ASHP Guidelines on Preventing Medication Errors with Chemotherapy and Biotherapy

Purpose and Definitions

The purposes of these guidelines are to define best practices for the safe use of chemotherapy and biotherapy agents and to assist practitioners in improving their medication-use systems to prevent medication errors and patient harm from these agents. Although the guidelines are intended primarily to address use of chemotherapy and biotherapy agents in cancer treatment, some recommendations may be more broadly applicable across the medication-use system. These guidelines supplement ASHP's Guidelines on Preventing Medication Errors in Hospitals and address error prevention within diverse healthcare settings.[1] Further, these guidelines provide updated general guidance to include a standard definition of a "medication error" and applicable aspects of recommendations from the National Coordinating Council on Medication Error Reporting and Prevention (NCC MERP). NCC MERP's definition of a medication error is:

> any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of the healthcare provider, patient, or consumer. Such events may be related to professional practice, healthcare products, procedures, and systems, including prescribing; order communication; product labeling, packaging, and nomenclature; compounding; dispensing; distribution; administration; education; monitoring; and use.[2]

For the purposes of these guidelines, chemotherapy and biotherapy agents are defined as any medication that (1) is listed in section 10:00 of the American Hospital Formulary Service[3] (AHFS) pharmacologic–therapeutic classification system; (2) has at least one FDA-labeled indication to prevent or treat cancer, even if not listed in AHFS 10:00; or (3) is an investigational medication being used to prevent or treat cancer. This definition includes medications administered by any route. For simplicity, the term "chemotherapy" is used throughout these guidelines to refer to any chemotherapy or biotherapy medication that is used for cancer treatment.

The variety of therapies used in the treatment of cancer will only increase as advances are made, and healthcare organizations will confront the challenge of defining the products that require special procedures for safe use. Given the complexity of cancer care, it is recommended that such a list be as inclusive as possible. While these guidelines focus on the safe use of chemotherapy in treating cancer patients, in some situations chemotherapy agents may be used for nonmalignant diseases. In general, these additional safety procedures should apply for all uses of a chemotherapy agent, regardless of indication. Although they are specific to use of chemotherapy for cancer treatment, many of the principles of these guidelines also apply to cancer supportive care (e.g., treatment for pain and nausea). Finally, for organizations that conduct clinical research, investigational chemotherapy agents should be included in all safety systems established for FDA-approved chemotherapy agents.

These guidelines provide wide-ranging recommendations for preventing errors with chemotherapy agents in healthcare organizations, with an emphasis on hospitals, infusion centers, and ambulatory care clinics that offer direct pharmacy services. Nevertheless, it is strongly recommended that the guidance also be adopted by other settings, including physician office practices, home care, and patients self-administering oral and injectable therapies at home. Other guidance on the safe use of chemotherapy in the ambulatory setting has been published by the American Society of Clinical Oncology (ASCO) and the Oncology Nursing Society (ONS).[4] These recommendations cover known procedural, technical, and behavioral elements that could systematically reduce a healthcare organization's vulnerabilities to errors. Given use of an electronic medical record (EMR) increased from 3.8% of hospitals in 2007 to 8% in 2011, and computerized provider order entry (CPOE) use increased from 4% of hospitals in 2005 to 34% of hospitals in 2011,[5] additional information on the unique considerations of using CPOE for chemotherapy ordering has been included in these guidelines.

Strict adherence to good practice recommendations is not sufficient. Because the complexities of chemotherapy use afford unlimited opportunities for system failures, continuous diligence to verify accuracy is critical by all persons responsible for medication-use functions for chemotherapy. These guidelines focus on the medication-use responsibilities shared by and unique to specific professional healthcare disciplines, progressing from general to specific applications. The structure of the guidelines, by necessity, includes the repetition of some material, repeated and enhanced in specific sections and recommendations for different healthcare professionals. With the growth in use and number of oral chemotherapy agents on the market, a greater responsibility for care management is now placed on the patient. It is essential that applicable sections of these guidelines extend to patients so they can participate in protecting their own safety.

The guidelines contain the following major sections:

1. Recommendations for healthcare organizations,
2. Recommendations for multidisciplinary monitoring of medication use and verification,
3. Recommendations for prescribing systems and prescribers,
4. Recommendations for medication preparation and dispensing systems and roles for pharmacists,
5. Recommendations for medication administration systems and roles for nurses,
6. Recommendations for patient education,
7. Recommendations for manufacturers and regulatory agencies, and
8. Recommendations for identifying and managing medication errors.

Because of the complexity of and differences in practice settings and organizational arrangements, aspects of these

guidelines may be more applicable to some practice settings than others. Pharmacists, physicians, nurses, and other healthcare providers should use their professional judgment in assessing and adapting the guidance to their own settings. These guidelines focus on safe use of a specific type of high-risk medications at various stages of the medication-use process and should be augmented as appropriate by other clinical and practice guidance, including ASHP statements and guidelines.

Background

Although the rate of medication errors for chemotherapy administered in the inpatient setting is not well documented, estimates of the frequency of errors with adult and pediatric chemotherapy in the ambulatory setting have been published. In one study, the overall chemotherapy error rate was 8.1 errors per 100 clinic visits.[6] For adults, errors were associated with 7.1% of clinic visits, and errors were associated with 18.8% of pediatric clinic visits. Errors occurred across all phases of the medication-use system, but administration (56%) and ordering (36%) errors were most common. Another study found a substantially lower rate (3%) of errors in chemotherapy orders in the outpatient infusion center at a major cancer center.[7] The error rate with oral chemotherapy agents is less well studied, but serious medication errors can occur with these therapies across all phases of the medication-use system.[8,9] Taylor and colleagues[10] documented a 9.9% error rate with oral chemotherapy given to pediatric patients with acute lymphoblastic leukemia. In this study, the errors occurred at the prescribing and administration steps.

Regardless of the exact rate of medication errors for chemotherapy agents, the safe use of these therapies presents unique challenges that demand additional safety systems. Chemotherapy agents often have a narrow therapeutic index, and they are used in complex, multidrug regimens. Complex dose calculations and adjustments are required, such as dosing per body surface area (BSA) and frequent adjustment according to renal function, toxicity, and other clinical parameters. Chemotherapy agents can cause serious toxicities at FDA-approved dosages and with FDA-approved administration schedules. Advocates for safe medication use, including oncology pharmacy specialists, have recommended that healthcare organizations improve their medication-use systems specifically to prevent medication errors with chemotherapy.[11-14]

Chemotherapy-related medication-error prevention remains a priority. Increasingly, many chemotherapy agents are administered outside the inpatient or ambulatory care setting. A growing number of patients are self-administering oral chemotherapy agents at home.[15] Thus, error-prevention strategies should be applicable to the diverse settings in which chemotherapy agents are used.

Surveys have indicated a need for improvement in medication-use systems for chemotherapy agents. One survey of major United States cancer centers indicated that the safety systems routinely used for infused chemotherapy agents are rarely applied to oral chemotherapy agents.[16] Another survey replicated this finding and indicated that many other recommended safety practices for chemotherapy agents are not followed.[17]

Recommendations for Healthcare Organizations

Optimal and comprehensive patient care, especially for patients receiving chemotherapy, requires the participation of multiple healthcare disciplines. Systems are necessary to coordinate the functions throughout the medication-use process of prescribing, preparing, dispensing, and administering of chemotherapy, and for educating and counseling patients.

Healthcare organizations where multiple disciplines are represented should establish committees with representatives from each discipline to develop policies and procedures for the medication-use process and to oversee its operation. These policies and procedures should include educational and competency requirements for persons with medication-use responsibilities; general system requirements that minimize vulnerabilities to errors; and periodic auditing of physicians', pharmacists', and nurses' proficiency with the system. Further, near misses and errors involving both commercial and investigational chemotherapy agents should be analyzed in all settings, and problems in the procedures that place patients at risk should be resolved.

Education, Competency, and Credentialing. All practice settings should establish policies and procedures ensuring that healthcare providers who prescribe, prepare, dispense, and administer chemotherapy and monitor patients receiving those medications are competent to perform those functions. For pharmacists and nurses, specific education and experience or board certification in a practice specialty may be included in the institution's credentialing process.

