Ontario
Cancer Care Ontario
Action Cancer Ontario

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

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 March 2021 placed Evidence-based Series (EBS) 12-2-2 IN REVIEW. This means that it is undergoing a review for currency and relevance. It is still appropriate for this document to be available while this updating process unfolds. 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**

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

PEBC Report Citation (Vancouver Style): Leung M, Bland R, Bladassarre F, Green E, Kaizer L, Hertz S, et al. Part 2: Administration of systemic treatment and management of preventable adverse events. Toronto (ON): Cancer Care Ontario; 2018 Nov 30 [In Review 2021 Mar 12]. Program in Evidence-based Care Practice Guideline Report No.: 12-12-2 IN REVIEW.

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

Table of Contents

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

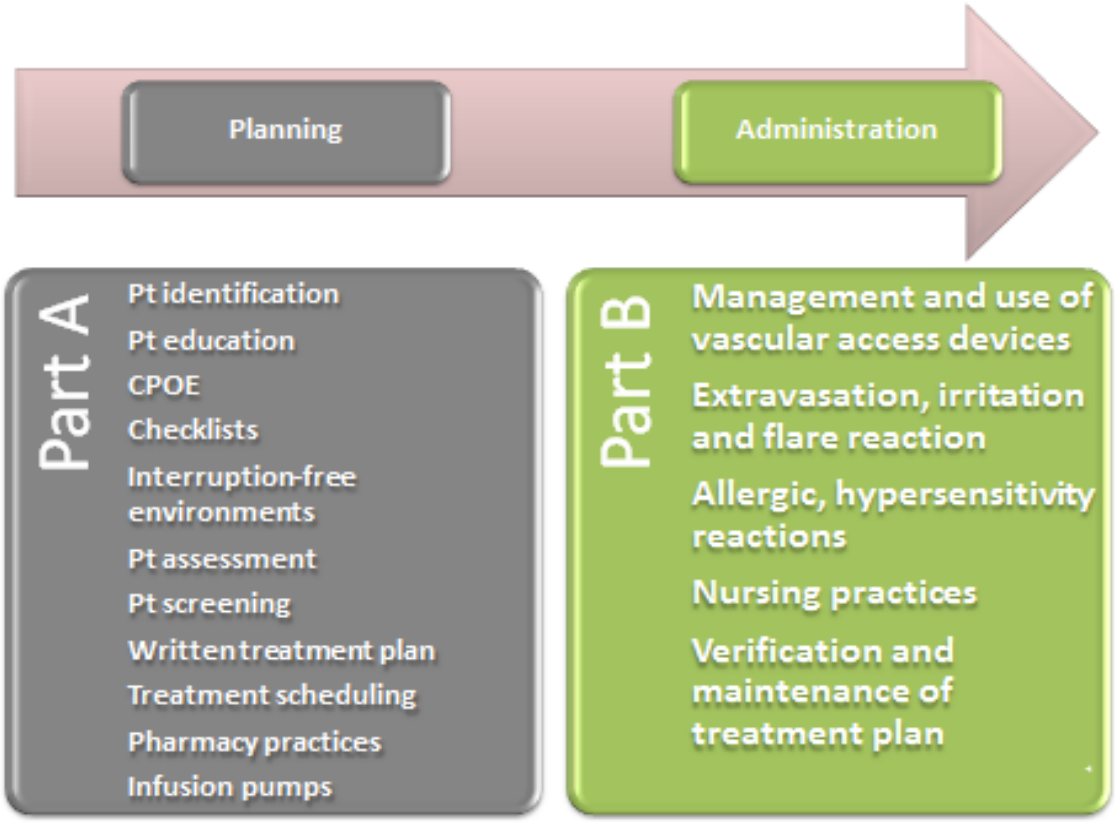
The goal of the Safe Administration of Systemic Cancer Treatment series is to provide recommendations that enable safe administration of chemotherapy with consideration for the "correct patient," "correct drug," "correct route," "correct dose," "correct time," "correct schedule" as well as adequate documentation.

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

REFERENCES

1. Browman GP, Levine MN, Mohide EA, Hayward RS, Pritchard KI, Gafni A, et al. The practice guidelines development cycle: a conceptual tool for practice guidelines development and implementation. J Clin Oncol. 1995;13(2):502-12 Comment in: Ann Oncol. 2002 Sep;13(9):1507-9; author reply: 9. Epub 1995 Feb 01.
2. Canadian Association of Nurses in Oncology. Standards and competencies for cancer chemotherapy nursing practice 2009, Jul 16, 2012 [cited 2012 Jul 16]. Available from: http://www.aqio.org/docs/normes_chimio_anglais.pdf.
3. O'Grady NP, Alexander M, Burns LA, Dellinger EP, Garland J, Heard SO, et al. Guidelines for the prevention of intravascular catheter-related infections. Clin Infect Dis. 2011;52(9):e162-93.
4. Camp-Sorrell D. Access device guidelines: recommendations for nursing practice and education, 3rd ed. Oncology Nursing Society; 2011.
5. O'Grady NP, Alexander M, Burns LA, Dellinger EP, Garland J, Heard SO, et al. Guidelines for the prevention of intravascular catheter-related infections 2011, Jun 7, 2012 [cited 2012 Jun 7]. Available from: http://www.cdc.gov/hicpac/pdf/guidelines/bsi-guidelines-2011.pdf.
6. European Oncology Nursing Society. Extravasation guidelines: guidelines implementation toolkit. [Internet]. Bussels, Belgium: EONS; 2007 [cited 2012 May 8]. Available from: http://www.cancernurse.eu/documents/EONSClinicalGuidelinesSection6-en.pdf.
7. National Institute for Clinical Excellence. Prevention and control of healthcare-associated infections in primary and community care. Internet: National Institute for Clinical Excellence, 2012 Mar 2012. Report No.: 149.
8. Camp-Sorrell D. State of the science of oncology vascular access devices. Semin Oncol Nurs. 2010;26(2):80-7.
9. Mermel LA, Allon M, Bouza E, Craven DE, Flynn P, O'Grady NP, et al. Clinical practice guidelines for the diagnosis and management of intravascular catheter-related infection: 2009 Update by the Infectious Diseases Society of America. Clin Infect Dis : an official publication of the Infectious Diseases Society of America. 2009;49(1):1-45. Epub 2009/06/06.
10. Baskin JL, Pui C-H, Reiss U, Wilimas JA, Metzger ML, Ribeiro RC, et al. Management of occlusion and thrombosis associated with long-term indwelling central venous catheters. Lancet. 2009;374(9684):159-69.
11. Fung-Kee-Fung M, Provencher D, Rosen B, Hoskins P, Rambout L, Oliver T, et al. Intraperitoneal chemotherapy for patients with advanced ovarian cancer: A review of the evidence and standards for the delivery of care. Gynecol Oncol. 2007;105(3):747-56.
12. Institute for Healthcare Improvement. What is a bundle? 2012 [cited 2012 Dec 13]. Available from: http://www.ihi.org/knowledge/Pages/ImprovementStories/WhatIsaBundle.aspx.
13. Debourdeau P, Kassab Chahmi D, Le Gal G, Kriegel I, Desruennes E, Douard MC, et al. 2008 SOR guidelines for the prevention and treatment of thrombosis associated with central venous catheters in patients with cancer: report from the working group. Ann Oncol. 2009;20(9):1459-71.
14. Kearon C, Akl EA, Comerota AJ, Prandoni P, Bounameaux H, Goldhaber SZ, et al. Antithrombotic therapy for VTE disease: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. Chest. 2012;141(2 Suppl):e419S-94S. Epub 2012/02/15.

15. Agency for Healthcare Research and Quality. CUSP Toolkit. U.S. Department of Health and Human Services; 2012 [cited 2012 Dec 14]; Available from: http://www.ahrq.gov/cusptoolkit/index.html.
16. New South Wales Government. EviQ, Cancer Treatments Online. Time out procedure checklist. 2010 [cited 2010 Sept 16]; Available from: https://www.eviq.org.au/Protocol/tabid/66/categoryid/217/id/6/Timeout+Procedure.aspx.
17. Wengstrom Y, Foubert J, Marguiles A, Roe H, Bugeia S. Extravasation guidelines 2007 2007 [cited 2012 Jul 10]. Available from: http://www.cancernurse.eu/documents/EONSClinicalGuidelinesSection6-en.pdf.
18. Wengstrom Y, Marguiles A. European Oncology Nursing Society extravasation guidelines. Stockholm: University of Stirling, 2008.
19. Leung M, Bland R, Baldassarre F, Green E, Kaizer L, Hertz S, et al. Safe administration of systemic cancer therapy. Part A: Safety during chemotherapy ordering, transcribing, dispensing, and patient identification. Toronto (ON): Program in Evidence-Based Care; 2012 [cited 2012 Jul 9]. Available from: https://www.cancercare.on.ca/toolbox/qualityguidelines/clin-program/systemic-ebs/
20. Easty AC, Fields A. Improving the safety of ambulatory intravenous chemotherapy in Canada 2011. [cited 2012 Jul 10]. Available from http://www.capca.ca/wp-content/uploads/IV-Ambulatory-Study-Final-Report-ENGLISH-Jan-14-2011_small.pdf.
21. Institute for Safe Medication Practices Canada. Fluorouracil incident root cause analysis. Toronto, On, Canada: ISMP; 2007 [cited 2010 Nov 10]. Available from: http://www.cancerboard.ab.ca/NR/rdonlyres/2FB61BC4-70CA-4E58-BDE1-1E54797BA47D/0/FluorouracilIncidentMay2007.pdf.
22. Rinke ML, Chen AR, Bundy DG, Colantuoni E, Fratino L, Drucis KM, et al. Implementation of a central line maintenance care bundle in hospitalized pediatric oncology patients. Pediatrics. 2012;130(4):e996-e1004. Epub 2012/09/05.

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

Name	Affiliation
Lorraine Martelli Provincial Head, Oncology Nursing Program CCO	CCO Toronto, ON
Melissa Lot Regional Oncology Nursing Lead, Erie St. Clair CCO	Windsor Regional Cancer Centre Windsor, ON
Sue Rieger Regional Oncology Nursing Lead, South West CCO	London Regional Cancer Centre London, ON
Margaret Mayer Regional Oncology Nursing Lead, Waterloo Wellington CCO	Grand River Regional Cancer Centre Kitchener, ON
Bonnie VanVeen Regional Oncology Nursing Lead, Hamilton Niagara Haldimand Brant CCO	Juravinski Cancer Centre Hamilton, ON
Laurie Van Dorn Regional Oncology Nursing Lead, Mississauga Halton Central West CCO	Carlo Fidani Regional Cancer Centre Mississauga, ON
Maritza Carvalho Regional Oncology Nursing Lead, Mississauga Halton Central West CCO	Carlo Fidani Regional Cancer Centre Mississauga, ON
Allyson Nowell Regional Oncology Nursing Lead, Toronto Central North CCO	Odette Cancer Centre Toronto, ON
Pam Savage Regional Oncology Nursing Lead, Toronto Central South CCO	Princess Margaret Cancer Centre Toronto, ON
Lisa Lun Regional Oncology Nursing Lead, Central CCO	Stronach Regional Cancer Centre at Southlake Newmarket, ON
Darrilyn Lessels Regional Oncology Nursing Lead, Central East CCO	R.S. McLaughlin Durham Regional Cancer Centre Oshawa, ON
Renee Hartzell Regional Oncology Nursing Lead, South East CCO	Cancer Centre of Southeastern Ontario Kingston, ON
Tennille Lecours Regional Oncology Nursing Lead, Champlain CCO	The Ottawa Hospital Cancer Centre Ottawa, ON
Alyson McQueen Regional Oncology Nursing Lead (interim), North Simcoe Muskoka CCO	Simcoe Muskoka Regional Cancer Centre Barrie, ON

Steffany Bourque Regional Oncology Nursing Lead, North East CCO	Northeast Cancer Centre Sudbury, ON
Karen Roberts Regional Oncology Nursing Lead, North West CCO	Regional Cancer Care Northwest Thunder Bay, ON
Lesley Moody Director, Person-Centered Care CCO	CCO Toronto, ON
Anita Rombough Group Manager, Oncology Nursing Program CCO	CCO Toronto, ON
Grace Kim Senior Specialist, Oncology Nursing Program CCO	CCO Toronto, ON
Jasmin Soobrian Senior Specialist, Oncology Nursing Program CCO	CCO Toronto, ON

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.

