipment and unused medication and for hand decontamination

Qualifying statement

The root-cause-analysis of the fluorouracil incident that occurred in Alberta in 2006 identified the lack of appropriate documentation and multitasking as contributing factors to the mistaken programming of the pump (21).

Useful resources for implementation

BC Cancer Agency protocol for the prevention and treatment of chemotherapy induced nausea and vomiting is available at: http://www.bccancer.bc.ca/NR/rdonlyres/8E898B5D-3F12-4623-8E32-5B3C429C58F7/56350/SCNAUSEA_Protocol_1Mar2012.pdf

RELATED GUIDELINES

PEBC EBS #12-10, Regional Models of Care for Systemic Treatment, 2007 (in review), available at: https://www.cancercareontario.ca/en/guidelines-advice/types-of-cancer/1186.
PEBC EBS #12-11, Patient Safety Issues: Key Components of Chemotherapy Labelling, 2009 available at https://www.cancercareontario.ca/en/guidelines-advice/types-of-cancer/1191.
PEBC EBS #16-3, Safe Handling of Cytotoxics, 2013 available at https://www.cancercareontario.ca/en/guidelines-advice/types-of-cancer/2161.

Funding

The PEBC is a provincial initiative of Cancer Care Ontario supported by the Ontario Ministry of Health and Long-Term Care. All work produced by the PEBC is editorially independent from the Ontario Ministry of Health and Long-Term Care.

Updating

All PEBC documents are maintained and updated
as described in the PEBC Document Assessment and Review Protocol.

Contact Information

For information about the PEBC and the most current version of all reports,

please visit the CCO website at http://www.cancercare.on.ca/ or contact the PEBC office at:
Phone: 905-527-4322 ext. 42822 Fax: 905-526-6775 E-mail: ccopgi@mcmaster.ca

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APPENDICES

Compendium of examples of procedures relevant to chemotherapy administration.

Appendix 1A. Example of a bundle for the control of catheter-related blood stream infections during maintenance of the line. Adapted from Rinke et al (22).

Central Line Maintenance Care Bundle
1. Daily assessment of line necessity and consolidation and/or elimination of catheter entries (CDC recommended)
2. Daily dressing/site assessment performed (CDC recommended)
3. Catheter entries: a. Hand hygiene performed before all catheter entries (CDC recommended) b. Nonsterile gloves worn for all catheter entries c. Cap scrubbed with alcohol (15 sec scrub and 15 sec dry) or Chlorhexidine Gluconate (CHG) (30 sec scrub and 30–60 sec dry) for each entry (CDC recommended)
4. Cap/tubing/dressing/needle changes: a. Sterile gloves and mask worn by provider/assistant b. Cap connection site scrubbed with alcohol or CHG before removal of old cap (CDC recommended) c. Dressing/needle site scrubbed with CHG (CDC recommended) d. For dressing/port needle changes, shield patient's face or tracheotomy from dressing change site e. Old and new cap/tubing/dressing/needle date and time clear
5. Catheter site care a. No iodine ointment (CDC recommended) b. Change needle every 7 days; unless soiled, loosened, dislodged, or infiltrated c. Change gauze dressings every 2 days; unless soiled, dampened, loosened (CDC recommended) d. Change clear dressing every 7 days; unless soiled, dampened, loosened (CDC recommended) e. Prepackaged dressing change kit
6. Catheter hub/cap/tubing care a. Replace administration sets, including add-on devices at 96 hours, unless soiled or suspected to be infected (CDC recommended) b. Replace tubing used to administer blood, blood products, or lipids at 24 hours (CDC recommended) c. Change caps at 72 hours but should be replaced when administration set is changed (CDC recommended) d. Prepackaged cap change kit/cart/central location

CDC=Centers for Disease Control and Prevention; Sec = seconds

Appendix 1B. Example of a preventative protocol and algorithm for the management of extravasation.

Suggestions for the choice of an optimal vein include: using the forearm, not the back of the hand, avoiding small and fragile veins, avoiding insertion on limbs with lymphedema or with neurological weakness, avoid veins next to joints, tendons, nerves or arteries, avoid the antecubital fossa.