Employers should evaluate prospective employees' training and previous practice experiences for knowledge and mastery of the skills that are essential prerequisites for working with chemotherapy. Prerequisites for preparing and administering chemotherapy should include discipline-appropriate training in how to safely handle chemotherapy agents to protect themselves, co-workers, and patients. Competency to appropriately educate patients and monitor adherence with prescribed therapy should be assessed. Deficiencies in applicants' training and experience must be identified and remedied before new employees assume patient-care responsibilities. Ongoing training for new and current employees should emphasize collaboration among healthcare providers to ensure optimal patient care, outcomes, and worker safety.

All healthcare providers who prescribe, prepare, dispense, and administer chemotherapy and monitor patients receiving those medications should be oriented in their practice setting before commencing patient-care responsibilities. Orientation should include an introduction of new employees to all the departments, service providers, and functions that affect patient care. Each provider's roles and responsibilities should be identified, and expectations should be clarified about how healthcare providers from different disciplines will communicate and work collaboratively with respect to the chemotherapy medication-use process.

Further, healthcare organizations should require that all personnel who prescribe, prepare, dispense, administer, and handle hazardous drugs or contaminated materials, and all persons who may be exposed to hazardous drugs or contaminated materials in the course of their duties, complete

job-appropriate training and evaluation. Employees should demonstrate competence, knowledge, and proficiency in techniques and procedures for safely handling (preventing exposure to oneself, other persons, and the environment, and managing accidental exposure) and disposing of hazardous drugs. Those competencies should be reassessed annually or more frequently if performance problems occur. It is the responsibility of medication-use system administrators and supervisory personnel to know the current government restrictions that limit or prohibit some healthcare providers from preparing and administering chemotherapy medications.

Healthcare providers who participate in the chemotherapy medication-use process and those who monitor patients receiving chemotherapy should be knowledgeable and have current information available about each of the following factors, relative to their scope of practice and job duties, on the chemotherapy used in their practice settings:

1. Names of chemotherapy drug formulations.
2. Indications and uses, and whether they comply with the FDA-approved labeling or approved compendia or are part of an investigational protocol.
3. Routes of administration.
4. Administration schedules.
5. Appropriate dosages, including dose adjustments for toxicity and, when applicable, constraints for the maximum dose of medication that can be safely given during a single administration, over a course of treatment, or cumulatively over a lifetime.
6. Appropriate storage conditions.
7. Potential adverse effects.
8. Potential drug interactions.
9. Procedures to use for handling hazardous substances.
10. Strategies for identifying and mitigating the risks of extravasation.

Every practice setting where cancer patients receive chemotherapy should provide opportunities for continuing professional and technical education related to chemotherapy management. A portion of the annual continuing education programs for healthcare providers specializing in oncology should be related to chemotherapy agents and their uses.

Providers who use drug-delivery devices (e.g., intravenous pumps and infusion controllers) to administer chemotherapy agents should be required to demonstrate competencies related to the clinical application, function (general use, operational limits, alarms), and care of these devices; problems that may occur with the devices; and troubleshooting.

Communication and Access to Information. Many errors occurring in the medication-use process are caused or aggravated by inadequate patient-specific information. Patients' medical records should be organized and made readily accessible for use by all providers who prescribe, dispense, and administer chemotherapy to enable independent confirmation that all prerequisite criteria have been met before commencing treatment. In some cases, individual disciplines may keep additional patient records that supplement the patient's primary medical record. For example, it has historically been the responsibility of pharmacists and pharmacies to maintain patient-specific medication profiles and records of medications that were prescribed and dispensed for each patient. Medication profiles for cancer patients should, at a minimum, include the following information:

1. Patient's name and a unique identifying code or number.
2. A brief medical history that identifies a patient's cancer diagnosis.
3. Known drug-related adverse events, allergies, and medication-, nutrient-, and food-related sensitivities.
4. Vital statistics that may affect treatment intensity, particularly those needed to calculate medication doses, including height, weight, BSA, age, sex, and pertinent laboratory values (e.g., serum creatinine, creatinine clearance, liver transaminases).
5. Data about all prescription, over-the-counter, and complementary and alternative medications used by a patient, including:
   - All relevant dates, including when the medication(s) were:
     - prescribed (if it differs from the date they were prepared and administered),
     - prepared and dispensed (if it differs from the date the medications were administered), and
     - administered (use planned date for patient self-administered agents);
   - Drug identity;
   - Drug dosage and reason(s) for any dose adjustments, as appropriate;
   - Total drug dosage administered per unit interval (e.g., day, week, treatment cycle);
   - Administration route;
   - Administration schedule as a function of the treatment plan (e.g., every 3 hours, days 1, 8, and 15, with the specific treatment dates);
   - Rate of administration (when relevant);
   - Prescribed duration of use (e.g., number of doses to administer; number of treatment hours, days, or weeks); and
   - The product manufacturer's identity, product lot numbers, and (when practicable) expiration dates for drugs dispensed from that facility.
6. Additional ingredients and diluting agents and the amounts used in extemporaneously compounded medications.
7. Primary references that describe the treatment regimen.
8. An up-to-date treatment history, including:
   - The treatment cycle or course number for each treatment repetition,
   - The dates on which a patient last received treatment,
   - How previous treatment was tolerated, and
   - The cumulative amount of drug previously administered for medications with established absolute cumulative dosage limits (e.g., anthracyclines, bleomycin) or constraints against repeated administration as a function of time.

Other settings, such as ambulatory, home, specialty, and managed care organizations are vulnerable to the same communication and interpretation errors that occur in hospitals. These settings and organizational arrangements, however,

could introduce additional opportunities for errors of omission and duplication when treatments and other services are provided at multiple locations and by more than one participating provider or group of providers. In hospitals and integrated health systems, patient-specific medical information has traditionally been communicated through a single comprehensive medical record. In contrast, providers in private practice, home care, and managed care organizations generally cannot rely on the availability of a comprehensive medical record, because medication prescribing, preparing, and administering may occur at geographically separate facilities.

Local policies should be developed to ensure that orders for a patient's chemotherapy medications are transmitted accurately and completely, that medication reconciliation takes place at all transitions in care, and that patient confidentiality is protected.[18] Electronic means of communication are recommended to transmit up-to-date, accurate, and comprehensive patient-specific medical information among providers. Thus, data entered into this electronic system by any one provider are immediately available to all. Until a single unifying network becomes available for all healthcare providers, portable printed and electronic records (including an accurate, updated patient medication list) that ensure patient safety and confidentiality must be devised.

Schedule Coordination. Because oncology patients often receive care from more than one healthcare provider, their primary provider, care coordinator, or patient navigator should coordinate patient care with other providers and facilities. Efficient organizational systems should have someone to coordinate a patient's healthcare needs with their various healthcare providers' schedules.

Standardize Medication Ordering. To the extent possible, medication prescribing, preparation, dispensing, and administration should be standardized. Healthcare organizations should adopt and incorporate national standards into their practice. Patient-care facilities should develop and use standardized preprinted medication-order forms or forms that are retrievable from a computerized database for requesting frequently used chemotherapy treatments and treatment-related services. Well-designed standardized, regimen-specific, medication-order forms decrease potential errors by organizing treatment information in a clear, consistent, and uniform format. As discussed further below, CPOE provides standardization opportunities and other potential benefits.

Standardized forms should be developed collaboratively with input from the healthcare providers who prescribe, prepare, and administer chemotherapy medications. Forms should be preprinted with the entire treatment plan and include items such as generic drug names, specifications for drug dosage and dosage modifications as a function of patient-specific variables, and administration routes and schedules. Forms should include the entire treatment plan, including oral medications that may be filled by an outside provider and patient self-administered. Prescription forms should also include space for prescribers to note laboratory test results that affect dosages, administration rates, and treatment duration. These forms may also permit prescribers to schedule laboratory tests and request other services for comprehensive patient care. A multidisciplinary process should be in place for the development, implementation and maintenance of these standard order forms, including independent double checks of the content. (An "independent double check" is a process in which two qualified individuals separately check, alone and apart from each other, an item or action, and then compare results to ensure the desired outcomes.[19]) These forms should include the revision date, as appropriate, to allow everyone involved to identify and validate that they are using the most current version.