References

1. BC Cancer Agency. Chemotherapeutic drugs, administration of. Vancouver: BC Cancer Agency; 2017 Jun. [cited 2018 Oct 24].
2. Cancer Care Nova Scotia. Administration of cancer chemotherapy. Halifax: Cancer Care Nova Scotia; 2011 Oct. [cited 2018 Oct 24].
3. Saskatoon Health Region. Chemotherapy drugs for cancer treatment: Administration, safe handing & disposal. ID #1065. Saskatoon: Saskatoon Health Region; 2015 Jan. Date Reaffirmed: Jan 2015. [cited 2018 Oct 24].
4. Fan M, Koczmara C, Masino C, Cassano-Piché A, Trbovich P, Easty A. Multiple intravenous infusions phase 2a: Ontario survey. Health Quality Ontario. Ont Health Technol Assess Ser. 2014 May;14(4):1–141. [cited 2018 Nov 2].
5. Pinkney S, Fan M, Chan K, Koczmara C, Colvin C, Sasangohar F, Masino C, Easty A, Trbovich P. Multiple intravenous infusions phase 2b: laboratory study. Health Quality Ontario. Ont Health Technol Assess Ser. 2014 May;14(5):1–163. [cited 2018 Nov 2].
6. 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 Jan 6. [cited 2018 Nov 2].
7. Canadian Association of Nurses in Oncology. National Strategy for Chemotherapy Administration. Standards and Competencies for Cancer Chemotherapy Nursing Practice. 2017 Sep [cited 2018 Nov 2].
8. CANO Standards and Cancer Care Nova Scotia Skills Checklist. 2015. [cited 2018 Nov 2].
9. Institute for Safe Medication Practices (ISMP). Targeted Medication Safety Best Practices for Hospitals: Frequently Asked Questions. 2014 Mar. [cited 2018 Nov 5].

10. Institute for Safe Medication Practices (ISMP). Targeted Medication Safety Best Practices for Hospitals. 2018-2019. [cited 2018 Nov 5].
11. Managing Overfill during Preparation and Delivery of Intravenous Medications. ISMP Canada Safety Bulletin. 2013 Aug 15;13(7):1-6. [cited 2018 Oct 24].
12. 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].
13. 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 Nov 2014; Revision date Nov 2017. [cited 2018 Oct 24].
14. Clinical Oncological Society of Australia. COSA guidelines for the safe prescribing, dispensing and administration of systemic cancer therapy. 2017. [cited 2018 Oct 24].
15. 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.
16. 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.
17. 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.

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

Evidence-Based Series #12-12-2: Section 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: Evidentiary Base

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: March 10, 2014

PURPOSE

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

INTRODUCTION

Assuring patient safety during chemotherapy administration is an important objective for health care institutions. Even when used properly, chemotherapeutic agents have the potential for serious adverse events and toxicity. At the point of receiving chemotherapy treatment and throughout treatment, the patient continues to be at risk of system failures in identification ("wrong patient" errors), scheduling ("wrong time" or "wrong schedule" errors), dispensing and prescribing ("wrong drug," "wrong route" or "wrong dose" errors) as reviewed in Part I of this series (1). However, there is added risk for complications from the vascular access device selected to deliver chemotherapy and from the early toxicities of the chemotherapy received.

Complications such as loss of catheter function, blood stream infections, venous thromboembolism, infusion reactions and extravasations can be associated with increased cost of care, hospitalization, morbidity or mortality. Some events are difficult to detect (2). Effective and timely recognition of such events can be challenging to the clinician when faced with the growing number of access devices and chemotherapy agents, all with their own unique characteristics and risks.

Increasing usage of peripherally inserted central (PICC) lines in ambulatory patients also places heavier reliance on the self-initiation and vigilance of patients and their caregivers should an adverse event arise. PICC lines allow the optimizing of chemotherapy administration, blood sampling, transfusions, antimicrobial therapy and nutrition (3).

However, treatment advantages are offset by the loss of rigorous monitoring and experienced assessments usually associated with the hospital environment.

Administering chemotherapy safely to a patient is dependent on clinician attentiveness to medication error prevention, early recognition of adverse events and timely response before they can cause serious harm. Patients want and need to be involved as they can detect some errors that occur during administration as well as adverse events that occur at home. (4). Reporting of errors is often inconsistent, while serious errors and adverse events cause substantial morbidity and mortality and become obviously "visible", those errors considered to have caused little harm are not always reported, although they can also impact the patient (5). At a Boston-based comprehensive cancer centre in the United States, 22% of the patients surveyed believed they experienced a recent unsafe episode in their plan of care despite only 1% having experienced injury due to medical error (6). Taking inadequate or inappropriate action can cause patient anxiety, discomfort, and breach of trust or perceptions of unsafe care during chemotherapy administration.

Reducing the risk of errors and adverse events in patients undergoing chemotherapy treatment requires standardized approaches and the implementation of evidence-based policies and procedures. Although there are published guidelines focused on the safe administration of chemotherapy, none of the guidelines provide a comprehensive summary and/or systematic review of the available evidence (7-10). Cancer Care Ontario (CCO) formed the Safe Administration of Chemotherapy Expert Panel to discuss best practices and review the current literature. The panel is composed of representatives from nursing, medicine and pharmacy. Through evidence and consensus, this document, promoted by the CCO Systemic and Nursing Programs, is to develop recommendations on patient-relevant issues that can be applied in the settings where people with cancer will receive systemic therapy.

In order to make recommendations as part of a clinical practice and organizational guideline, the Working Group of the Safe Systemic Cancer Treatment Administration Panel developed this evidentiary base upon which those recommendations are based.

METHODS, SUMMARY RESULTS AND DISCUSSION

The following section presents how the recommendations shown in Section 1 were built from the available evidence and from the expertise of the Working Group. Three areas of interest were identified that covered:

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

After the areas of interest were established, the documents that had already been identified from the general search conducted when Part A of this series was prepared and that had been marked as relevant for topics in this Part 2 document were examined.

For area of interest 1): Oncology Nursing Society (ONS) guideline, 2003 (11), Gullatte, 2007 (12). Both of these resources were edited books and were both based on narrative reviews. For Area of interest 2) and 3): EviQ bundle (13), the Journal of Infusion Nursing Standards (14-17), the 2003 ONS guideline (11), the European Oncology Nursing Society, 2007 (EONS) and 2008 guidelines (18,19), Schulmeister, 2009 (20) the ONS position statement (21) and the American Society of Clinical Oncology Standards (ASCO) (22).

Many of these guidelines were out of date, as it was pointed out by the clinicians in the Working Group that instrumentation and techniques have changed substantially since the early 2000s. As well, many of these guidelines were not based on a systematic review of the evidence, or they were not applicable to Ontario; therefore, the Working Group included the ASCO Standards document (22) and a second systematic search was undertaken on April 19, 2012.

The web sites searched are reported in Section 3 of this document. Our own files and the reference lists of included documents were also searched. The search terms used for Medline are reported in Appendix 1.

Guidelines selection

As in Part A of this series (see Methods document at https://www.cancercareontario.ca/en/guidelines-advice/types-of-cancer/1196), we organized the selection process of guidelines in two steps.

At step 1, performed by the methodologist (FB), and one clinician (of ML, RB, SH, JC, MT, LK, AB, MC, or EG), we included documents that were:

- relevant to Ontario,
- specific to their objectives,
- included a systematic review of the evidence,
- published during or after 2006,
- had recommendations about the long-term use of access devices and their complications, and
- published in English.

We excluded guidelines that:

- covered topics already addressed in other existing Cancer Care Ontario guidelines,
- included an exclusively pediatric population,
- covered exclusively temporary central catheters placed in acute care settings.

At step 2 of the process, the Working Group examined the guidelines selected and, based on their expertise, decided to exclude those that were:

- not current,
- clinically not relevant,
- reports of procedure manuals,
- not related to the intravenous or intraperitoneal administration,
- focused on access devices used for hemodialysis, on intensive care unit patients and on the administration of parenteral nutrition.

Search results

The search of the bibliographic sources generated 96 documents. Fifteen guidelines represented by 16 publications were selected after the two-step process (13,18,23-36).

Quality assessment

The quality of the guidelines was measured independently using the AGREE II tool (37) by Working Group members (AB, EG, ML, RB, SH), the methodologist (FB) and one of the PEBC students (EK) in pairs. The Working Group met on August 16, 2012 to discuss the results of the quality assessment, and the results of the AGREE II evaluation are reported in Appendix 2.

Synthesizing the evidence

For each area of interest, the Working Group used specific, clinically relevant questions to structure this document, including topics of relevance for the recommendations. These questions are presented in Table 1 with a reference to the guidelines that have been used as the evidence base for the recommendations.

Table 1. Areas of Interest That Encompass the Administration of Systemic Cancer Treatment and the Management of Preventable Adverse Events with the Evidence Base that Supports the Recommendations.

Questions	Evidence Base
Area of interest 1: Selection, use and management of vascular access devices, including potential complications, during the administration of systemic cancer treatment	
What are the most effective and safe access devices to administer chemotherapy?	• Centers for Disease Control and Prevention (CDC) (28), • European Oncology Nursing Society Extravasation guidelines (EONS) (38) • Oncology Nursing Society (ONS) (24)
When is access assessed?	• ONS (24), • National Institute for Clinical Excellence (NICE) (31) and • CDC guideline (28) • Baskin et al (23) • Fung-Kee-Fung et al (27) • Mermel et al (32) • Debourdeau et al (26) • American College of Chest Physicians (ACCP) (30)
What options are presented to patients?	
What are the most effective techniques for insertion and management of access devices to prevent infection, lumen occlusion and venous thrombosis as well as for reducing error rates?	
What are the most effective intravenous (IV) access devices for patients (central vs. peripheral devices)?	
What are the indications for insertion of a peripheral access device in the delivery of chemotherapy?	
Area of interest 2: Extravasation, phlebitis, flare, allergy and hypersensitivity complications of chemotherapy administration	
What are the best strategies for the prevention of extravasation?	• EONS Extravasation guidelines (18,19) • ONS (24)
What are the best strategies for the detection and differential diagnosis of extravasation?	
What are the best strategies for the management of extravasation once it has occurred?	
What are the best strategies for documenting extravasation?	
What are the best strategies for the prevention and treatment of irritation and flare reaction?	
What are the best strategies for the prevention and treatment of allergic/hypersensitivity reactions to chemotherapy?	
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	
What are the most effective nursing strategies for reducing errors of administration of systemic cancer treatment agents to cancer patients while using volumetric pumps and other devices (e.g., elastomeric pumps)?	• ONS (24) • ASCO standards (22)
What are the most effective strategies for double checking calculations prior to administration of chemotherapy drugs?	
What are the best strategies for the preparation and administration of pre-medications?	
What are the best strategies to prevent errors during the administration of systemic cancer therapy?	
What are the best strategies for post care (e.g., hydration)?	
What are the best strategies for management of error-related toxicity?	
What are the best strategies for the verification and maintenance of treatment (e.g., identification of needs, support measures to help	

maintain the treatment)?	

EONS = European Oncology Nursing Society

DISCUSSION AND CONCLUSIONS

The practice of chemotherapy administration is very complex, variable and context dependent. Often, interventions are based on tradition or manufacturers' recommendations (39). Many high-quality guidelines exist that describe the techniques and procedures, which meet the interest of clinical practitioners for highly detailed description of practices. The Working Group, instead of repeating the content of existing guidelines in this provincial guideline, strived to highlight the challenging areas for organizations and for clinicians and to provide reference to existing useful tools for implementation.

The guidelines used as the basis for this evidence-based series were found and selected through a systematic process, and their content was sifted through the experience of the Working Group to create the recommendations presented here.

This area of practice is highly technical, and the risk exists of losing the centredness that is due to the cancer patient while giving technologies a front-stage place. With the approach adopted, the Working Group hoped to provide food-for-thought for organizations that are creating procedure manuals and for clinicians who work in this area.