Example of an algorithm for management of a suspected extravasation
(adapted from EONS guideline for extravasation (6))

1. Stop the infusion immediately, DO NOT remove the cannula
2. Disconnect infusion from the cannula/needle
3. Leave the cannula/needle in place and try to aspirate as much of the drug as possible from the cannula with a 10-ml syringe. Avoid applying direct manual pressure to suspected extravasation area
4. Mark the affected area and take digital images of the site
5. Remove the cannula/needle
6. Collect the extravasation kit, notify the physician on service and seek advice from the chemotherapy team to start drug-specific approaches as soon as possible if it is required (see below)
7. Administer pain relief if required and complete required documentation

EONS = European Oncology Nursing Society

Example of Drug-Specific Approaches to Treatment(adapted from EONS guideline for extravasation (6))**:**

A. Localize and neutralize To be used with the following drugs**:** **Amsacrine** **Actinomycin** **Carmustine** **Dacarbazine** **Doxorubicin** **Epirubicin** **Idarubicin** **Mitomycin C** **Mustine** **Streptozotocin**	**B. Disperse and dilute** To be used with the following drugs: **Vinblastine** **Vincristine** **Vindesine** **Vinorelbine** **Oxaliplatin** **Aminophilline** **Calcium solutions** **Hypertonic glucose** **Phenytoin** **TPN** **X-ray contrast media**
8. LOCALIZE: **Apply a cold pack to the affected area for 20 minutes, 4 times daily for 1-2 days.**	**8. DISPERSE** **Apply a warm compress to the affected area for 20 minutes, 4 times a day for 1-2 days.**
9. NEUTRALIZE: **Neutralize the drug by using the specific antidote. The antidote should be given as per the specific directions provided by the manufacturer. (Note: only anthracyclines, mitomycin C and mustine have specific antidotes at the present time).**	**9. DILUTE** **Give several subcutaneous injections of 150-1500 IU of hyaluronidase diluted in 1 mL sterile water around the extravasated area to dilute the infusate.**
10. Remove the cannula (delivering the antidote) after confirming no more antidote will be prescribed or given.	**10. Document the incident using extravasation documentation sheet.**
11. Elevate the limb.	**11. Arrange follow-up for the patient as appropriate.**
12. Document the incident using extravasation documentation sheet.	
13. Arrange follow-up for the patient as appropriate	

Appendix 1C. Antidotes studied for specific cytotoxic drug extravasations. Adapted from EONS guideline for extravasation (6)

Extravasated Drug	Suggested Antidote	Suggested Dose	Level Of Evidence
Anthracyclines	Dexrazoxane hydrochloride	Initiate as soon as possible within 6 hours after an extravasation. Administered IV daily for 3 days based on BSA (1000 mg/m^2 on Day 1 and Day 2 (maximum dose 2000 mg), 500 mg/m^2 on day 3 (maximum dose 1000 mg)). Reduce dose if renal function impaired (CrCl <40 mL/min). Refer to product monograph.	Efficacy in biopsy-verified anthracycline extravasation has been confirmed in clinical trials.
Anthracyclines	Topical DMSO (99%)	Apply locally as soon as possible. Repeat every 8 hours for 7 days.	Suggested as a possible antidote in many literature sources. Due to lack of evidence, it is recommended that this is further studied.
Mitomycin C	Topical DMSO (99%)	Apply locally as soon as possible. Repeat every 8 hours for 7 days.	Suggested as a possible antidote in many literature sources. Due to lack of evidence, it is recommended that this is further studied.
Mechlorethamine (Nitrogen mustard)	Sodium thiosulfate	2 mL of a solution made from 4 mL sodium thiosulfate + 6 mL sterile water for subcutaneous injection.	Little evidence to support use; one study suggests protective effect.
Vinca alkaloids	Hyaluronidase	150-1500 IU subcutaneously around the area of extravasation.	Suggested as a possible antidote. Due to lack of evidence, it is recommended that this is further studied.
Taxanes	Hyaluronidase	150-1500 IU subcutaneously around the area of extravasation.	Suggested as a possible antidote. Due to lack of evidence, it is recommended that this is further studied.