Standardized medication-order forms, including prescriptions for oral therapies administered by patients, simplify and expedite medication ordering by requiring prescribers to supply only patient-specific information, such as

1. Patient's name and unique identifying number (e.g., medical record number) or date of birth according to institutional policies regarding patient identification.
2. Date and time the order was generated.
3. Time and date treatments are to be administered.
4. Cycle and day number.
5. Current patient-specific laboratory values (as defined by institutional policy regarding the timeframe for which laboratory test results are considered acceptable to use to determine whether chemotherapy can be initiated).
6. Patient-specific dosing parameters (i.e., height, weight, dosing weight, BSA).
7. Medication generic name.
8. Planned medication dosages and administration rates as a function of patient-specific factors and the calculated doses and rates to be administered.
9. Route of administration (including the venous access device type, if applicable).
10. Patient's allergies and medication and nutrient sensitivities.
11. Prescriber's name and signature.
12. Prescriber's telephone, pager, or fax number (or another means to communicate with the prescriber).

Preprinted forms should specify, by protocol number or publication reference, the treatment that is to be administered.[11,20,21]

For investigational chemotherapy treatments, standardized forms should also include the study name, protocol number, and patient-specific study number, as applicable. Color-coded forms, for example, may be used to designate different types of treatment, such as commercially marketed chemotherapy and investigational medications.

Standardized order forms eliminate many of the issues related to misinterpreting medication orders that are commonly associated with nonstandardized orders; however, healthcare providers must be aware that interpretation errors may still result from illegible handwriting. Multipurpose preprinted forms that list chemotherapy medications alphabetically may also contribute to prescribing errors when two similar drug names appear in close proximity. Since lined paper can obscure the details of a prescriber's orders, preprinted forms should be printed on unlined paper.

Self-replicating forms (e.g., carbon copies, no-carbon required paper) can produce copies that are difficult to read, and these forms should be avoided. Further, poor quality fax transmissions of these order sets should also be avoided. Providers who prepare and administer medications on the basis of a copy of a prescriber's order should be wary of ambiguous notations, artifact markings, and omissions on the

copy. Each facility should restrict chemotherapy ordering (e.g., access to medication-order forms) to providers with the appropriate clinical privileges. Healthcare organizations that depend on standardized forms should review all forms on a regularly defined schedule and must ensure that only the most current versions of standardized forms are available and that obsolete forms are recalled and destroyed.

CPOE. CPOE should be implemented to further enhance the safety of the chemotherapy-use process. CPOE offers an opportunity to introduce new safety features into the chemotherapy prescribing process, but implementation of CPOE for chemotherapy providers appears to lag other areas.[5,22,23]

CPOE provides many of the same safety and convenience features as preprinted orders, such as order legibility, standardization across practitioners, chemotherapy scheduling and sequencing, and inclusion of support care medications and some patient demographics. CPOE also provides additional benefits that are not available with a paper system. For example, the ability to control user access to various sections of the system can be very useful in managing prescriber privileges, especially to limit which staff may order chemotherapy or prescribe specific investigational drugs. CPOE improves efficiency by allowing data to be accessed by different providers in different locations at the same time, and it serves as a guide for the ordering provider via clinical decision support features and serves to structure workflow (i.e., specific steps in subsequent preparation, dispensing, and administration). CPOE provides benefits over a paper system, including additional safety checks not possible with paper, but diligence by the prescriber and careful independent checks of the resulting orders are still essential when using CPOE for chemotherapy.

CPOE for chemotherapy must be implemented with great care. CPOE represents a major change in an organization's chemotherapy use process and workflow, and it may introduce new errors that may not have existed in the traditional handwritten process.[24] In a well-established and mature chemotherapy-use system, one must be certain that the dramatic changes produced by CPOE do not threaten the safety of the chemotherapy-use process during the implementation period.

To gain the benefits of CPOE, there are several key principles of implementation and continued development that must be considered, such as standardization, reduction in ambiguity, safety over convenience, and an evaluation of workflow effects.[25,26] When feasible, formal process redesign methods should be applied before implementing CPOE for chemotherapy. Given the patient safety risks involved, a formal failure modes and effects analysis (FMEA) should be considered, as such an approach has been successfully used.[23,27] When reviewing the capabilities of a CPOE system, pertinent patient data must be available to all providers. These data include provider notes, laboratory values, flow sheets that show prior chemotherapy and medications administered, and consent forms, among others. Workflow should be considered when determining how data are displayed and in what order the data are presented. This workflow begins at the point the order is entered by the prescriber, followed by pharmacist review, nurse review, drug administration, and the documentation of the effect on the patient. The number and type of checks required to verify the order should be reviewed with consideration of the CPOE capabilities and workflow. Some institutional chemotherapy policies dictate a final review and approval (informally known as "OK to Give" or final sign-off) of the chemotherapy order by an attending physician or other senior clinician.

Clinical decision support is another important consideration for CPOE.[26] Clinical decision support can guide the prescriber through various phases of the ordering process and include specific chemotherapy considerations based on individual patient parameters, such as laboratory values, comorbid conditions, hydration requirements, and the need for supportive care medications (e.g., antiemetics). Appropriate alerts, such as allergies, drug interactions, duplicate therapies, and maximum doses, should be incorporated as appropriate and be consistent with the institution's overall plan for implementing clinical decision support alerts. The duration of the order set, a cycle or specific weeks of therapy, should be standardized, and clear criteria to treat or continue treatment must be documented for the patient to continue treatment.

Users should plan for improvements and alterations to the CPOE system after implementation. Changes should be considered by a multidisciplinary team and include provider feedback as well as data from continuous monitoring of the order entry process, including safety reporting and near-miss data. Continuous review and improvement are multidisciplinary processes and need to include both clinicians and information systems staff.[28]

Implementing CPOE for chemotherapy is an important step, and CPOE should be leveraged to provide guidance for prescribers ordering chemotherapy. By definition, the prescriber is entering orders directly into the system, and safety can be improved because there is usually no intermediary who must interpret the orders and enter them into another information system. Since CPOE clearly reflects and communicates the intent of the prescriber, properly planned CPOE should give prescribers the ability to select a specific regimen or protocol that delineates the necessary information to produce a clear and accurate drug regimen.[28] These custom ordering screens are typically called "order sets" or "templates," and they are essential to safely using CPOE for chemotherapy.[23]

Depending on the system and resources devoted to order sets, additional information (e.g., requirements for laboratory values, supportive care, dose reductions, or dose-limiting parameters) may be part of the order sets. Information such as dosing (e.g., mg/kg or mg/m^2, diluents, or concentration, if appropriate) should be part of the order set to facilitate dose verification by the pharmacist. The system may also be able to prevent ordering the wrong route of administration or append a warning message to specific orders, averting such potentially deadly mistakes as inadvertently prescribing vincristine intrathecally.

Transitioning complex order sets from paper to a CPOE system poses various challenges. Care must be taken in designing ordering templates, because an undetected design error may result in multiple mistakes. Prescribers and investigators (in the case of an investigational protocol ordering set) should be involved in the checking of the template, and ideally they should be asked to sign off on the particular ordering screens before they are put into wide use. The building of these orders sets is not a simple process, especially pediatric order sets and investigational drug regimens.[29]

Cancer chemotherapy often includes a complicated sequencing of drugs and scheduling of the regimen. Growth factors need to be scheduled at the proper time to be effective and not interfere with the mechanism of action of the chemotherapy or biotherapy regimen. Unfortunately, if there is a delay in the scheduled administration times, some systems may not allow a simple click or two to reschedule multiple days and doses, in contrast to older methods in which a prescriber could just write "delay chemotherapy by 6 hours."

If possible, the CPOE system and electronic health record should allow for an electronic check and documentation of the independent checks by the pharmacist, nurse, and any others involved in the chemotherapy use process. A notation in the system alerting the nurse or prescriber that the order is under review by the pharmacist is very helpful. Systems should allow senior physician final approval (i.e., "OK to give" or final sign-off) before action is taken by the pharmacy.