REFERENCES

1. Leung M, Bland R, Baldassarre F, Green E, Kaizer L, Hertz S, et al. Safe administration of systemic cancer therapy. Part A: Safety during chemotherapy ordering, transcribing, dispensing, and patient identification. Toronto (ON): Cancer Care Ontario; 2012 Jul 9. Program in Evidence-based Care Practice Guideline Report No.: 12-12-1
2. Chopra V, Flanders SA, Saint S. The problem with peripherally inserted central catheters. JAMA. 2012;308(15):1527-8.
3. Chopra V, Anand S, Krein SL, Chenoweth C, Saint S. Bloodstream infection, venous thrombosis, and peripherally inserted central catheters: reappraising the evidence. Am J Med. 2012;125(8):733-41. Epub 2012/07/31.
4. Schwappach DL, Wernli M. Chemotherapy patients' perceptions of drug administration safety. J Clin Oncol. 2010;28(17):2896-901. Epub 2010/05/12.
5. Mazor KM, Roblin DW, Greene SM, Lemay CA, Firneno CL, Calvi J, et al. Toward patient-centered cancer care: Patient perceptions of problematic events, impact, and response. J Clin Oncol. 2012;30(15):1784-90.
6. Weingart SN, Price J, Duncombe D, Connor M, Sommer K, Conley KA, et al. Patient-reported safety and quality of care in outpatient oncology. Jt Comm J Qual Patient Saf. 2007;33(2):83-94. Epub 2007/03/21.
7. Jacobson JO, Polovich M, McNiff KK, LeFebvre KB, Cummings C, Galioto M, et al. American Society of Clinical Oncology/Oncology Nursing Society chemotherapy administration safety standards. Oncol Nurs Forum. 2009;36(6):651-8.
8. Carrington C, Michael M, Koczwara B, Stevenson B, Siderov J, Searle C, et al. Guidelines for the safe prescribing, dispensing and administration of cancer chemotherapy: Clinical Oncology Society of Australia; 2008 [cited 2010 Nov 10]. Available from: http://www.docstoc.com/docs/34823429/Guidelines-for-the-Safe-Prescribing-Dispensing-and-Administration-.

9. Polovich M, Whitford JM, Olsen M. Chemotherapy and biotherapy guidelines and recommendations for practice. 3rd ed. Pittsburgh: Oncology Nursing Society; 2009.
10. ASPH Council on Professional Affairs. ASHP guidelines on preventing medication errors with antineoplastic agents. Am J Health-Syst Pharm. 2002;59(17):1648-68.
11. Cope D, Ezzone S, Hagle M, McCorkindale D, Moran A, Sanoshy J, et al. Access Device Guidelines: Recommendations for nursing practice and education. Pittsburgh, PA: Oncology Nursing Society; 2003.
12. Gullatte MM. Clinical guide to antineoplastic therapy: A chemotherapy handbook. 2nd ed. Pittsburgh, PA: Oncology Nursing Society; 2007.
13. New South Wales Government. EviQ, Cancer Treatments Online. Time out procedure checklist. 2010 [cited 2010 Sept 16]; Available from: https://www.eviq.org.au/Protocol/tabid/66/categoryid/217/id/6/Timeout+Procedure.aspx.
14. Anonymous. Infusion nursing standards of practice. J Infus Nurs. 2007;30(3).
15. Gorski LA. Infusion nursing standards of practice. J Infus Nurs. 2007;30(3):151-2.
16. Gorski LA. Infusion nursing standards of practice. J Infus Nurs. 2007;30(1):20-1.
17. Infusion Nurses Society. Infusion Nursing Standards of Practice. J Infus Nurs. 2006;29(1 Suppl):S1-92.
18. Wengstrom Y, Foubert J, Marguiles A, Roe H, Bugeia S. Extravasation guidelines 2007 2007 [cited 2012 Jul 10]. Available from: http://www.cancernurse.eu/documents/EONSClinicalGuidelinesSection6-en.pdf.
19. Wengstrom Y, Marguiles A. European Oncology Nursing Society extravasation guidelines. Stockholm: University of Stirling, 2008.
20. Schulmeister L. Vesicant Chemotherapy Extravasation Antidotes and Treatments. 2009.
21. Oncology Nursing Society. Oncology services in the ambulatory setting. Oncology Nursing Society. Oncol Nurs Forum. 2001;28(1):14.
22. Jacobson JO, Polovich M, McNiff KK, Lefebvre KB, Cummings C, Galioto M, et al. American Society Of Clinical Oncology/Oncology Nursing Society chemotherapy administration safety standards. J Clin Oncol. 2009;27(32):5469-75.
23. Baskin JL, Pui C-H, Reiss U, Wilimas JA, Metzger ML, Ribeiro RC, et al. Management of occlusion and thrombosis associated with long-term indwelling central venous catheters. Lancet. 2009;374(9684):159-69.
24. Camp-Sorrell D. Access device guidelines: recommendations for nursing practice and education. 3rd ed. Oncology Nursing Society; 2011.
25. Cummings-Winfield C, Mushani-Kanji T. Restoring patency to central venous access devices. Clin J Oncol Nurs. 2008;12(6):925-34.
26. Debourdeau P, Kassab Chahmi D, Le Gal G, Kriegel I, Desruennes E, Douard MC, et al. 2008 SOR guidelines for the prevention and treatment of thrombosis associated with central venous catheters in patients with cancer: report from the working group. Ann Oncol. 2009;20(9):1459-71.
27. Fung-Kee-Fung M, Provencher D, Rosen B, Hoskins P, Rambout L, Oliver T, et al. Intraperitoneal chemotherapy for patients with advanced ovarian cancer: A review of the evidence and standards for the delivery of care. Gynecol Oncol. 2007;105(3):747-56.
28. O'Grady NP, Alexander M, Burns LA, Dellinger EP, Garland J, Heard SO, et al. Guidelines for the prevention of intravascular catheter-related infections, 2011 [cited 2012 Jun 7]. Available from: http://www.cdc.gov/hicpac/pdf/guidelines/bsi-guidelines-2011.pdf.

29. O'Grady NP, Alexander M, Burns LA, Dellinger EP, Garland J, Heard SO, et al. Guidelines for the prevention of intravascular catheter-related infections. Clin Infect Dis. 2011;52(9):e162-93.
30. Kearon C, Akl EA, Comerota AJ, Prandoni P, Bounameaux H, Goldhaber SZ, et al. Antithrombotic therapy for VTE disease: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. Chest. 2012;141(2 Suppl):e419S-94S. Epub 2012/02/15.
31. National Institute for Clinical Excellence. Prevention and control of healthcare-associated infections in primary and community care. Internet: National Institute for Clinical Excellence, 2012 Mar 2012. Report No.: 149.
32. Mermel LA, Allon M, Bouza E, Craven DE, Flynn P, O'Grady NP, et al. Clinical practice guidelines for the diagnosis and management of intravascular catheter-related infection: 2009 Update by the Infectious Diseases Society of America. Clin Infect Dis: an official publication of the Infectious Diseases Society of America. 2009;49(1):1-45. Epub 2009/06/06.
33. Johnston J, Armes S, Barringer E, Dickeson P, D'Onofrio L, Giff C, et al. Assessment and device selection for vascular access. Internet: Registered Nurses' Association of Ontario; 2008 [cited 2012 Jun 8]. Available from: http://rnao.ca/sites/rnao-ca/files/Assessment_and_Device_Selection_for_Vascular_Access.pdf.
34. Registered Nurses' Association of Ontario. Care and maintenance to reduce vascular access complications. Toronto, Ontario, Canada: Registered Nurses' Association of Ontario; 2005 [cited 2012 Jun 12]. Available from: http://rnao.ca/sites/rnao-ca/files/Care_and_Maintenance_to_Reduce_Vascular_Access_Complications.pdf.
35. Vescia S, Baumgartner AK, Jacobs VR, Kiechle-Bahat M, Rody A, Loibl S, et al. Management of venous port systems in oncology: a review of current evidence. Ann Oncol. 2008;19(1):9-15.
36. Canadian Association of Nurses in Oncology. Standards and competencies for cancer chemotherapy nursing practice, 2009 [cited 2012 Jul 16]. Available from: http://www.aqio.org/docs/normes_chimio_anglais.pdf.
37. The AGREE Research Trust. The Appraisal of Guidelines for Research & Evaluation (AGREE) instrument: The AGREE Research Trust; 2001 [cited 2009 July 29]; Available from: http://www.agreetrust.org/instrument.htm.
38. European Oncology Nursing Society. Extravasation guidelines: guidelines implementation toolkit. [Internet]. Bussels, Belgium: EONS; 2007 [cited 2012 May 8]. Available from: http://www.cancernurse.eu/documents/EONSClinicalGuidelinesSection6-en.pdf.
39. Camp-Sorrell D. State of the science of oncology vascular access devices. Semin Oncol Nurs. 2010;26(2):80-7.

APPENDICES

Appendix 1. Systematic search for guidelines.

Updated search conducted on April 19, 2012: Search strategy
Database: Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations and Ovid MEDLINE(R) <1946 to Present>
Search Strategy:
---

1 exp practice guidelines/
2 exp Guideline/
3 guideline?.tw,pt,sh.
4 (practice guideline or guideline?).mp,pt.
5 consensus.sh,tw,pt.
6 1 or 2 or 3 or 4 or 5
7 Catheterization, Peripheral/ or Catheterization, Central Venous/ or Infusions, Intravenous/ or Fluid Therapy/ or intravenous therapy.mp. or Infusions, Parenteral/ or Injections, Intravenous/
8 6 and 7
9 limit 8 to (English language and yr="2006 -Current")

Appendix 2. Results of AGREE II evaluation.

1	Baskin JL, Pui C-H, Reiss U, Wilimas JA, Metzger ML, Ribeiro RC, et al. Management of occlusion and thrombosis associated with long-term indwelling central venous catheters. Lancet. 2009;374(9684):159-69. http://www.thelancet.com/journals/lancet/article/PIIS0140-6736%2809%2960220-8/abstract	2 reviewers recommend the use of the guideline, 2 reviewers recommend its use with modifications **Summary AGREE II scores:** Domain 1: Scope and purpose 60% Domain 2: Stakeholder involvement 19% Domain 3: Rigour of development 47% Domain 4: Clarity of presentation 78% Domain 5: Applicability 13% Domain 6: Editorial independence 71%
2	Camp-Sorrell D. Access device guidelines: recommendations for nursing practice and education. 3rd ed: Oncology Nursing Society; 2011. (Book)	3 reviewers recommend the use of this guideline, and 1 reviewer recommends its use with modifications **Summary AGREE II scores:** Domain 1: Scope and purpose 83% Domain 2: Stakeholder involvement 50% Domain 3: Rigour of development 60% Domain 4: Clarity of presentation 85% Domain 5: Applicability 52% Domain 6: Editorial independence 90%
3	Cummings-Winfield C, Mushani-Kanji T. Restoring patency to central venous access devices. Clin J Oncol Nurs. 2008;12(6):925-34. http://www.ons.org/Publications/VJC/media/ons/docs/publications/VJC/restoringpatencycytocvads.pdf This document has been excluded because of low quality.	3 reviewers recommended not to use this guideline; 1 reviewer recommends its use with modifications **Summary AGREE II scores:** Domain 1: Scope and purpose 74% Domain 2: Stakeholder involvement 40% Domain 3: Rigour of development 35% Domain 4: Clarity of presentation 71% Domain 5: Applicability 45% Domain 6: Editorial independence 25%
4	Debourdeau P, Kassab Chahmi D, Le Gal G, Kriegel I, Desruennes E, Douard MC, et al. 2008 SOR guidelines for the prevention and treatment of thrombosis associated with central venous catheters in patients with cancer: report from the working group. Ann Oncol. 2009;20(9):1459-71. http://annonc.oxfordjournals.org/content/20/9/1459.full.pdf	3 reviewers recommend the use of this guideline, 1 reviewer recommends its use with modifications **Summary AGREE II scores:** Domain 1: Scope and purpose 74% Domain 2: Stakeholder involvement 31% Domain 3: Rigour of development 77% Domain 4: Clarity of presentation 92%