Appendix 1d. Participants in 2018 modifications made by the CCO Oncology Nursing Program

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Appendix 1e. CCO Oncology Nursing Program Modifications

In November 2018 the Oncology Nursing Program made modifications to specific sections pertaining to infusions to align them with current practice. This is not a full update of the guideline.

Literature Search:

A search was initially undertaken for guidance on the administration of low-volume, high-concentration monotherapies. The search was subsequently expanded to cover safe administration of intravenous systemic therapy for cancer patients (including chemotherapy, biologics, and targeted therapy).

A search of grey literature resources was done using the Canadian Agency of Drugs and Technologies in Health (CADTH) checklist "Grey Matters" as well as an environmental scan of known guideline producers. PubMed and the Cochrane Library were also searched. The search was international in scope but restricted to English language documents.

Results:

The search found 22 documents that warranted a full-text review. Of these, 17 contained relevant information and were included. The documents (with links to URLs) are summarized in the Table.

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Guidance on safe administration of intravenous systemic therapy for cancer patients

Document	URL	Relevant information
BC Cancer Agency. Chemotherapeutic drugs, administration of. Vancouver: BC Cancer Agency; 2017 Jun [cited 2018 Oct 24].	http://www.bccancer.bc.ca/health-professionals/clinical-resources/nursing/nursing-practice-references	Includes guidance on safe handling, checking drug orders, and administration of chemotherapeutic drugs.
Cancer Care Nova Scotia. Administration of cancer chemotherapy. Halifax: Cancer Care Nova Scotia; 2011 Oct [cited 2018 Oct 24].	http://www.cdha.nshealth.ca/nova-scotia-cancer-care-program-16	Standards and policies for administration of systemic therapy including administration, preparation, and safe handling.
Saskatoon Health Region. Chemotherapy drugs for cancer treatment: Administration, safe handing & disposal. ID #1065. Saskatoon: Saskatoon Health Region; 2015 Jan. Date Reaffirmed: January 2015 [cited 2018 Oct 24].	https://www.saskatoonhealthregion.ca/about/Pages/Policies-Nursing-Manual.aspx	Policies and procedures for the administration, safe handling, and disposal of systemic therapy.
Health Quality Ontario Fan M, Koczmara C, Masino C, Cassano-Piché A, Trbovich P, Easty A. Multiple intravenous infusions phase 2a: Ontario survey. Ont Health Technol Assess Ser. 2014 May;14(4):1–141 [cited 2018 Nov 2].	https://www.hqontario.ca/Portals/0/Documents/evidence/reports/full-report-phase2a-mivi-140505-en.pdf	Survey of Ontario hospitals using multiple intravenous infusions. The survey investigated policies and procedures relating to secondary infusions, intravenous (IV) line identification, IV line setup and removal, dead volume management, IV bolus administration, and pump-specific issues.
Health Quality Ontario Pinkney S, Fan M, Chan K, Koczmara C,	https://www.hqontario.ca/Portals/0/Documents/evidence/reports/full-report-	Laboratory study to identify the risks associated with administering and

Colvin C, Sasangohar F, Masino C, Easty A, Trbovich P. Multiple intravenous infusions phase 2b: laboratory study. Ont Health Technol Assess Ser. 2014 May;14(5):1–163 [cited 2018 Nov 2].	phase2b-mivi-140505-en.pdf	managing multiple IV infusions.
Canadian Agency for Drugs and Technologies in Health. Rapid Response Report. Medication Administration via Direct Intravenous Push versus Minibags: Comparative Clinical Effectiveness and Guidelines. 2017 January 6 [cited 2018 Nov 2].	https://www.cadth.ca/sites/default/files/pdf/htis/2017/RB1049%20IV%20Push%20vs%20Minibag%20Final.pdf	A rapid response review comparing IV push versus minibags. Limited evidence and does not directly pertain to cancer systemic therapy.
Canadian Association of Nurses in Oncology. National Strategy for Chemotherapy Administration. Standards and Competencies for Cancer Chemotherapy Nursing Practice¤. 2017 September [cited 2018 Nov 2].	https://cdn.ymaws.com/www.cano-acio.ca/resource/resmgr/standards/2018CANO_NSCA_Toolkit__V6.pdf	Provides standards for practice, education, and continuing competence of oncology nurses prepared by the National Strategy for Chemotherapy Administration. Includes recommended content to include in cancer chemotherapy policies and competencies for nursing practices, and a self-assessment tool.
CANO Standards and Cancer Care Nova Scotia Skills Checklist. 2015 [cited 2018 Nov 2].	file:///C:/Users/walkerc/Downloads/cano-standards-and-detailed-skills-checklist.pdf	Includes the CANO self-assessment tool (see above) and a Cancer Care Nova Scotia checklist for safe handling and disposal of hazardous drugs.
Institute for Safe Medication Practices (ISMP)	https://forms.ismp.org/tools/bestpractices/faq/FAQ-BP1.pdf	Frequently asked questions regarding administration of vincristine in a minibag.