Careful thought is necessary and critical when using a CPOE system, and the potential for error still exists. Prior to order entry, the prescriber must consider whether a dose reduction is needed based on a change in laboratory values or organ function. If an investigational protocol is involved, the prescriber must select the correct cycle or dose level, if dose escalation is necessary. CPOE systems may be able to guide the prescriber, but they cannot make the correct choice for him or her. Another potential source of error is the auto-calculation feature of some systems. The system can utilize the latest height and weight to calculate BSA or use the patient's weight to calculate the proper dose. However, an incorrect height or weight entry can result in a dosing error. It is easy for prescribers to miss small but significant changes that could result from data entry errors. Systems may be able to prevent data entry error by displaying an alert when data differ from a previous entry by a certain percentage or final dose amount.

Emergency contingency plans for how to communicate chemotherapy orders in the event the CPOE is not available (e.g., power outage, system failure) should be developed and tested. Whenever possible, the contingency plan should replicate the CPOE process (e.g., paper orders replicating CPOE screens) as much as possible to minimize introduction of new risks. Training and awareness of the emergency contingency plan should be part of the orientation and annual competency plan for all providers.

Implementation of a CPOE system presents many new challenges for the health (or patient) care team. Although remotely entering orders in a CPOE system may be convenient for some, it may also reduce the face-to-face contact of writing in the chart during rounds or while on the patient-care unit, reducing the opportunity for personal interactions between healthcare professionals. While CPOE has been shown to prevent prescribing errors, it is not a panacea, and diligence and independent checks are still essential to a safe chemotherapy process using CPOE. Knowing some of its pitfalls in advance will aid in the design and use of all the features available in a CPOE system, especially for high-risk therapies such as chemotherapy. The success of CPOE depends on having high-level administrative, clinical, financial, and information technology support. It is critical front-line staff have a significant role in the development, implementation, and monitoring of CPOE.[28]

Verbal Orders for Chemotherapy Medications. Except for discontinuing treatment, medication-use systems should not permit healthcare providers to use or accept verbal orders to commence or modify a chemotherapy medication.[11,12,30] Verbal communication for chemotherapy orders, whether face-to-face or over the telephone, circumvent an essential checkpoint in the order-verification process, whether they are communicated directly to persons who prepare medications or received and reported by one or more intermediaries.[31]

Stat Orders for Chemotherapy Medications. It is rarely necessary to begin chemotherapy treatment as quickly as possible (i.e., "stat"). In general, stat orders for chemotherapy may compromise essential order-verification safeguards and are almost never appropriate. Except for urgently required treatments, chemotherapy medication preparation and administration should be scheduled when staffing is adequate to ensure that appropriate safety checks are performed during compounding, verification, and administration. It is essential that patient care is not compromised under any circumstances.

Standardize Dosage Calculation. Medication-use systems should establish whether drug dosages should be routinely calculated as a function of actual, ideal (lean), or adjusted body weight and develop standardized criteria that direct dosage calculation as a function of this weight. ASCO has produced guidelines for dosing chemotherapy in obese patients that suggest using actual body weight if the intent is cure.[32] Institutions should consider this information when deciding on dose calculation standards. Institutions should also define policies for other situations, such as in pediatric or hematopoietic stem cell transplant patients, where adjusted-weight dosing is used, or when cure is not the goal. Investigational protocols may specify treatment parameters different from institutional parameters. In all cases, the treatment plans and medication orders should indicate whether patients' actual or ideal body weight was used in calculating drug dosages and identify the equation from which dosages were calculated.

Methods should be standardized for calculating BSA and ideal body weight, rounding calculated results (e.g., drug dosages and administration rates), and changing dosages and administration rates in response to changes in patients' weight and stature. For dosage and administration rates calculated from pharmacokinetic data, the mathematical equations that describe how calculated values were derived should appear in the treatment plans and medication orders.

Standardize the Content of Medication Orders. Standards should be established for the content of an acceptable medication order, requirements for patient-specific measurements, and data that must be included on medication-order forms.[33,34] The following standards are recommended:

1. All orders for patient-care services should be clearly dated and timed.
2. When ordering chemotherapy medications, the generic drug name (as approved by the United States Adopted Names [USAN] program) should be used. Brand names are not acceptable unless they aid in identifying combination drug products or a particular

drug formulation (e.g., to distinguish between liposomal and nonliposomal product formulations).

3. The dosage form should be specified.
4. Orders for medications should include the patient-specific data from which drug doses are calculated (height, weight, BSA, laboratory test results). When drug dosages and schedules are modified for current or anticipated pathologies, treatment plans and medication orders should explicitly identify the factors on which treatment modifications are based. If the order is for chemotherapy as part of the clinical trial, identifying information for the protocol should be included in the order.
5. Drug dosages and calculated doses should be expressed in metric notation. The word units should never be abbreviated in medication orders where drug dosages and administration rates are expressed in biological activity units (e.g., aldesleukin, asparaginase, bleomycin). Leading zeros (e.g., 0.3 mg) should be used for numbers less than one. Trailing zeros should never be used.
6. Medication orders should specify the drug dosage and calculated dose according to the "container rule" (i.e., the specified and calculated dose is the amount prepared in and administered from a single container).[20]
7. Administration vehicle solutions and volumes should be specified, unless standard solutions and volumes have been established.
8. The administration route should be specified.
9. The administration rate should be specified, when relevant.
10. The administration schedule and the duration of treatment should be specified. Treatment plans and medication orders should specify the interval between repeated doses, the days on which each dose is to be given within a treatment cycle or course, and the total length of a treatment cycle or course.
11. The dates and times when drug administration is to commence, or the temporal sequence in which each medication is to be administered, should be specified. When 1200 is written as 12 a.m. or 12 p.m., it may be incorrectly interpreted. Directions indicating events for 1200 should be written as 12:00 noon or 12:00 midnight, or expressed in the 24-hour system.
12. The medical record should contain a justification for the chemotherapy treatment plan (e.g., a reference to FDA product labeling, the primary literature, institutionally approved guidelines, national consensus guidelines, or an investigational protocol); similar information may be included in the medication order to provide additional clarification.
13. Although healthcare providers have traditionally used abbreviations, acronyms, and nicknames to describe chemotherapy medications and treatment regimens, the practice is potentially dangerous and should be avoided. Abbreviations for drug names, scheduling information, and directions for medication use should be prohibited in medication orders. Nonstandard abbreviations, Latin abbreviations, and apothecaries' weights and measures should not be used in orders for chemotherapy medications. Whenever possible, measurement units should be expressed in metric notation.

Therefore, a medication order that complies with these recommendations would appear as follows for a patient with a BSA of 2 m^2: Methotrexate injection 100 mg/m^2/dose = 200 mg in 100 mL 5% dextrose injection/dose, administer by continuous intravenous infusion over 24 hours, every 48 hours for three doses days 1, 3, and 5. Start at 0800 on April 1, 2014.

Establish Dosage Limits and Acceptable Routes of Administration. Medication-use systems should include utilization limits for chemotherapy medications. Constraints should be developed to limit maximum chemotherapy drug dosages and administration routes and schedules. Multidisciplinary peer review should be completed before established drug administration limits are exceeded.[11,12] These constraints should include the maximum amount of a chemotherapy drug that may be administered as a single dose, the maximum amount that may be administered during a defined time interval (including maximum administration rates for parenterally administered medications and maximum dose per day for oral therapy), and the routes by which each drug should be administered.[35] For example, some institutions cap the dose of vincristine at 2 mg or limit the lifetime dose of doxorubicin to 550 mg/m^2 in patients with normal cardiac function.

Constraints for dosage and administration rate may be defined by treatment regimens and protocols and may vary among protocols. In contrast, the types of treatments administered in some practice settings may be consistently similar, permitting the establishment of absolute maximum dose limits within that practice setting.

Limits should also be established for the maximum amount of a chemotherapy drug that may be administered during one treatment course or cycle and, when appropriate, the maximum amount of drug that may be administered to a single patient within his or her lifetime.[11] In addition, dosage limits should be established for chemotherapy medications used in specific combination regimens (defined for each drug) in which clinical toxicities may be exacerbated by combining agents with overlapping adverse-effect profiles.