		Domain 5: Applicability 9% Domain 6: Editorial independence 42%
5	Fung-Kee-Fung M, Provencher D, Rosen B, Hoskins P, Rambout L, Oliver T, et al. Intraperitoneal chemotherapy for patients with advanced ovarian cancer: A review of the evidence and standards for the delivery of care. Gynecol Oncol. 2007;105(3):747-56. http://dx.doi.org/10.1016/j.ygyno.2007.02.015	2 reviewers recommend not to use this guideline, 2 reviewers recommend its use with modifications
6	O'Grady NP, Alexander M, Burns LA, Dellinger EP, Garland J, Heard SO, et al. Guidelines for the prevention of intravascular catheter-related infections, 20112011 Jun 7, 2012 [cited 2012 Jun 7]. Available from: http://www.cdc.gov/hicpac/pdf/guidelines/bsi-guidelines-2011.pdf, *AND* O'Grady NP, Alexander M, Burns LA, Dellinger EP, Garland J, Heard SO, et al. Guidelines for the prevention of intravascular catheter-related infections. Clinical Infectious Diseases. 2011;52(9):e162-93. http://cid.oxfordjournals.org/content/52/9/e162.extract	4 reviewers recommend the use of this guideline **Summary AGREE II scores:** Domain 1: Scope and purpose 83% Domain 2: Stakeholder involvement 74% Domain 3: Rigour of development 72% Domain 4: Clarity of presentation 88% Domain 5: Applicability 68% Domain 6: Editorial independence 92%
7	Wengström Y, Foubert J, Marguiles A, Roe H, Bugeia S. Extravasation guidelines 2007, *AND* Wengstrom Y, Marguiles A. European Oncology Nursing Society extravasation guidelines. Stockholm: University of Stirling, 2008.	2 reviewers recommend the use of this guideline, 2 reviewers recommend its use with modifications because it is out of date.
8	Kearon C, Kahn SR, Agnelli G, Goldhaber S, Raskob GE, Comerota AJ, et al. Antithrombotic therapy for venous thromboembolic disease: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines (8th ed).[Erratum appears in Chest. 2008 Oct;134(4):892]. Chest. 2008;133(6 Suppl):454S-545S. http://chestjournal.chestpubs.org/content/133/6_suppl/454S.full.pdf Supplementary material: http://journal.publications.chestnet.org/data/Journals/CHEST/23443/Data_supp_v141_i2_pe419S_112301.pdf	4 reviewers recommend the use of this guideline **Summary AGREE II scores:** Domain 1: Scope and purpose 93% Domain 2: Stakeholder involvement 69% Domain 3: Rigour of development 91% Domain 4: Clarity of presentation 94% Domain 5: Applicability 74% Domain 6: Editorial independence 90%

9	National Institute for Clinical Excellence. Prevention and control of healthcare-associated infections in primary and community care. Internet: National Institute for Clinical Excellence, 2012 Mar 2012. Report No. 149. http://www.nice.org.uk/nicemedia/live/13684/58656/58656.pdf	4 reviewers recommend the use of this guideline. However, it has been noted that this is for home care, and that it is entirely based on the more recent CDC 2009 guideline. **Summary AGREE II scores:** Domain 1: Scope and purpose 85% Domain 2: Stakeholder involvement 89% Domain 3: Rigour of development 83% Domain 4: Clarity of presentation 81% Domain 5: Applicability 83% Domain 6: Editorial independence 83%
10	Mermel LA, Allon M, Bouza E, Craven DE, Flynn P, O'Grady NP, et al. Clinical practice guidelines for the diagnosis and management of intravascular catheter-related infection: 2009 Update by the Infectious Diseases Society of America. Clin Infect Dis. 2009;49(1):1-45. Epub 2009/06/06. http://www.ncbi.nlm.nih.gov/pubmed/19489710	3 reviewers recommend the use of this guideline, 1 reviewer recommends its use with modifications **Summary AGREE II scores:** Domain 1: Scope and purpose 93% Domain 2: Stakeholder involvement 64% Domain 3: Rigour of development 87% Domain 4: Clarity of presentation 93% Domain 5: Applicability 34% Domain 6: Editorial independence 94%
11	Johnston J, Armes S, Barringer E, Dickeson P, D'Onofrio L, Giff C, et al. Assessment and device selection for vascular access. Internet: Registered Nurses' Association of Ontario; 2008 [cited 2012 Jun 8]. Available from: http://rnao.ca/sites/rnao-ca/files/Assessment_and_Device_Selection_for_Vascular_Access.pdf This guideline has been excluded because it is generic and it is specified in the text that nurses who work in oncology settings will need more specific recommendations.	1 reviewer recommends not to use the guideline 1 reviewer recommends its use with modifications because it is not focussed on oncology 2 reviewers recommend the use of this guideline **Summary AGREE II scores:** Domain 1: Scope and purpose 86% Domain 2: Stakeholder involvement 69% Domain 3: Rigour of development 82% Domain 4: Clarity of presentation 92% Domain 5: Applicability 91% Domain 6: Editorial independence 83%
12	Registered Nurses' Association of Ontario. Care and maintenance to reduce vascular access complications. Toronto, Ontario, Canada: Registered Nurses' Association of Ontario;	2 reviewers recommend the use of this guideline 2 reviewers recommend its use with modifications (not focussed on oncology)

	2005 [cited 2012 Jun 12]. Available from: http://rnao.ca/sites/rnao-ca/files/Care_and_Maintenance_to_Reduce_Vascular_Access_Complications.pdf	**Summary AGREE II scores:** Domain 1: Scope and purpose 92% Domain 2: Stakeholder involvement 54% Domain 3: Rigour of development 86% Domain 4: Clarity of presentation 88% Domain 5: Applicability 79% Domain 6: Editorial independence 77%
13	EviQ bundle https://www.eviq.org.au/. You need to register to enter, but it is free: at the site in the previous link, you can access procedures; at the link below you can access the 2007 guideline: .https://www.eviq.org.au/LinkClick.aspx?fileticket=fqkfYc6p9Bk%3d&tabid=60 This guideline has been excluded because the online tool has examples of procedures, the 2007 document has been considered out of date.	3 reviewers recommend not to use this guideline, 1 reviewer recommends its use
14	Canadian Association of Nurses in Oncology. Standards and competencies for cancer chemotherapy nursing practice 2009 [cited 2012 Jul 16]. Available from: http://www.aqio.org/docs/normes_chimio_anglais.pdf	4 reviewers recommend the use of this document. However, it was noted that this is not a guideline per se, and many of the AGREE criteria do not apply. **Summary AGREE II scores:** Domain 1: Scope and purpose 78% Domain 2: Stakeholder involvement 67% Domain 3: Rigour of development 52% Domain 4: Clarity of presentation 76% Domain 5: Applicability 27% Domain 6: Editorial independence 29%
15	Vescia S, Baumgartner AK, Jacobs VR, Kiechle-Bahat M, Rody A, Loibl S, et al. Management of venous port systems in oncology: a review of current evidence. Ann Oncol. 2008;19(1):9-15. http://annonc.oxfordjournals.org/content/19/1/9.full.pdf+html This document has been excluded because of low quality	3 reviewers would not recommend the use of this guideline **Summary AGREE II scores:** Domain 1: Scope and purpose 78% Domain 2: Stakeholder involvement 29% Domain 3: Rigour of development 44% Domain 4: Clarity of presentation 60% Domain 5: Applicability 29% Domain 6: Editorial independence 13%

Evidence-Based Series #12-12-2: Section 3

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: Development Methods, Recommendations Development and External Review Process

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: March 10, 2014

THE PROGRAM IN EVIDENCE-BASED CARE

The Program in Evidence-Based Care (PEBC) is an initiative of the Ontario provincial cancer system, Cancer Care Ontario (CCO) (1). The PEBC mandate is to improve the lives of Ontarians affected by cancer through the development, dissemination, and evaluation of evidence-based products designed to facilitate clinical, planning, and policy decisions about cancer care.

The PEBC supports a network of disease-specific panels, termed Disease Site Groups (DSGs), as well as other groups or panels called together for a specific topic, all mandated to develop the PEBC products. These panels are comprised of clinicians, other health care providers and decision makers, methodologists, and community representatives from across the province.

The PEBC produces evidence-based and evidence-informed guidelines, known as Evidence-Based Series (EBS) reports, using the methods of the Practice Guidelines Development Cycle (1,2). The EBS reports consists of an evidentiary base (typically a systematic review), an interpretation of and consensus agreement on that evidence by our Groups or Panels, the resulting recommendations, and an external review by Ontario clinicians and other stakeholders in the province for whom the topic is relevant. The PEBC has a formal standardized process to ensure the currency of each document, through the periodic review and evaluation of the scientific literature and, where appropriate, the integration of that literature with the original guideline information.

This EBS is comprised of the following sections:

- *Section 1: Guideline Recommendations*. Contains the clinical and organizational recommendations derived from a systematic review of the clinical and scientific literature and its interpretation by the Group or Panel involved and a formalized external review in Ontario by review participants.

- *Section 2: Evidentiary Base*. Presents the comprehensive evidentiary/systematic review of the clinical and scientific research on the topics discussed and the conclusions reached by the Working Group.
- *Section 3: Development Methods, Recommendations Development, and External Review Process*. Summarizes the EBS development process, the recommendations development process and the results of the formal external review of the draft version of the EBS.

FORMATION OF THE GUIDELINE DEVELOPMENT WORKING GROUP

CCO's Systemic Treatment and Nursing Programs asked the PEBC to develop a guideline on the safe administration of systemic cancer treatment. In consultation with the Systemic Treatment and Nursing Programs, a Working Group was identified. This Working Group consisted of three registered nurses, two pharmacists, two hematologists, three medical oncologists, and one health research methodologist. The Working Group and the Systemic Treatment and Nursing Programs also formed the Safe Chemotherapy Administration Guideline Development Group. This group would take responsibility for providing feedback on the guideline as it was being developed requiring changes as necessary before approving it.

OBJECTIVES AND RESEARCH QUESTIONS

This Working Group developed the following objectives for this guideline in consultation with the Systemic Treatment and Nursing Programs.

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 of the administration of systemic treatment to adult cancer patients.

From these objectives, and according to three areas of interest, the following research questions were derived to direct the search for available evidence to inform recommendations to meet the objective.

1) **Area of interest 1: Selection, use and management of vascular access devices, including potential complications, during the administration of systemic cancer treatment**
   - What are the most effective and safe access devices to administer chemotherapy?
   - When is access assessed?
   - What options are presented to patients?
   - What are the most effective techniques for insertion and management of access devices to prevent infection, lumen occlusion and venous thrombosis as well as for reducing error rates?
   - What are the most effective intravenous (IV) access devices for patients (central vs. peripheral devices)?
   - What are the indications for insertion of a peripheral access device in the delivery of chemotherapy?

Area of interest 2: Extravasation, phlebitis, flare, allergy and hypersensitivity complications of chemotherapy administration

- What are the best strategies for the prevention of extravasation?

- What are the best strategies for the detection and differential diagnosis of extravasation?
- What are the best strategies for the management of extravasation once it has occurred?
- What are the best strategies for documenting extravasation?
- What are the best strategies for the prevention and treatment of irritation and flare reaction?
- What are the best strategies for the prevention and treatment of allergic/hypersensitivity reactions to chemotherapy?

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

- What are the most effective nursing strategies for reducing errors of administration of systemic cancer treatment agents to cancer patients while using volumetric pumps and other devices (e.g., elastomeric pumps)?
- What are the most effective strategies for double independent checking calculations prior to administration of chemotherapy drugs?
- What are the best strategies for the preparation and administration of pre-medications?
- What are the best strategies to prevent errors during the administration of systemic cancer therapy?
- What are the best strategies for post care (e.g., hydration)?
- What are the best strategies for management of error-related toxicity?
- What are the best strategies for the verification and maintenance of treatment (e.g., identification of needs, support measures to help maintain the treatment)?

GUIDELINE REVIEW

Almost all PEBC document projects begin with a search for existing guidelines that may be suitable for adaptation. The PEBC defines adaptation, in accordance with the ADAPTE Collaboration, as "the use and/or modification of (a) guideline(s) produced in one cultural and organizational setting for application in a different context" (3). This includes a wide spectrum of potential activities from the simple endorsement, with little or no change, of an existing guideline, to the use of the evidence base of an existing guideline with *de novo* recommendations development.