Targeted Medication Safety Best Practices for Hospitals: Frequently Asked Questions March 2014 [cited 2018 Nov 5].		
Institute for Safe Medication Practices (ISMP) Targeted Medication Safety Best Practices for Hospitals. 2018-2019 [cited 2018 Nov 5].	https://www.ismp.org/sites/default/files/attachments/2017-12/TMSBP-for-Hospitalsv2.pdf	2018-2019 best practices for safe administration of medication including vinca alkaloids and high-alert IV medications.
Managing Overfill during Preparation and Delivery of Intravenous Medications. ISMP Canada Safety Bulletin. 2013 Aug 15;13(7):1-6. [cited 2018 Oct 24].	http://www.ismp-canada.org/download/safetyBulletins/2013/ISMPCSB2013-07_ManagingOverfillIntravenousMedications.pdf	ISMP safety bulleting on the various methods of preparing IV medications and the issue of overfill in IV bags.
National Health Service Education for Scotland. Education and Training Framework for the Safe Use of Systemic Anti-Cancer Therapy (SACT). 2014 Feb. [cited 2018 Nov 5].	https://www.nes.scot.nhs.uk/media/2534050/sact-framework.pdf	Framework for education and training across Scotland for all healthcare workers involved in delivery of anti-cancer therapy.
Guideline and Procedure Manual for the Safe Use of Systemic Anti-Cancer Therapy Version – 2.0 Authorised by the NHS Lanarkshire Systemic Anti-Cancer Therapy Group. Approved November 2014 Revision date November 2017. [cited 2018 Oct 24].	Google words from the citation to obtain link.	Provides guidance on all aspects of systemic therapy including prescribing, preparation, dispensing, administration, extravasation, storage, disposal, and safety.
Clinical Oncological Society of Australia. COSA guidelines for the safe prescribing, dispensing and administration of systemic	https://wiki.cancer.org.au/australia/COSA:Cancer_chemotherapy_medication_safe	Recommendations and best practices regarding safe administration of systemic cancer therapy. Includes responsibilities,

cancer therapy. 2017. [cited 2018 Oct 24].	ty_guidelines	competencies, and procedures for prescriber, pharmacist, and nurse.
Corbitt N, Malick L, Nishioka J, Rigdon A, Szoch S, Torr P. Instituting Vincristine Minibag Administration: An Innovative Strategy Using Simulation to Enhance Chemotherapy Safety. J Infus Nurs. 2017 Nov/Dec;40(6):346-352.		Description of a single institution's process to to prepare, deliver, and administer vinca alkaloids using a minibag.
Neuss MN, Gilmore TR, Belderson KM, Billett AL, Conti-Kalchik T, Harvet BE, Hendricks C, LeFebvre KB, Mangu PB, McNiff K, Olsen M, Schulmeister L, Von Gehr A, Polovich M. 2016 Updated American Society of Clinical Oncology/Oncology Nursing Society Chemotherapy Administration Safety Standards, Including Standards for Pediatric Oncology. Oncol Nurs Forum. 2017 Jan 6;44(1):31-43.		Standards for safe administration of chemotherapy, supported by a systematic review and external consultation.
Cooper DM, Rassam T, Mellor A. Non-flushing of IV administration sets: an under-recognised under-dosing risk. Br J Nurs. 2018 Jul 26;27(14):S4-S12.		A study examining the frequency, volume, and dose of drug discarded within administration sets in 6 clinical areas using IV infusion in 1 hospital