Chemotherapy drug-use limits should appear prominently in printed treatment descriptions (e.g., protocol summaries, care maps, schematic treatment diagrams) and on printed medication-order forms and computer-based medication-order templates. Active clinical decision support that alerts healthcare providers whenever an order for chemotherapy medications exceeds defined limits would be ideal.[36] For patients who receive chemotherapy medications for which cumulative dosage limits have been established, cumulative dosage data should be constantly updated in their permanent medical records and in any supplementary records. Patients' cumulative dosage data should be audited and independently confirmed by healthcare providers when verifying orders for chemotherapy medications.[11,37]

In each healthcare organization, the medication-use system should include a multidisciplinary committee that oversees matters related to medication-use limits. The committee should proactively develop and establish policies and procedures for resolving disagreements related to patient treatment among providers; whether medications should be prepared, dispensed, and administered if a discrepancy cannot be resolved; and how medication-use-related disputes are to be resolved. Committee membership should comprise

all providers who have responsibilities in the medication-use process in the organization.[11]

Investigational Chemotherapy Medications. Cancer patients often receive investigational (i.e., experimental) anticancer treatments at facilities participating in clinical trials. Consideration must be given to ensure that the same safety precautions and checks that are used for FDA-approved chemotherapy therapies apply similarly to prescribing, preparing, dispensing, and administering oral and parenteral investigational medications and monitoring patients who receive those therapies.

Facility administrators should ensure that adequate staff is maintained to support an investigational drug program.[31] Ideally, nurses and pharmacists should be involved early in the process of developing clinical protocols involving the use of commercially marketed and investigational chemotherapy medications.[38] Early involvement helps ensure that chemotherapy regimens are expressed in a fashion to mitigate errors, and investigational medications are prepared and administered in accordance with local policies and procedures. Nurses and pharmacists should be voting members on regulatory and review committees that evaluate the scientific and ethical treatment of patients receiving chemotherapy medications and monitor investigational therapies (e.g., institutional review boards).[11]

Because a protocol governs and supplies the rules for drug use in clinical trials, an up-to-date copy of the study protocol should be available for review at all sites where medications are prepared and administered. All staff should be informed through inservice education programs before new protocols are implemented. Inservice programs and study-related information should be provided by persons associated with the investigational study (e.g., principal investigator, associate investigators, protocol chairperson, study-coordinating personnel). If an investigational protocol is to be conducted at more than one site within a health system, procedures should be developed to ensure that up-to-date information is available at all study sites where patients receive protocol-directed care.

Procedures for supplying healthcare providers with information about patients' dose assignments, drug dosage, and schedule modifications should also be devised. A separate procedure should be established allowing independent dose-checking activity among all disciplines involved in the medication-use process for investigational drugs.

Intrathecal Administration. Administration of chemotherapy via the intrathecal route is necessary for certain treatment regimens. Given the high risk associated with intrathecal administration (e.g., vincristine intrathecal administration is fatal), specific considerations apply to intrathecal administration of chemotherapy:

1. Prescribing should be limited to providers with institutional privileges to prescribe chemotherapy.
2. Drug labels should clearly indicate that the chemotherapy is only intended for intrathecal administration, including ancillary labels. Vinca alkaloid drugs must contain label warnings to avoid intrathecal administration.
3. Medications that will be administered intrathecally should be placed in separate bags from medications administered by other routes (e.g., intravenous, subcutaneous, intramuscular) in the pharmacy. Upon delivery to the unit, intrathecal medications should be stored separately from medications with other routes of administration.
4. Providers administering intrathecal chemotherapy should do so in a setting that has been designated for that procedure. An independent double check by two qualified individuals should be completed prior to administration.

Recommendations for Multidisciplinary Monitoring of Medication Use and Verification

Independent medication-order verification is an essential safeguard that ensures the accuracy and appropriateness of medical treatment. It is imperative that healthcare providers resolve any questions related to medication orders before treatment commences. Providers should recognize that medication-order verification and other system safeguards ensure patients' safety.[11,20,37] Lack of information about patients and their medications has been described as the most frequent cause of medication errors.[24,39] In order to independently verify prescribers' orders for medications, all persons who prepare and administer chemotherapy medications and those who monitor patients who have received chemotherapies should also have access to complete, up-to-date copies of treatment protocols and patient-specific data, including home medication lists.[11,30,37] Drug information and reference materials should be readily available to all persons who provide patient care.

Each healthcare provider has a responsibility to share information with other providers and consultants to ensure patient safety and an optimal treatment outcome. Policies that regulate treatment verification standards should describe how prescribers, medically responsible and senior authorizing physicians, pharmacists and pharmacy technicians, nurses, and other persons who are responsible for transcribing and transmitting medication orders should interact and communicate information.

Providers who prescribe, prepare, dispense, and administer chemotherapy medications should perform independent double checks at defined points in the chemotherapy use process. Treatment-verification systems may incorporate computerized medication-order safety checks but should also include independent manual double checks.[11,31] Ideally, computerized systems (e.g., CPOE) are used to calculate and verify dosages and the rate and route of administration for chemotherapy drug orders and to screen medication orders for compliance with dosage limits. In addition to facilitating chemotherapy-order processing, computer software can also serve as a double check on prescribers' orders. Systems requiring pharmacists to transcribe prescribers' medication orders into a computerized or manual drug-ordering system should have a second person, preferably a pharmacist, recheck all order-processing documents and product labeling before a drug product is dispensed. In situations in which a pharmacist is not available, a prescriber or nurse may serve as the second check.

Providing medications to patients includes five discrete steps: prescribing, preparation, dispensing, adminis-

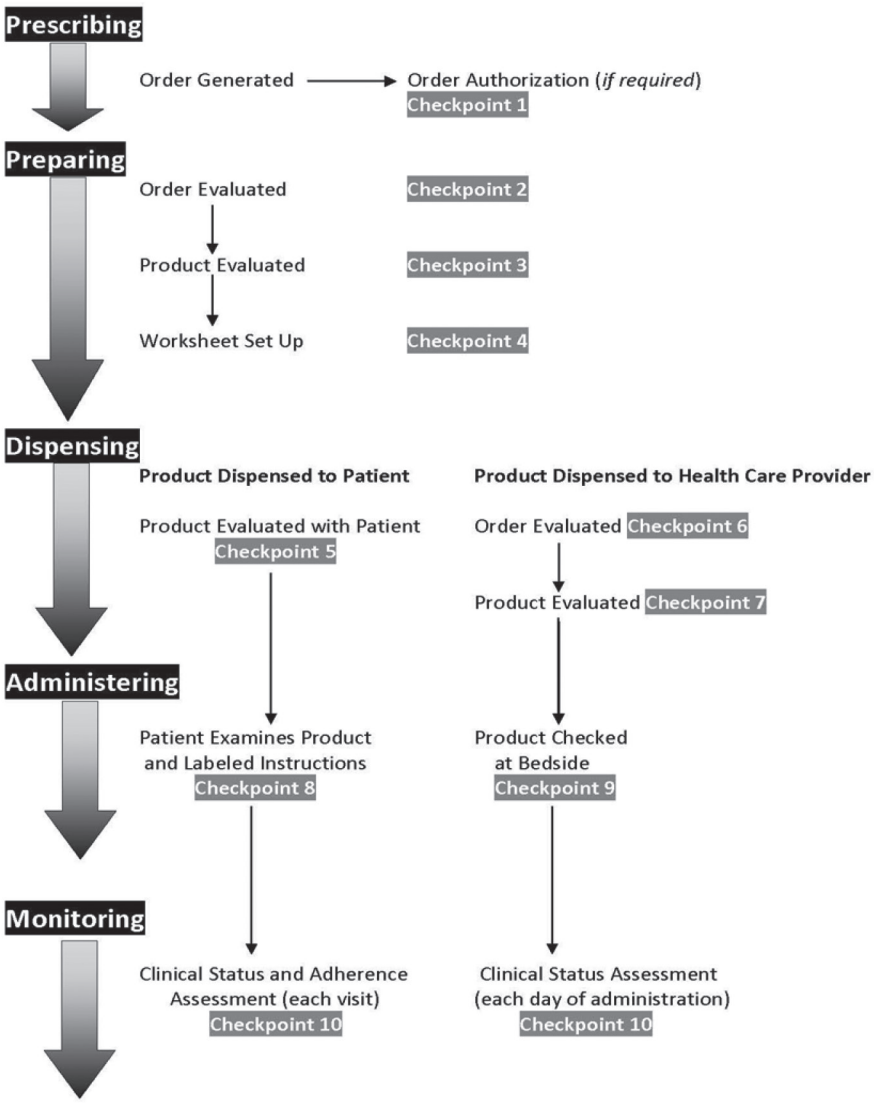
tration, and monitoring. The ideal verification system has ten established checkpoints to ensure that an chemotherapy drug is accurately prescribed, prepared, dispensed, and administered to the patient for whom it was intended (Figure 1). Different individuals should complete each check so that no single person bears responsibility for checking his or her own work.