For this document, the results of the general search for guidelines conducted at the start of the two part series was reviewed; a second search was conducted in April 2012 including the Canadian Partnership Against Cancer Standards and Guideline Evidence database (4), the MEDLINE and EMBASE databases (Ovid interface), the National Guidelines Clearinghouse (5), the National Institute for Health and Care Excellence (NICE) (6), the New Zealand Guidelines Group (http://www.health.govt.nz/about-ministry/ministry-health-websites/new-zealand-guidelines-group), the Association for Professionals in Infection Control and Epidemiology Inc. (APIC) (http://www.apic.org/), the Association for Vascular Access (AVA) (http://www.avainfo.org/website/article.asp?id=280986), the Canadian Association of Nurses in Oncology (CANO) (http://www.cano-acio.ca/) the Centers for Disease Control (CDC) (http://www.cdc.gov/), the Evidence-based Practice in Infection Control (http://www.chica.org/links_evidence_guidelines.php), the Infusion Nurses Society (http://www.ins1.org/i4a/pages/index.cfm?pageid=1), the Oncology Nurses Society (http://www.ons.org/), the Vascular Access Society (http://www.vascularaccesssociety.com/), the Joint Commission

(http://www.jointcommission.org/), the Vascular Access Society (http://www.vascularaccesssociety.com/), the Registered Nurses Association of Ontario (RNAO) (http://rnao.ca/), the Scottish Intercollegiate Guideline Network (SIGN) (http://www.sign.ac.uk/), the BC Cancer Agency (http://www.bccancer.bc.ca/default.htm), the Alberta Cancer Board (http://albertacancer.ca/), Accreditation Canada (http://www.accreditation.ca/en/), EviQ Cancer Treatments Online (https://www.eviq.org.au/), The Agency for Healthcare Research and Quality M&M (http://www.webmm.ahrq.gov/), the Institute of Safe Medication Practices Canada (ISMP Canada) (http://www.ismp-canada.org/), the Quality Healthcare Network (http://www.qhn.ca/), the Guidelines Advisory Committee (http://www.gacguidelines.ca/), the International Pharmaceutical Federation (https://www.fip.org/) and the Infectious Diseases Society of America (http://www.idsociety.org/Index.aspx). An untargeted search of the Google® search engine was also conducted with the key words "chemotherapy, extravasation, infections, thrombosis, complications"; the results reported in the first five pages retrieved were examined. The reference lists of included guidelines were scanned for additional references.

Only guidelines published in or after 2006 that were based on a systematic review of the literature and that were relevant to Ontario and to the objectives and the research questions were considered. Guidelines that were considered relevant were then evaluated for quality using the AGREE II instrument.

Seventy guidelines were identified from the above described searches and their full text examined for the existence of an evidence base and for their relevance to the systemic cancer treatment administration in the context of Ontario. Fifteen of these guidelines (7-21) were selected as applicable to the context in Ontario and the AGREE II tool (22,23) was applied to them.

The remaining documents were not considered because their recommendations were not reported to be based on a systematic review of the evidence, they were outdated, or because they were not addressing specifically the safety questions asked in this document.

The Working Group agreed with the content of the selected guidelines, and links to them have been provided in this document for readers interested in the details regarding individual procedures. Additional links to implementation tools are also provided.

INITIAL RECOMMENDATIONS

Using the evidentiary base in Section 2, the Working Group developed a set of initial recommendations. These initial recommendations were developed through a consideration of the quality and the potential for bias in the selected guidelines and the likely benefits and harms. This process is described in detail for each topic area described below.

Key Evidence for Benefits and Harms

The following guidelines were used as a base for the recommendations in each area of interest:

Area of interest 1) Selection, use and management of vascular access devices, including complications, during the administration of systemic cancer treatment.

- Centers for Disease Control and Prevention (CDC) (24)
- European Oncology Nursing Society (EONS) (25)

- Oncology Nursing Society (ONS) (26)
- National Institute for Clinical Excellence (NICE) (27)
- Baskin et al (7)
- Fung-Kee-Fung (12)
- Mermel et al (16)
- Debourdeau et al (11)
- American College of Chest Physicians (15)

Area of interest 2): Extravasation and other complications of chemotherapy administration.

- EONS (25)
- ONS (26)

Area of interest 3): Nursing practices during and just after the administration of systemic cancer treatment agents, including verification and maintenance of the treatment plan.

- ONS (26)
- ASCO standards (13)

Aggregate Evidence Quality and Potential for Bias

The Working Group strived to provide guidance for both organizations and clinicians in this very complex and technical area of practice while striving not to make a procedure manual of this guideline. The high quality, evidence-based guidelines forming the backbone of this document were retrieved and selected through a systematic process, and appropriate references and links to them have been provided.

This process was intended to reduce bias, and at the same time to integrate the expertise of the Working Group with the available evidence, in order to produce guidance that is sound and applicable to Ontario.

Values of the Working Group

The Working Group considered the values of patient-centred care and context-specific flexibility in weighing benefits compared to harms, and then made a considered judgement.

Considered Judgement

The content of this document provides a framework to organizations and clinicians for the safe administration of systemic treatment to cancer patients. This area of practice is very complex and very technical; specific details of the involved procedures can be found in the evidence-based guidelines that are referenced here. Additional reference to relevant tools for the implementation of safe practices is also provided. The format of this document is intended to meet the needs of multiple users in diverse contexts while keeping the patient at the centre of focus and using the best available evidence.

INITIAL (DRAFT) RECOMMENDATIONS

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) 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) (9) 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 who participate in the care of persons with cancer and are receiving chemotherapy.
- Education of professionals to develop 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 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.
- Standards for all major processes involved in the prescribing and administration of chemotherapy. For example: how chemotherapy is prescribed; the use of standardized chemotherapy protocols with supporting references and documentation when there are protocol deviations; a process for order verification and independent double-checking; preparation and chemotherapy dispensing; pre-treatment assessment; selection of catheter, its maintenance and removal; monitoring, patient education and discharge, documentation.
- Safe handling of hazardous drugs, including equipment for personal protection; drug administration; cancer chemotherapy spill management and waste disposal; and for drug preparation that meets provincial and national occupational health and safety standards.
- Safe labelling and timing of chemotherapy drugs.
- Education and promotion of self-management in persons receiving chemotherapy (e.g., on prevention, management and reporting of side effects and adverse events).
- Prevention, early detection and management of complications related to the catheter/device use and to the drug administered.

Justification: The above recommendations are based on the CANO document and integrated with 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 complications, during the administration of systemic cancer therapy;

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)

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.

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 generally recommended dwell duration times of different devices.

Table 1. Vascular and Non-Vascular Access Devices. (Adapted from O'Grady 28 and Camp-Sorrell 8)

Catheter type	Entry Site	Length	Comments
VASCULAR DEVICES			
Peripheral intravenous catheters	Usually inserted in veins of forearm or hand.	<15 cm.	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.	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.	Account for majority of catheter related blood stream infections (CRBSI).
Peripherally inserted central venous catheters (PICC)	Inserted into basilic, cephalic, or brachial veins and enter the superior vena cava.	≥20 cm depending on patient size.	Lower rate of infection than non-tunneled CVCs.
Tunneled central venous catheters	Implanted into subclavian, internal jugular, or femoral veins.	≥8 cm depending on patient size.	Cuff inhibits migration of organisms into catheter tract; lower rate of infection than non-tunneled CVC.

Totally implantable	Tunneled beneath skin and have subcutaneous port accessed with a needle; implanted in subclavian or internal jugular vein	≥8 cm depending on patient size	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 por s	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	*Implanted peritoneal ports:* Low risk of displacement, more expensive, does not allow for high pressure forced irrigation.

Table 2. Access devices dwell time

Line type	Time
Peripheral lines	Short duration (days)
Non tunneled catheters	Approximately up to 6 weeks
PICC lines	Approximately 12 months
Tunneled catheters	Several years
Implanted ports	Indefinite
Intra-peritoneal catheters	Indefinite

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 3 below presents important factors to consider in the appropriateness of device selection and device insertion with some examples.

Table 3. Factors that impact catheter selection

Related factors	Specific Examples
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. Patient factors 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 which informed our recommendations were the Centers for Disease Control and Prevention (CDC) (19), the European Oncology Nursing Society (EONS) Extravasation guidelines (25) and the Oncology Nursing Society (ONS) (8) documents. Concepts from these guidelines were integrated with the Working Group expert consensus; the intent was to be as succinct as possible given that many factors often limit choices.

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 (8) (book available for purchase), and CDC (19) (available at http://www.cdc.gov/hicpac/pdf/guidelines/bsi-guidelines-2011.pdf) and EONS available at http://www.cancernurse.eu/documents/EONSClinicalGuidelinesSection6-en.pdf.

Examples of type of equipment include peripheral or central access device, 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 clear dressing to secure the cannula, and not covering with a bandage).

B. Prevention and detection of complications

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 and thrombosis/occlusion, or extravasation.

The Working Group recognizes the risk of experiencing complications with an access device is proportionate to the number of underlying contributing factors and the combination thereof.

Table 4 highlights preventable complications for each type of device, and the underlying factors and processes that may contribute to these adverse events. Extravasation, infiltration and flare reactions will be addressed separately and in detail in "Area of Interest 2): Extravasation, allergy and hypersensitivity complications of chemotherapy administration"

Table 4. Factors that may contribute to complications by catheter type

Type Of Catheter And Possible Complications	Factors That May Contribute To Complications
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 (how well performed); • Patient and carer's education (how well performed); • Health care workers education.
Central catheters:	
• Catheter migration • Catheter failure • Pinch-off syndrome • Catheter fracture • Damage to the catheter • Infection • Occlusion • Thrombosis	• Ultrasound placement of the catheter (used or not used) • Fluoroscopic guidance and/or radiographic confirmation of catheter tip placement • Development of, and adherence to, regular flushing/locking protocol(s) (used or not) • Level of awareness of manufacturers' warnings and labels • Consultation/communication among team members • Aseptic techniques (how well performed) • Patient's and carer's education and follow-up support • Health care workers education • Patient's level of activity
Intraperitoneal catheters:	
• Leakage around the exit site of the external catheter • Tunnel or exit site infection	• Development of, and adherence to, regular flushing/locking protocol(s) • Level of awareness of manufacturers' warnings

• Catheter dislodgement • Catheter failure • Nonfunctioning catheter • Bleeding • Bowel obstruction, perforation or fistula • Infection	and labels • Consultation/communication among team members • Aseptic techniques (how well performed) • Patient's and carer's education and follow-up support • Health care workers education

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

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

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 failure mode and effects analyses on incident events.

Justification

The guidelines which informed our recommendations are the ONS (8), the National Institute for Clinical Excellence (NICE) (17) and the CDC guideline (19). These recommendations are integrated with the expert opinion of the Working Group.

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 or evolving (29).

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 which may contribute to catheter-related complications.

Justification

The guidelines which informed our recommendations are the ONS guideline (8), the National Institute for Clinical Excellence (NICE) (17) available at http://www.nice.org.uk/nicemedia/live/13684/58656/58656.pdf, the Mermel et al document (16), the Baskin document (7), the CDC guideline (19) available at http://www.cdc.gov/hicpac/pdf/guidelines/bsi-guidelines-2011.pdf as well as the standards developed by Fung-Kee-Fung et al for intraperitoneal chemotherapy (12). Devices' insertion techniques are beyond the scope of this document. Interested readers can refer to the above mentioned guidelines.

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.

Justification:
The guidelines that have been used to inform our recommendations have been chosen through a rigorous and systematic review process (see Section 2 of this document). The guidelines that have been used are: For infective complications ONS, CDC, NICE and Mermel et al (8,16,17,19); for thrombotic/occlusive complications: Baskin et al, ONS, Debourdeau et al, and ACCP (7,8,11,15) and ONS for extravasation, phlebitis, irritation, flare reaction and allergic reactions (8).

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 5.

Table 5 Factors that may lead to catheter-related infection 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.
	• 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 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	• 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.	• 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/thrombosis, the Working Group recommends:

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

Health professionals should monitor for the appearance of signs and symptoms of local and systemic catheter-related bloodstream 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.

The treatment of infections, occlusion and thrombosis is beyond the scope of this document. Also, patientrelated factors (such as underlying hypercoagulable state) and thrombosisprovoking factors (such as type of chemotherapy type given i.e., immunomodulatory drugs, L-asparaginase) are beyond the scope of this document.

Useful resources for implementation

The CUSP toolkit (30) 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

AREA OF INTEREST 2): Extravasation, allergy, 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 in 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 this figure may be substantial (25). Extravastion should be considered both in the ambulatory setting and in the home setting 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 also may 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 6 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 6 Factors that may put cancer patients at risk of extravasation at different points of care

A. Factors That Are Conducive To Extravasation	
Point of care 1: catheter insertion	• Peripheral vein wall puncture
Point of care 2: during catheter access and use	• 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 sub cutaneous 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 1: catheter insertion	Not applicable

Point of care 2: during catheter access and use	• Failure to give pre-meds or to identify whether patient has taken pre-meds appropriately
	  • Infusion too fast
	  • Concentration
	  • Drug related (rituximab)

E. Factors That Are Conducive To Allergic Reactions	
Point of care 1: catheter insertion	Not applicable
Point of care 2: during catheter access and use	• Previous number of cycle • Drug related • Previous history of reactions to same drug
Point of care 3: Maintenance (device not in use)	• Patient education

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

Health professionals should be mindful of factors that can put patients at increased risk of extravasation, phlebitis, infiltration, flare, hypersensitivity reactions and allergic reactions and 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 1 of this document) and should be educated about the risk of vesicant extravasation and actions that patients can take.

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, hypersensitivity/flare reaction, as well as for signs and symptoms of 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 case 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 cytotoxic 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.

Justification

Health professionals involved in the administration of chemotherapy should be aware of the extravasation policy and procedure and of the contents and whereabouts of the extravasation kit and a replacement kit. They should have an understanding of the precautionary steps to be taken to avoid extravasation. The training about cytotoxic handling with special attention to new agents and to techniques and devices of administration should be maintained on an ongoing basis. Examples of topics for organizational policies are 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.

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 (21,31).

Useful resources for implementation

- EviQ portal (18) 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

Qualifying statement

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 do the procedure safely. These protocols are institution specific and are developed with the input from all the members of the health care team. The protocols may contain tools that are useful in the various phases of administration of chemotherapy as well for reporting.

Two guidelines represented by three publications were selected that were relevant for this topic area, and applicable to Ontario: the EONS guideline (21,31) available at http://www.cancernurse.eu/documents/EONSClinicalGuidelinesSection6-en.pdf, and the ONS guideline (8).

The recommendation about educating patients to what they can do in case of extravasation has been endorsed by the working group from the EONS Extravasation guidelines (21,31).

Patients are a primary source of information in that they can report the first symptoms

that allow for detecting extravasation. Participation of patients in the care process has also been recommended in Part 1 of this series (32).

Qualifying statement

Beyond 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 that have been shown to be effective and that can be implemented at each point of care to insure that all the risk factors have been taken into consideration include checklists, and patient involvement in their care (see Part 1 of this series) (32).

AREA OF INTEREST 3): Nursing practices during and just after the administration of systemic cancer treatment agents in the hospital setting, including verification and maintenance of the treatment plan.

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

C. Administration with volumetric and elastomeric pumps; double checking of calculations.

- For elastomeric pumps, improved staff and patient education is required to ensure that the pumps infuse at a rate as close to the nominal rate as possible. This includes:
  - User-specific education materials for pharmacy staff, nurses and patients.
  - Ordering physicians 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 be all programmed using the same units which 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, 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 any leakage or contamination prior to use, and throughout the infusion period. If the infusion is occurring at home, the patient should be educated on performing this check periodically.
- 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 for several days beyond the administration of a cytotoxic drug.

Qualifying statement

Factors that have been recognized as causes for variations in the flow rate of elastomeric pumps (33) are:

- 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 et al report (33) available at: http://www.capca.ca/wp-content/uploads/IV-Ambulatory-Study-Final-Report-ENGLISH-Jan-14-2011_small.pdf.
- EviQ portal (18) available at: https://www.eviq.org.au/.
- Camp-Sorrell: "Access device guidelines: recommendations for nursing practice and education" (8).
- BC cancer agency policies and procedures available at: http://www.bccancer.bc.ca/NR/rdonlyres/4478D9DB-662B-43C2-8839-6D3C374D3FAE/54559/UpdateDec2011_30Nov2011.pdf

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

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, 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 provider 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.

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/hypersensitivity reactions can be excluded.
- Protocols and procedures are followed for the safe disposal of used equipment and unused medication, and for the decontamination of hands.

Qualifying statement

The root-cause-analysis of the fluorouracil incident occurred in Alberta in 2006, (34) identified the lack of appropriate documentation and multitasking as contributing factors to the mistaken programming of the pump.

Useful resources for implementation

BC cancer agency protocols for pre- and post- chemotherapy care available at: http://www.bccancer.bc.ca/NR/rdonlyres/8E898B5D-3F12-4623-8E32-5B3C429C58F7/56350/SCNAUSEA_Protocol_1Mar2012.pdf

INTERNAL REVIEW

Almost all PEBC documents undergo internal review. This review is conducted by the Expert Panel and the Report Approval Panel. The Working Group was responsible for incorporating the feedback and required changes of both of these panels, and both panels had to approve the document before it could be sent to External Review.

Expert Panel Review and Approval

The following individuals acted as the Expert Panel for this document: Rose Bortolussi, Venetia Bourrier, Flay Charbonneau, Daniela Gallo-Hershberg, Susan Glick, Caroline Hamm, Karen Janes, Gregory Knight, Kara Laing, Jonathan Noble, Jill Petrella, Andrew Robinson, and Susan Walisser. The members of this group were required to submit conflict of interest declarations prior to reviewing the document. These declarations are described in Appendix 1. The document must be approved by formal vote. In order to be approved, 75% of the Safe Chemotherapy Administration Expert Panel membership must cast a vote or abstain, and of those who voted, 75% must approve the document. At the time of the voting, the Safe Chemotherapy Administration Expert Panel members could suggest changes to the document, and possibly make their approval conditional on those changes. In those cases, the Working Group would be responsible for considering the changes, and if those changes could be made without substantially altering the recommendations, the altered draft would not need to be re-submitted for approval again.

The Safe Chemotherapy Expert Panel reviewed the document between August 23, and September 25, 2013. During this review, the Safe Chemotherapy Expert Panel provided the following key feedback:

- Extend the recommendations to cancer patients in any settings, not exclusively ambulatory hospital.

- Minor changes in the wording of the recommendations and of the text in general to improve clarity and consistency.

In response to this feedback, the Working Group made the following changes:

- The phrase "in a hospital setting" was removed throughout the document.
- Changes in the wording were made to improve clarity and consistency of language.

On September 26 in a teleconference meeting the Safe Chemotherapy Administration Working Group decided together on the changes to be made in response to feedback and formally approved them unanimously.

Report Approval Panel Review and Approval

The purpose of the Report Approval Panel (RAP) review is to ensure the methodological rigour and quality of PEBC documents. The RAP consists of nine clinicians with broad experience in clinical research and guideline development, and the Director of the PEBC. For each document, three RAP members review the document: the Director and two others. RAP members must not have had any involvement in the development of the guideline prior to Internal Review. All three RAP members must approve the document, although they may do so conditionally. If there is a conditional approval, the Working Group is responsible for ensuring the necessary changes are made, with the Assistant Director of Quality and Methods, PEBC, making a final determination that the RAP's concerns have been addressed.

In June 2013 the RAP reviewed this document. The RAP conditionally approved the document in September, 2013. Key issues raised by the Report Approval Panel included the following:

1) Although the document is very well written and well organized, and it is useful, it does not provide specific enough guidance.
2) A change to the core recommendation has been suggested as follows:
To optimize the highest level of professional practice (dictated by professional bodies, such as ONA or CANO) to ensure optimal safety of chemotherapy administration, it is recommended:

- ***that institutions develop, implement and monitor specific policies and procedures for the safe admin of chemotherapy***
- ***that these policies and procedures be developed by DATE***
- ***that development of policies and procedures be considered as a quality indicator for part of Cancer System Quality Index***

The Working Group made some changes in the wording of the recommendations to align with RAP suggestions; however, the document was not substantially changed. This was discussed with Dr. Melissa Brouwers, Dr. Sheila McNair and Mr. Hans Messersmith and the RAP agreed with the position of the Working Group.

External Review by Ontario Clinicians and Other Experts

The PEBC external review process is two-pronged and includes a targeted peer review that is intended to obtain direct feedback on the draft report from a small number of

specified content experts and a professional consultation that is intended to facilitate dissemination of the final guidance report to Ontario practitioners.

Following approval of the document at Internal Review, the Safe Chemotherapy Administration Expert Panel circulated the draft document with recommendations modified as noted under Internal Review, above, to external review participants for review and feedback. Appendix 2 summarizes the draft recommendations and supporting evidence developed by the *Safe Administration of Chemotherapy Expert Panel* as submitted for External Review.

Methods

Targeted Peer Review: During the guideline development process, nine targeted peer reviewers from Ontario considered to be clinical and/or methodological experts on the topic were identified by the working group. Several weeks prior to completion of the draft report, the nominees were contacted by email and asked to serve as reviewers. Three reviewers agreed and the draft report and a questionnaire were sent via email for their review. The questionnaire consisted of items evaluating the methods, results, and interpretive summary used to inform the draft recommendations and whether the draft recommendations should be approved as a guideline. Written comments were invited. The questionnaire and draft document were sent out on November 15, 2013. Follow-up reminders were sent at two weeks (email) and at four weeks (telephone call). The Safe Chemotherapy Administration Expert Panel reviewed the results of the survey.

Professional Consultation: Feedback was obtained through a brief online survey of health care professionals who are the intended users of the guideline. All oncology nurses, medical oncologists, pharmacists in oncology, radiation oncologists and interventional radiologists in the PEBC database were contacted by email to inform them of the survey. All the participants were from Ontario. Participants were asked to rate the overall quality of the guideline (Section 1) and whether they would use and/or recommend it. Written comments were invited. Participants were contacted by email and directed to the survey website where they were provided with access to the survey, the guideline recommendations (Section 1) and the evidentiary base (Section 2). The notification email was sent on November 15, 2013. The consultation period ended on January 10, 2014. The Safe Chemotherapy Administration Expert Panel reviewed the results of the survey.

Results

Targeted Peer Review: Three responses were received from three reviewers. Key results of the feedback survey are summarized in Table 1.

Table 1. Responses to nine items on the targeted peer reviewer questionnaire.