Prescribing Chemotherapy Medications (Checkpoint 1). Healthcare providers who prescribe, prepare, and administer chemotherapy drugs should be familiar with the entire treatment regimen. A prescriber should order all the medications necessary for the entire treatment regimen, including hydration and supportive care orders, at the same time and prior to administration of any of the medications. When prescribing chemotherapy regimens based on a patient's weight (or BSA, which relies on weight), weight data and trends in patient weight should be evaluated to be sure the correct information is used. In CPOE, order sets may assist in completing all relevant orders of a treatment regimen at the same time. Requiring all treatment details in advance ensures that orders can be checked for completeness and accuracy and compliance with planned treatment.

Institutions should establish policies regarding whether chemotherapy may be prescribed by physicians-in-training (e.g., medical fellows) and nonphysician healthcare providers with prescribing privileges (e.g., nurse practitioners, physician assistants). If the institution allows prescriptions by these individuals, these orders should be verified by at least one medically responsible person, other than the prescriber, who is knowledgeable about medical oncology.

When orders for chemotherapy drugs must be countersigned by a second medically responsible individual, the person who countersigns the medication orders should critically evaluate each order for a chemotherapy treatment. This is checkpoint 1. The orders should be compared with patient-specific data and verified against original reference sources that describe the treatment regimen (e.g., a published article,

Figure 1. Medication-order verification system. These established checkpoints ensure a chemotherapy medication is accurately prescribed, prepared, dispensed, administered, and monitored.



validated standard reference text, investigational protocol). If the patient is taking part in an investigational study, verification of enrollment onto the trial and of informed consent should be reviewed.

Preparing Chemotherapy Medications (Checkpoints 2–4). Checkpoint 2 requires persons receiving a prescriber's order for chemotherapy medications to review the original medication orders and independently verify them against published standards (e.g., product package labeling, reports published in professional journals, treatment protocols, standard reference textbooks) and determine appropriateness based on patient-specific information. The dose per container and the total course dose should be verified at this checkpoint.

Because erroneous information sometimes appears in published information, orders for noninvestigational chemotherapy medications should be verified against the primary reference in which the specific treatment was described (e.g., published reports, study protocols, meeting proceedings). If a primary reference is not available, the treatment regimen should be confirmed with a resource that previously had been validated as accurately describing the planned treatment (locally compiled handbooks, guides, and compendia) or at least two alternative publications, including reviews and reference textbooks.[11,34] Investigational drug doses and administration schedules must be verified against a study protocol that was approved by all relevant regulatory agencies and study sponsors (e.g., institutional review board, National Cancer Institute, FDA). Protocol amendments should be distributed immediately and be readily available for reference. In addition, order templates should be updated as soon as possible, especially for drug dose or preparation changes.

Although preprinted order forms and CPOE preclude the necessity of repeatedly verifying drug names, dosages, routes, and schedules, all medication orders should be evaluated for completeness, compliance with the planned regimen, and, during repeated courses, deviations from previous treatments by following these recommendations:

1. The date a patient was last treated and the next planned treatment date should be compared to ensure that an appropriate interval has elapsed since treatment was last administered.
2. Measurements from which a patient's medication dosage and administration rate are calculated should be confirmed (e.g., height, weight, BSA). Institutions should develop policies and procedures regarding when patient-specific data (e.g., height, weight, BSA) should be re-measured. It is important to review trends in height and weight as a double check to ensure there were no errors in documentation.
3. Appropriate laboratory test and physical assessment values should be evaluated and primary treatment references should be consulted to determine whether they are within acceptable ranges or if treatment modifications are indicated.
4. A patient's allergy, drug sensitivity, and adverse drug effect histories and his or her current medication profile should be evaluated for potential drug interactions with planned chemotherapy treatment.

For patients who receive treatment in clinical trials in which more than one primary or ancillary treatments are prescribed (e.g., dose- and duration-escalating studies), treatment assignment and dosage and administration schedule modifications should be confirmed with at least one person directly associated with the clinical trial, other than the prescriber (e.g., the principal investigator, an associate investigator, research nurses or pharmacists, a study coordinator or chairperson). The prescriber should be consulted when expected treatment modifications were not ordered or when nonstandard modifications were prescribed.

Instructions for diluents, drug administration sequence and duration, number of doses, and starting date and time should be checked. To ensure that appropriate ancillary and supportive medications that facilitate chemotherapy drug delivery and those required by protocol have been prescribed and are complete and accurate (e.g., premedications, hydration, cytoprotectant and "rescue" medications, antiemetics, hematopoietic growth factors), their orders should be reviewed and confirmed. Discrepancies between prescribed medications and planned treatment should be brought to the prescriber's attention and resolved before medication preparation proceeds.

At checkpoint 3, after treatment orders have been verified, all work related to medication-order processing and preparation accuracy should be routinely documented in a standardized format, either on paper or electronically. Drug preparation work sheets (sometimes referred to as work cards or admixture or compounding logs, sheets, and cards) identify the drug products prepared for each patient and the persons who prepared and checked the medications. Although layout and design may vary among work sheets, and data may be organized as a continuous log in which each drug product appears on separate, consecutive lines or as a separate record for each patient, all work sheets should detail the techniques used in preparing the drug products. They should also identify special preparation and dispensing information, such as the indication of special product containers, requirements for filtration, the need for special diluents, intermediate dilution steps, and how and when administration sets should be attached to the drug product container. Order processing, drug preparation, and processing records should be confirmed by a second individual (preferably a pharmacist).[11,12] The calculations written on preparation work sheets should be independently verified by a second healthcare provider who did not prepare the work sheet. Independent verification should include checking the work sheet for completeness and accuracy of content, with particular attention given to special preparation instructions. A checklist, whether paper or electronic, that identifies the necessary elements in chemotherapy drug preparation may be a helpful reference (Figure 2).[11] Technology can serve as a surrogate checklist, if practitioners follow procedures in using appropriately developed and applied software.

At checkpoint 4, drug products should be checked, after preparation, against both the preparation work sheet and the original order by an individual who was not involved in preparing the work sheet. Checklists may also be helpful for this step.[11]

Dispensing Chemotherapy Medications (Checkpoint 5). Checkpoint 5 requires persons dispensing medications to patients or caregivers for outpatient use to verify a patient's

Figure 2. Chemotherapy drug preparation checklists.

Checklist for Initial Setup of Chemotherapy Drug Work Card

This form should be completed on paper or electronically by the pharmacist checking the work card. Place check mark (or N/A) in each space after each check is completed. Your check marks and initials at the bottom of this work sheet are your personal assurance that you checked all these items for accuracy in the setup and transcription of information onto the work card. Each drug requires a separate checklist.

Patient _____ Drug _____

Start date _____

Administration time _____

Stop date _____

Duration _____

Correct drug name _____

Number of doses _____

Dose _____

Drug concentration _____

Drug volume _____

Diluent _____

Volume of diluent _____Overfill _____Drug in overfill ____

Expiration time _____

Special delivery devices (tubing, cassette, container, etc.)

Correct route of administration _____

Correct line type, as appropriate _____

Correct mixing instructions (special directions, e.g., "Do Not Filter") _____

Auxiliary label information (e.g., "Do Not Refrigerate," "Use In-line Filter," "For Intrathecal Use Only") _____

Correct total volume _____

Pharmacist's initials _____ Date _____

This record should remain with the work card for the duration of the order and be saved for the supervisor for review after discontinuation of the order.