	Reviewer Ratings (N=3)				
Question	Lowest Quality (1)	(2)	(3)	(4)	Highest Quality (5)
1. **Rate the guideline development methods.**			1	1	1
2. Rate the guideline presentation.		1	1		1
3. Rate the guideline recommendations.				2	1
4. Rate the completeness of reporting.			1	1	1
5. Does this document provide sufficient information to inform your decisions? If not, what areas are missing?*			1	2	
6. What are the barriers or enablers to implementation of this guideline?	Skipped				

7. Rate the overall quality of the guideline report.				1	2
	Strongly Disagree (1)				Strongly Agree (5)
8. I would make use of this guideline in my professional decisions.			1	1	1
9. I would recommend this guideline for use in practice.			1	1	1

Summary of Written Comments

The main points contained in the written comments were:

Comment	Response/Modification
Question 1	
Methods are clearly stated and the process of identifying and selecting the evidentiary base was clear.	None needed
Recommendations are consistent with literature and standards. Clearly identify what nurses are to consider and what patients' education should be undertaken.	None needed
Stakeholders: Excellent. A required 75% approval seems low. Am I correct that primary trials were not reviewed (just consensus/guideline documents)? While significantly more work, including primary data would strengthen the methods. The guideline review itself was quite thorough	The topics covered were too many and existing literature of good quality: looking at primary literature would have meant duplication of effort.
Question 2	
Suggest to renumber or retitle this. Part 2 Section 1, Section 2 is confusing. Perhaps letters Part 2 Section A?	This suggestion has not been implemented because the document has been known from its inception as is.
A bit repetitive. The organizational schema used beyond the main was not apparent, making it difficult to access specific materials	Headings levels have been re-arranged.
Question 3	
It is very important that policy and procedures development be recognized as a quality indicator and that the impact of implementation is assessed. Competency and education of all providers is important. Assessment tool development is critical.	No changes needed
Great work on the extravasation section…long overdue.	No changes needed
Question 4	
Seems very thorough.	No changes needed
Passed on objectives - work is complete.	No changes needed

Some potentially helpful items (e.g., list of vesicants) were missing. Detail provided was hit and miss, depending on topic.	This provincial guideline is not intended to provide procedural detail, and what is provided, in appendices, is meant as an example. New drugs will come out that are not in the list, that's why it is a good idea to keep it as an example.
Question 5	
Tracking relevant data will be important to assess quality. Literature on data elements to collect on an EHR and how data is managed, reported and integrated into a provincial metric is critical as each region adopts different types of EHRs	Need to discuss
Too many referrals to other documentation or sites, versus including them in yours -See #4 -Would like to see a grading of strength of the recommendations/evidence these recommendations were based on	The documents to which we refer in this guideline are resources that contain more detail for the specific procedures than we would have been able to include in this guideline without making it an unmanageable document and a procedure manual. The evidence that supports the recommendations is listed in Table 1, Section 2. The critical appraisal of the included guidelines was performed using the AGREE II tool, and the results of this appraisal, done by two members of the working group, is reported in Section 2, Appendix 2.
Question 6	
This report provides lots of ideas. Implementation would be greatly enabled by reporting outcomes in CSQI. A barrier to implementation is existing workload.	No changes needed.
Many topics in one guideline and at times confusion but should not limit its implementation	No changes needed
Additional comments	
There needs to be flexibility in how this guideline is implemented in various jurisdictions such as small communities or geographically isolated locations. It will be especially important to monitor safety in these settings.	No changes needed

Professional Consultation: Fifteen responses were received. Key results of the feedback survey are summarized in Table 2.

Table 2. Responses to four items on the professional consultation survey.

	Number 15 (%)				
General Questions: Overall Guideline Assessment	Lowest Quality (1)	(2)	(3)	(4)	Highest Quality (5)
1. Rate the overall quality of the guideline report.*		1(7)		12 (80)	2 (13)
	Strongly Disagree (1)	(2)	(3)	(4)	Strongly Agree (5)
2. I would make use of this guideline in my professional decisions.**		2 (13)	1 (7)	10 (67)	2 (13)
3. I would recommend this guideline for use in practice.*		1 (7)		9 (60)	5 (33)

4. What are the barriers or enablers to the implementation of this guideline report?

- Resources and funding.
- Barriers, cost, compliance. Enablers: best practice, safety to all involved.
- Enablers: implementation task group, communication, and documentation.
- Very long and detailed. However, many of the sub-topics are unique and require separate discussion, as here. Likely to be a reference work rather than a true aid in daily care. Users may remove those sections of the report of particular reference to their needs, rather than file the whole report.
- Some of the guidelines are beyond the scope of the Regional Cancer Programs and will involve collaboration with other programs.
- Putting the information in table format makes it easy for healthcare professionals to review; good layout; language is clear.
- Pg. 20 - Post care; recommendation that patient going home with ambulatory pump should be observed until the proper functioning of the pump can be verified is difficult to implement. For 7 days elastomeric pump -- it will take few hours before any significant change can be observed, and we do not want staff to open the system to verify it.
- Time and workforce.
- Processes will need to be defined for each cancer centre and measurements taken to ensure the guideline is being followed - that takes resources and time - which I think will be the biggest barrier. Enabler will be the focus on safety.
- Very comprehensive guideline; no perceived barriers.
- I found the set-up this guideline difficult to use. The recommendations don't stand out from the additional information that informs the recommendations. Only one of the tables of information is cited. Much of the information I would use in my practice is in the tables, and I would like to know the sources. The table of contents should be expanded - use sublayers so that information can be found better. Titles of subsections need to be clearer and easier to interpret. Possibly consider using different fonts when wanting certain information to be visible. I find the document so difficult to read because content doesn't stand out. Not all the links are useful in the document. For example, the link for the CANO standards isn't to their website, and AGIO.com when you open it appears to have adds for searching through. Other links for additional resources, it would be ideal to put the names of the resources with the links. I'm not sure what to look for, and if the links change, I won't be able to find anything that relates to the resource you are referring to. It is missing information

that people want to use in practice - it does not indicate what the evidence says about extravasation antidotes - only provides another organizations antidotes. Does CCO agree with these?
- None identified.

Additional comments
- -Table 3 Intra-peritoneal catheter --> there is a duplicate row (last section) -Table 5, section A - point of care #2 --> fibrin sheath on CVC and inadequate staff education - Not really understanding Table 5, section E - point of care #3 - between maintenance and patient education as factor conducive for allergic reaction. - Page 19, last bullet in the box --> What constitutes as "several days"? Most recommended 48 hrs post chemo.
- Some specific comments - 1) Page 10 in "the box" I wonder if specific recommendation should be that the decisions are made in collaboration with the patient? 2) Page 12 where it talks about failure mode and effects analysis - this is pretty specific - I wonder if it shouldn't be broadened to maybe "route cause analysis." 3) Page 12 - third box, mentions care bundles for treatment, but on page 10, it says that treatment is out of scope. 4) Page 16 - E - Is there a number of previous cycles?, what does "drug specific" mean - maybe different wording is needed? What does "patient education" mean - is it lack of patient education? 5) Page 18 - last box - "improved staff and patient education" - improved from what? Should it just asy "for elastomeric pumps, staff and patient education is required...." 7) Page 19 - "prior to chemo administration a final check of patient and drug info...." does this include patient id? Does this mean that there needs to be two independent checks of pt id before the drug is given? Not sure
- needs clarity.
- Please add more specifics for oral administration on page 5. I think too many groups separate out oral, and forget that there is relevance in the document for oral therapies. Also on page 5, I think it would be valuable to add the frequency for continuing competency programs. Yearly is what the professional colleges recommend, and multiple oncology professional organizations, including CANO. Extravasation management on page 15 should include the inpatient setting as a potential site. I think further information on page 19 in the recommendation should be included in relation to management of bodily fluids - in relation to caregivers/family and patients, and unregulated caregivers. Many individuals can be at risk for exposure, and cancer patients are receiving these treatments at home, in long-term care organizations, on in hospitals in non-oncology settings and risk of exposure without proper education is a big issue. CCO should comment further on this. I think in relation to the language used for the skills and training that RNs need for checking, that we should use the language of competency. The RN must be competent to be able to the final check. - p. 19 Page 20 - For the post-care box, I'm wondering if consideration was given to demonstrating understanding - being knowledgeable about how to manage complications for when they are at home. They need to be knowledgeable before they leave.

Modifications/Actions
- Boxes enclosing the recommendations have been shaded to make recommendations stand out.
- Nothing was added in regard to oral therapy, because this topic was out of scope for this document.

- On page 5: The specific frequency (annually) of the program to evaluate maintenance of competency programs for professionals caring for persons receiving chemotherapy has been added.
- The evidence sources of Tables 3, 4 and 5 have been referenced to Table 1, Section 2, combined with the expert opinion of the working group members.
- A reference has been made to PEBC EBS #16-3: Safe handling of cytotoxics, 2013, for information regarding handling body fluids in the clinical and home setting.
- Table 5.E has been modified to clarify what the factors conducive to allergic reactions could be in Point of Care 2, by adding lack or patient education, and of previous documentation. Point of care 3 (maintenance) has been deleted. In the corresponding recommendation, a line has been introduced requiring standardized policies for managing hypersensitivity reactions, allergic reactions, and extravasation.
- Wording has been changed to the recommendation on page 18 to clarify.

CONCLUSION

This EBS report reflects the integration of feedback obtained through the external review process with final approval given by the Safe Chemotherapy Administration Expert Panel and the Report Approval Panel of the PEBC. Updates of the report will be conducted in accordance with the PEBC Document Assessment and Review Protocol.

Conflict of Interest

In accordance with the PEBC Conflict of Interest (COI) Policy, the guideline authors, Safe Chemotherapy Administration Expert Panel members, and internal and external reviewers were asked to disclose potential conflicts of interest.

For the Working Group members, 10 members members declared they had no conflicts of interest, and two (SS) declared conflicts. SS declared to have received more than $5,000 in a single year from Novartis, and RB declared to work for Innomar Strategies Inc. since 2012.

For the Safe Chemotherapy Administration Expert Panel, nine members declared they had no conflicts of interest, and three (VB, KJ and GK) declared conflicts. VB declared to be co-investigator on a study of IV chemotherapy and to have received funding from Cancer Agencies; declared to be Director of Pharmacy Services and Provincial Oncology Drug Program for Cancercare Manitoba. KJ declared to be co-investigator for study (Improving the Safety of Ambulatory Intravenous Chemotherapy in Canada) funded by CPSI, CAPCA, ISMP and five provincial cancer agencies)2008-2010). GK declared to have received travel and conference support greater than $5,000 to attend a meeting in 2012

The COI declared above did not disqualify any individuals from performing their designated role in the development of this guideline, in accordance with the PEBC COI Policy. To obtain a copy of the policy, please contact the PEBC office by email at ccopgi.mcmaster.ca

ACKNOWLEDGEMENTS

The Safe Chemotherapy Administration Expert Panel would like to thank Ms. Umangjot Bharaj who helped completing the appendices.

REFERENCES

1. Browman GP, Levine MN, Mohide EA, Hayward RS, Pritchard KI, Gafni A, et al. The practice guidelines development cycle: a conceptual tool for practice guidelines development and implementation. J Clin Oncol. 1995;13(2):502-12 Comment in: Ann Oncol. 2002 Sep;13(9):1507-9; author reply: 9. Epub 1995 Feb 01.
2. Browman GP, Newman TE, Mohide EA, Graham ID, Levine MN, Pritchard KI, et al. Progress of clinical oncology guidelines development using the Practice Guidelines Development Cycle: the role of practitioner feedback. J Clin Oncol. 1998;16(3):1226-31. Epub 1998 Mar 21.
3. The ADAPTE Collaboration. The ADAPTE Process: REsource Toolkit for Guideline Adaptation. Version 2.0 [cited July 19, 2014]. Available from http://www.g-i-n.net. 2009.
4. Canadian Partnership Against Cancer [Internet]. Toronto, ON. SAGE - Standards and Guidelines Evidence. Available at: http://www.partnershipagainstcancer.ca/[cited 2013 July 25]. Available from: http://www.partnershipagainstcancer.ca/.
5. US Department of Health and Human Services. National Guideline Clearinghouse. Agency for Healthcare Research and Quality; 2013; Available from: http://www.guideline.gov/index.aspx.
6. National Institute for Health and Care Excellence [Internet]. London: National Institute for Health and Care Excellence; c2013 Londonupdated 2013 July 24; Available from: http://www.nice.org.uk/.
7. Baskin JL, Pui C-H, Reiss U, Wilimas JA, Metzger ML, Ribeiro RC, et al. Management of occlusion and thrombosis associated with long-term indwelling central venous catheters. Lancet. 2009;374(9684):159-69.
8. Camp-Sorrell D. Access device guidelines: recommendations for nursing practice and education. 3rd ed: Oncology Nursing Society; 2011.
9. Canadian Association of Nurses in Oncology. Standards and competencies for cancer chemotherapy nursing practice2009 Jul 16, 2012 [cited 2012 Jul 16]. Available from: http://www.aqio.org/docs/normes_chimio_anglais.pdf.
10. Cummings-Winfield C, Mushani-Kanji T. Restoring patency to central venous access devices. Clin J Oncol Nurs. 2008;12(6):925-34.
11. Debourdeau P, Kassab Chahmi D, Le Gal G, Kriegel I, Desruennes E, Douard MC, et al. 2008 SOR guidelines for the prevention and treatment of thrombosis associated with central venous catheters in patients with cancer: report from the working group. Ann Oncol. 2009;20(9):1459-71.
12. Fung-Kee-Fung M, Provencher D, Rosen B, Hoskins P, Rambout L, Oliver T, et al. Intraperitoneal chemotherapy for patients with advanced ovarian cancer: A review of the evidence and standards for the delivery of care. Gynecol Oncol. 2007;105(3):747-56.
13. Jacobson JO, Polovich M, McNiff KK, LeFebvre KB, Cummings C, Galioto M, et al. American Society of Clinical Oncology/Oncology Nursing Society chemotherapy administration safety standards. Oncol Nurs Forum. 2009;36(6):651-8.
14. Johnston J, Armes S, Barringer E, Dickeson P, D'Onofrio L, Giff C, et al. Assessment and device selection for vascular access. Internet: Registered Nurses' Association of Ontario; 2008 [cited 2012 Jun 8]. Available from: http://rnao.ca/sites/rnao-ca/files/Assessment_and_Device_Selection_for_Vascular_Access.pdf.
15. Kearon C, Akl EA, Comerota AJ, Prandoni P, Bounameaux H, Goldhaber SZ, et al. Antithrombotic therapy for VTE disease: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. Chest. 2012;141(2 Suppl):e419S-94S. Epub 2012/02/15.