Supervisor's initials _____ Date _____

Continued on next page

identity when a medication is dispensed. Patients who self-administer their medications or personal caregivers should visually examine the medication, confirm whether its appearance meets their expectations, and compare its instructions with information they received from their healthcare providers (e.g., a chemotherapy calendar).

Dispensing and Administering Chemotherapy Medications (Checkpoints 6–9). At checkpoint 6, before starting treatment, each chemotherapy medication should be checked independently against the prescriber's orders by at least two individuals who are trained and competent to administer chemotherapy medications. All dosage- and administration-rate-related calculations should be independently verified. This includes any infusion pump rate settings, which should be checked at the initiation of each container of the infusion, periodically throughout the infusion, and whenever a new nurse assumes care for the patient. Healthcare providers should routinely confirm that the medication will be administered to the intended patient by comparing a patient's name and unique identifying code or number with medication labels (e.g., alpha–numeric characters or bar codes) and that a drug product's identity, ancillary components (e.g., additional medications, diluent, and vehicle solutions), route of administration, and schedule are correct.

At checkpoint 7, healthcare providers should examine the medication container and note whether the content's general appearance is what was expected. Many parenteral chemotherapy products have distinctive colors, and product coloration should be confirmed before administration.

At checkpoint 8, patients who self-administer their medications (or receive it from personal caregivers) should carefully read the container's label to confirm the product's identity and review its instructions for use (schedule of dosing, whether to take with or without food) each time they take a medication.

At checkpoint 9, patients should be encouraged to ask questions about their treatment before its administration and compare its appearance and medication label with information they received about the treatment. Patient identification using two identifiers should occur prior to chemotherapy administration. Whenever possible, barcode-driven administration should be used.[40]

In ambulatory care practice, it is common for patients to receive parenteral chemotherapy medications in a setting where a physician and a nurse (or other healthcare profes-

Figure 2 (*continued*)

Checklist for Preparing and Labeling Chemotherapy Drugs

For each order you check, verify that each element is correct with a check mark.

Patient _____ Drug _____

Date _____

Label check

Patient name is same as on front of work card _____

Drug name on label matches drug name written on back of work card _____

Dose on label matches dose written on back of work card_____

Diluent on label matches diluent written on back of work card _____

Volume of diluent on label matches volume of diluent on back of work card _____

Correct date to prepare _____

Expiration date and time _____

Correct time (expiration date not greater than administration time) _____

For each drug/additive

Correct drug used _____Proper protocol supply ____

Drug concentration in each vial _____

Additives, such as sodium bicarbonate solution, for which large stock bottles are used (which remain in hood) are visually checked, lot number is verified, and technician is asked to verify volume used _____

Drug volume for dose verified _____

Drug lot number on each vial matches lot number written on work card _____

Calculations are checked _____

Drug has not expired _____

For each diluent

Correct diluent _____Volume of diluent _____

Diluent has not expired _____

Special instructions followed

Air purged from bag ____

Tubing affixed/primed to end of line _____

Diluent for reconstitution _____

Correct container _____Proper overfill ___Drug in overfill ___

Final miscellaneous steps

Chemotherapy work card checklist is in card pocket _____

Solution is inspected for impurities/floaters_____

Label is initialed (on left-hand side of label just below last additive or drug) **after** being affixed to correct admixture _____

Total volume to be infused _____ Red chemo i.v. seal _____

"Caution chemo" label ____ Other auxiliary labeling ____

Zip-lock bag _____

Work card is initialed _____

Pharmacist's initials _____ Date _____

Supervisor's initials _____ Date _____

sional) complete all tasks related to prescribing, preparing, administering, and monitoring treatment without a pharmacist's participation. Under these circumstances, the healthcare providers involved should perform independent double checks and be involved in the entire process. The person preparing chemotherapy medications should work from written orders.

Monitoring (Checkpoint 10). Chemotherapy agents are usually expected to produce adverse events, so it is sometimes difficult to detect possible medication errors resulting from failure at one of the prior checkpoints. However, a vigilant healthcare team might discover a potential error sooner if they are knowledgeable about the expected adverse effects and are vigilant for either exaggerated or unexpected adverse effects.

For all chemotherapy agents administered at a healthcare institution, the patient's clinical status should be assessed on each day of chemotherapy administration. Vital signs should be taken and a standardized assessment for possible toxicities should be performed.

For oral chemotherapy agents, assurance that patients understand how to take their chemotherapy medicine should be assessed initially and then at each patient encounter. An assessment for adherence should be performed at each clinic visit. Patients should be taught how to recognize and report expected and unexpected toxicities.

Recommendations for Prescribing Systems and Prescribers

Chemotherapy prescribing is complicated by numerous medical publications that report indications, dosages, and administration schedules inconsistent with FDA-approved product labeling. Chemotherapy treatments frequently involve off-label uses based on preliminary reports, promising information from abstracts, and compendia information. Prescribers must exercise great care in correctly interpreting this information and clearly communicating orders for chemotherapy medications with other healthcare providers.

Health-system administrators should require orders for all chemotherapy medications and other high-risk drugs prescribed by physicians-in-training or nonphysician prescribers to be countersigned by a senior physician with expertise in the specialty to safeguard against errors in interpretation and prescribing. Healthcare providers seeking privileges for prescribing chemotherapy drugs should complete an orientation to local policies and procedures related to prescribing chemotherapy before they are permitted to order them for patient care.

Healthcare providers should locally develop standardized dosage and administration schedule modifications for each chemotherapy medication. Treatment modifications may be appropriate for patients with the following characteristics: (1) preexisting pathologies that predispose a patient to adverse effects from treatment with particular chemotherapies (e.g., withholding or decreasing bleomycin dosages in patients with preexisting pulmonary dysfunction or cardiotoxic agents in patients with congestive heart failure); (2) a history of severe, prolonged, or cumulative adverse effects after previous chemotherapy treatments; (3) impaired physiological function that predisposes patients to altered pharmacodynamic responses (e.g., renal or hepatic impairment); (4) low or decreased performance status; and (5) patients on multiple medications with a potential for a drug interaction with a particular chemotherapy.

Healthcare providers should also establish for their institutions standardized guidelines for prescribing drugs that are routinely administered concomitantly with chemotherapy medications. Medication-use guidelines for supportive care and ancillary agents (e.g., antiemetics, hydration, chemoprotectants) should be made accessible to all healthcare providers who prescribe, prepare, and administer chemotherapy drugs and for persons who perform clinical monitoring.

When generating medication orders in a setting where preprinted ordering forms, CPOE, and other electronic and mechanical means (e.g., e-prescribing) are not available, prescribers should legibly print the names of medications, dosages, routes of administration, and administration schedules in plain block letters and Arabic numerals. Medication orders should include the indications for which they are prescribed (e.g., for sore mouth, for nausea, for chronic lymphocytic leukemia).

When chemotherapy treatment (ordering, preparing, and administering) is coordinated at a single location, it is the prescriber's responsibility (or in the conduct of clinical trials, it is the principal investigator's responsibility) to provide information about the treatment (e.g., protocols, publication reprints) to those who prepare and administer medications and monitor patient outcomes. It remains the prescriber's responsibility to answer questions and provide information to other healthcare providers when treatment is implemented in a place that is geographically separate from the prescriber's location. Prescribers, clinical investigators, and medically responsible staff should provide to healthcare providers who prepare and administer chemotherapy medications a complete printed (or electronically reproduced) copy of the treatment regimen.