16. Mermel LA, Allon M, Bouza E, Craven DE, Flynn P, O'Grady NP, et al. Clinical practice guidelines for the diagnosis and management of intravascular catheter-related infection: 2009 Update by the Infectious Diseases Society of America. Clinical infectious diseases : an official publication of the Infectious Diseases Society of America. 2009;49(1):1-45. Epub 2009/06/06.
17. National Institute for Clinical Excellence. Prevention and control of healthcare-associated infections in primary and community care. Internet: National Institute for Clinical Excellence, 2012 Mar 2012. Report No.: 149.
18. New South Wales Government. EviQ, Cancer Treatments Online. Time out procedure checklist. 2010 [cited 2010 Sept 16]; Available from: https://www.eviq.org.au/Protocol/tabid/66/categoryid/217/id/6/Timeout+Procedure.aspx.
19. O'Grady NP, Alexander M, Burns LA, Dellinger EP, Garland J, Heard SO, et al. Guidelines for the prevention of intravascular catheter-related infections 2011 [cited 2012 Jun 7]. Available from: http://www.cdc.gov/hicpac/pdf/guidelines/bsi-guidelines-2011.pdf.
20. Registered Nurses' Association of Ontario. Care and maintenance to reduce vascular access complications. Toronto, Ontario, Canada: Registered Nurses' Association of Ontario; 2005 [cited 2012 Jun 12]. Available from: http://rnao.ca/sites/rnao-ca/files/Care_and_Maintenance_to_Reduce_Vascular_Access_Complications.pdf.
21. Wengstrom Y, Foubert J, Marguiles A, Roe H, Bugeia S. Extravasation guidelines 2007 [cited 2012 Jul 10]. Available from: http://www.cancernurse.eu/documents/EONSClinicalGuidelinesSection6-en.pdf.
22. The AGREE Collaboration. Development and validation of an international appraisal instrument for assessing the quality of clinical practice guidelines: the AGREE project. Qual Saf Health Care. 2003;12(1):18-23. Epub 2003 Feb 07.
23. The AGREE Research Trust. The Appraisal of Guidelines for Research & Evaluation (AGREE) instrument.: The AGREE Research Trust; 2001 [cited 2009 7/29/2009]; Available from: http://www.agreetrust.org/instrument.htm.
24. Centers for Disease Control and Prevention (CDC). Atlanta: CDC 24/7: Saving Lives. Protecting People.; [updated 2013 July 29; cited 2013 July 29]. Available from: http://www.cdc.gov/.
25. European Oncology Nursing Society. Extravasation guidelines: guidelines implementation toolkit. [Internet]. Bussels, Belgium: EONS; 2007 [cited 2012 May 8]. Available from: http://www.cancernurse.eu/documents/EONSClinicalGuidelinesSection6-en.pdf.
26. Oncology Nursing Society. Prevention and reporting of medication errors. Oncology Nursing Society. Oncol Nurs Forum. 2001;28(1):15-6.
27. National Institute for Clinical Excellence. Guidance on the use of ultrasound locating devices for placing central venous catheters. Internet: National Institute for Clinical Excellence, 2005 Contract No.: No. 49.
28. O'Grady NP, Alexander M, Burns LA, Dellinger EP, Garland J, Heard SO, et al. Guidelines for the prevention of intravascular catheter-related infections. Clin Infect Dis. 2011;52(9):e162-93.
29. Camp-Sorrell D. State of the science of oncology vascular access devices. Semin Oncol Nurs. 2010;26(2):80-7.
30. Agency for Healthcare Research and Quality. CUSP Toolkit. U.S. Department of Health and Human Services; 2012 [cited 2012 Dec 14]; Available from: http://www.ahrq.gov/cusptoolkit/index.html.
31. Wengstrom Y, Marguiles A. European Oncology Nursing Society extravasation guidelines. Stockholm: University of Stirling, 2008.
32. Leung M, Bland R, Baldassarre F, Green E, Kaizer L, Hertz S, et al. Safe administration of systemic cancer therapy. Part A: Safety during chemotherapy ordering, transcribing,

dispensing, and patient identification. Toronto (ON): Program in Evidence-Based Care; 2012 2012 Jul 9].
33. Easty AC, Fields A. Improving the safety of ambulatory intravenous chemotherapy in Canada 2011.
34. Institute for Safe Medication Practices Canada. Fluorouracil incident root cause analysis. Toronto, On, Canada: ISMP; 2007 [cited 2010 Nov 10]. Available from: http://www.cancerboard.ab.ca/NR/rdonlyres/2FB61BC4-70CA-4E58-BDE1-1E54797BA47D/0/FluorouracilIncidentMay2007.pdf.

Appendix 1. Members of the Safe Chemotherapy Administration Panel and declaration of conflict of interest.

Working Group Members	
Mova Leung Pharmacy Clinical Leader, Oncology Peel Regional Cancer Centre Credit Valley Hospital 2200 Eglinton Avenue W, Rm 2F-342 Mississauga, ON L5M 2N1 *Declared no conflict of interest.*	Rosemary Bland Clinical Manager Systemic Therapy Juravinski Regional Cancer Centre Level 2, Room 2-0854 699 Concession Street Hamilton, ON L8V 5C2 *Declared working at Innomar Strategies Inc since 2012.*
Fulvia Baldassarre Research Coordinator Program in Evidence-based Care Cancer Care Ontario McMaster University, Henderson Site G Wing, 2nd Floor, Rm 220 711 Concession Street, Hamilton, ON L8V 1C3 *Declared no conflict of interest.*	Esther Green Provincial Head Nursing and Psychosocial Oncology Cancer Care Ontario 620 University Avenue Toronto, ON M5G 2L7 *Declared no conflict of interest.*
Leonard Kaizer Medical Oncologist Credit Valley Hospital Peel Regional Cancer Centre 2200 Eglinton Avenue West Mississauga, Ontario L5M 2N1 *Declared no conflict of interest.*	Sherrie Hertz Program Manager, Systemic Treatment Program Cancer Care Ontario 620 University Avenue West Mississauga, Ontario L5M 2N1 *Declared no conflict of interest.*
Jill Craven Manager of Pharmacy Services LRCP London Regional Cancer Centre 790 Commissioners Road East London, ON N6A 4L6 *Declared no conflict of interest.*	Maureen Trudeau Medical Oncologist Odette Cancer Centre Sunnybrook Health Sciences Centre 2075 Bayview Avenue, Room T2 023 Toronto, ON M4N 3M5 *Declared no conflict of interest.*
Angela Boudreau Registered Nurse Sunnybrook Regional Cancer Centre 2075 Bayview Avenue Toronto, Ontario M4N 3M5 *Declared no conflict of interest.*	Matthew Cheung Hematologist, Internist Odette Cancer Centre Sunnybrook Health Sciences Centre 2075 Bayview Avenue, Room T2-031 Toronto, ON M4N 3M5 *Declared no conflict of interest.*
Simron Singh Medical Oncologist Odette Cancer Centre	Vishal Kukreti Hematologist, Oncologist Department of Hematology

Sunnybrook Health Sciences Centre 2075 Bayview Avenue, Room T2-047 Toronto, ON M4N 3M5 *Declared to have received ≥ $5,000 in a single year from Novartis*	Princess Margaret Hospital 5th Floor, 610 University Ave. Toronto, ON M5G 2M9 *Declared no conflict of interest.*
Ronjon Raha Peel Regional Cancer Centre 2200 Eglinton Avenue West Mississauga, ON L5M 2N1 *Declared no conflict of interest.*	
Members of the Expert Panel	
Rose Bortolussi Pharmacy Technician Odette Cancer Centre Toronto, ON *Declared no conflict of interest.*	Venetia Bourrier Oncology Pharmacist Cancer Care Manitoba Winnipeg, MB *Declared to be co-investigator on a study of IV chemotherapy and to have received funding from Cancer Agencies. Declared to be Director of Pharmacy Services and Provincial Oncology Drug Program for Cancercare Manitoba. Declared to have received grant funding from pharmaceutical companies.*
Flay Charbonneau Manager Pharmacy Sunnybrook Regional Cancer Centre Toronto, ON *Declared no conflict of interest.*	Daniela Gallo-Hershberg Pharmacist North York General Hospital Toronto, ON *Declared no conflict of interest.*
Susan Glick Patient representative *Declared no conflict of interest.*	Caroline Hamm Medical Oncologist Regional Cancer Centre Windsor, ON *Declared no conflict of interest.*
Karen Janes Advanced Practice Nurse BC Cancer Agency Vancouver, BC *Declared to be co-investigator for study (Improving the Safety of Ambulatory Intravenous Chemotherapy in Canada) funded by CPSI, CAPCA, ISMP and five provincial cancer agencies)2008-2010)*	Gregory Knight Medical Oncologist Grand River Regional Cancer Centre Kitchener, ON *Declared to have received travel and conference support >$5,000 to attend a meeting in 2012*
Kara Laing Director of Medical Oncology	Jill Petrella Quality Coordinator

Dr. H. Bliss Murphy Cancer Centre St. John's, NL *Declared no conflict of interest.*	Cancer Care Nova Scotia Halifax, NS *Declared no conflict of interest.*
Andrew Robinson Medical Oncologist Regional Cancer Program Sudbury, ON *Declared no conflict of interest.*	Susan Walisser Chief of Oncology Pharmacy BC Cancer Agency Vancouver, BC *Declared no conflict of interest.*

Appendix 2. Recommendations submitted for external review.

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:

4)Selection, use and management of vascular access devices, including potential complications, during the administration of systemic cancer treatment

5)Extravasation, phlebitis, flare, allergy and hypersensitivity complications of chemotherapy administration

6)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) 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 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
- Standards for all major processes involved in the prescribing, dispensing and administration of chemotherapy. For example: how chemotherapy is prescribed, the use of standardized chemotherapy protocols (with supporting references and documentation when there are protocol deviations), a process for order verification and independent double-checking, chemotherapy preparation and dispensing, pre-treatment assessment, catheter selection, maintenance and removal, 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:

C. Selection and management of peripheral and central venous access devices and intra-peritoneal catheters
D. 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 intra-peritoneal, intra-vesicular, intra-pleural, intra-ventricular 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 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. Patient factors 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 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. 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 • 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 carers' education and follow-up support • Health care workers' education

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-centered 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 failure mode and effects 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. 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

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

F. 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
G. 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
H. 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
I. 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
J. Factors that are conducive to allergic reactions	
Point of care 2: during catheter access and use	• Previous number of cycles • Drug specific • Previous history of reactions to same drug or drugs in the same chemical class
Point of care 3: Maintenance (device not in use)	• Patient education

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 1 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.

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 procedure, 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 1 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 1 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.

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

- For elastomeric pumps, improved 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 performing this check periodically
- 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 for several days beyond the administration of a cytotoxic drug

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 et al 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/NR/rdonlyres/4478D9DB-662B-43C2-8839-6D3C374D3FAE/54559/UpdateDec2011_30Nov2011.pdf

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

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

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 protocols for pre- and post- chemotherapy care available at: http://www.bccancer.bc.ca/NR/rdonlyres/8E898B5D-3F12-4623-8E32-5B3C429C58F7/56350/SCNAUSEA_Protocol_1Mar2012.pdf

RELATED GUIDELINES

PEBC EBS #16-1, Managing Central Venous Access Devices in Cancer Patients, 2006 (in review).

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.

DRAFT RECOMMENDATIONS were approved for external review January 3, 2014.