General Guidelines for Prescribing Chemotherapy Medications.[11,13,20,41] The following are general guidelines for prescribing chemotherapy drugs:

1. Instructions for medication regimens should be explicit, complete, clear, and easy to follow. Treatment regimens should be described accurately and consistently in all written, published, or circulated materials in which chemotherapy medication use is described.
2. The patient's medical record should contain a justification for the chemotherapy treatment plan (e.g., FDA product labeling, a primary literature reference, institutionally approved guidelines, national consensus guidelines, or an investigational protocol).
3. Medication-use systems should require healthcare providers to use standardized vocabulary and nomenclature for describing treatment with chemotherapy medications. "Tall Man" lettering should be used for written and electronic orders.
4. Prescribers should use uniform and consistent notations to express quantifiable amounts (dosage, concentration, volume, and time).
5. Prescribers should never trail a whole number with a decimal point followed by a zero (e.g., write "5 mg," not "5.0 mg").
6. When writing amounts less than one, the expression should be written with a leading zero preceding the decimal point (e.g., "0.125 mg").
7. All treatment plans and medication orders should identify the dosage (as a function of body weight, BSA, or other dosing factors) and the calculated dose. Total course dose should be included in circumstances in which a single infusion container is designed to provide multiple days of treatment (e.g. 7-day cladridine infusion).
8. When treatment day enumeration is arbitrary, day 1 typically describes the day treatment commences. In contrast, hematopoietic progenitor-cell transplantation regimens often include day 0, and significant treatment-related events before and after a progenitor-cell graft is administered are distinguished by negative (minus) and positive (plus) prefixes, respectively.
9. All medications that are a part of the treatment regimen (e.g., oral chemotherapies) should be included, indicating where the product will be filled or dispensed.

10. Recommendations for proper medication storage should also be included. Cancer patients must often travel long distances to receive care, so guidance and support (provision of coolers and ice packets for refrigerated medications) to properly store medications when in transit as well as at home.

In some cases, CPOE can be used to promote best practices (e.g., eliminating the use of trailing and leading zeros [items 4 and 5 above]).

Specific Recommendations for Parenterally Administered Medications.[20] Healthcare providers should adhere to the following guidelines for parenteral chemotherapy drugs:

1. In treatment plans and orders, doses should be expressed as the total amount of medication to be administered from a single container (i.e., the total amount of medication per syringe, bag, or other container).
2. For medication admixtures that can be prepared in more than one way, practitioners should institute *a priori*, standard, and consistent methods directing how each medication will be prepared and administered.
3. When a medication with extended stability is administered from a single container for more than 24 hours, a prescriber's order for treatment should specify the amount of medication to be administered during each 24-hour interval.[20] For example, a medication order for a patient with a BSA of 2 m^2 should read: Drug XYZ (8 mg/m^2/day × 3 days) 48 mg in 150 mL 0.9% sodium chloride injection by continuous intravenous infusion over 72 hours. Start on 04/01/2001 at 0800 (total dose/cycle = 48 mg).

Specific Recommendations for Orally Administered Chemotherapy Medications.[20,42] Prescribing orally administered chemotherapy agents presents unique challenges for healthcare providers due to the greater responsibility placed upon patients to manage their own care and patients' perception that these agents may be less dangerous than parentally administered agents. Healthcare providers should adhere to the following recommendations when oral medications are the prescribed chemotherapy treatment or when oral chemotherapy is included as part of the treatment regimen:

1. In treatment plans and medication orders, drug doses and schedules should be described as the amount of medication to be taken per dose, not as a total daily dose that is to be taken in divided doses.
2. In treatment plans, medication orders, and instructions to a patient, the number of doses to be administered or taken should be clearly identified.
3. Doses for solid orally administered dosage forms should specify whether and how doses are to be rounded to the nearest capsule or tablet strength. If the calculated dose can't be provided based on the available dosage forms, the following alternatives can be considered:
   a. whether tablet formulations should be broken (if not a hazardous drug);
   b. whether an alternative dosage method or formulation is appropriate; or
   c. whether alternate day dosing is appropriate based on the pharmacokinetic and pharmacodynamic properties of the medication. The goal of alternate day dosing is to fulfill the total weekly dose rather than giving the exact daily dose (e.g., if an agent is to be given 175 mg daily for 2 weeks, but the drug is only available in 50 mg capsules, consider alternate day dosing by giving 200 mg on one day and 150 mg on the next day). If alternate day dosing is used, then instructions that say "take X tablets on odd days and X tablets on even days" should be avoided, as two consecutive odd days may occur when transitioning from one month to another. For example: January 31 and February 1.
4. Only the quantity needed to cover the administration period until the next clinical evaluation should be ordered.
5. If appropriate, instructions should address how medications are to be taken with respect to food ingestion and indicate whether particular types of food may affect medication activity.
6. Oral chemotherapy medication orders should be included with parenteral chemotherapy orders to allow for appropriate screening and safety checks.
7. Oral chemotherapy medication orders should be included on the patient's home medication list to allow for appropriate screening and safety checks.
8. Oral chemotherapy medication orders should be communicated to the pharmacist for appropriate screening and safety checks.
9. Patient instructions should address what to do if a dose is missed.
10. Patients should be provided with explicit instructions regarding what adverse effects to expect, which ones require a telephone call to a provider, and who and where to call.
11. Instructions should describe safe handling, storage, and disposal of oral chemotherapy.
12. Essential ancillary medications and supportive care that accompany a chemotherapy treatment regimen should be explicitly identified.
13. Refills on oral chemotherapy medications should be discouraged, when feasible.
14. Patients should be appropriately educated regarding access and cost issues (e.g., regarding specialty pharmacies, prior authorization, out-of-pocket costs, and options for pharmaceutical manufacturer or copay assistance).

Recommendations for Medication Preparation and Dispensing Systems and Roles for Pharmacists

For each practice setting, persons representing the various healthcare disciplines that prescribe, prepare, and administer chemotherapy medications should participate in planning and managing local medication-use systems.

Standardized Medication Preparation Guidelines. Healthcare providers should establish standardized guidelines for reconstituting, diluting, admixing, packaging, and labeling

commonly used chemotherapy and other medications that are routinely administered with chemotherapy. Each practice facility should also establish a standardized method for labeling multidose vials and reconstituted drug products. Standardized medication preparation guidelines should be prominently displayed (e.g., as a chart) for easy accessibility in areas where orders are processed and medications prepared. Policies should be developed for prescribing of oral chemotherapy that are not being dispensed by the health system. Instructions for patient counseling, safe handling, and disposal should be included in these policies.

Policies and procedures should be developed for situations in which medications are prepared at facilities that are geographically removed from where treatment is administered. Procedural protocols should describe requirements for medication packaging, storage conditions during transportation, duration of transport, and handling after delivery. Medication couriers should receive training in organizational policies for handling medications and should immediately report when conditions and handling practices deviate from procedural standards. In addition, handling procedures should ensure patient confidentiality and provide guidelines for emergency situations, such as hazardous-drug spills.

Persons who prepare and dispense chemotherapy medications should ensure timely drug delivery to patients and patient-care areas after receiving written orders. If dispensing is delayed for any reason, healthcare providers awaiting the medications should be notified.[11]

Quality Assurance and Improvement. In collaboration with healthcare providers who prescribe and administer medications, pharmacists and persons who prepare and dispense chemotherapy should take the initiative in developing and managing quality-assurance and quality improvement programs for their medication-use systems. These programs should include surveillance and reporting systems, FMEAs, and root-cause analysis, when appropriate, that track potential and actual medication errors, evaluate the proximal causes of errors among processes and systems, and identify preventive measures.[11,43] The major advantage of multidisciplinary participation is that each discipline's perspectives and methods for conceptualizing system flaws and solutions can be incorporated in designing strategies for preventing medication errors. Confidential reporting is essential to the success of a medication-error surveillance and reporting system. Only by understanding what causes and contributes to errors can the number of errors be reduced. In designing a medication-error surveillance and reporting system, strategic emphasis should be placed on understanding why errors occur and not on blaming or censuring personnel.[44] Further, proactive assessment of the chemotherapy-use process should be conducted.

Orientation on Medication-Error Reduction. Pharmacy supervisors and managers should develop an orientation program about medication errors commonly associated with chemotherapy medications for training of pharmacy personnel who prepare and dispense chemotherapy. Pharmacists should develop ongoing interprofessional educational programs that focus awareness on potential medication errors with chemotherapy medications, strategies for preventing errors, and local and national medication-error reporting and evaluation systems for all practitioners who have direct patient contact.

Pharmacists should engage the support of medical and nursing administrators and supervisors to encourage their staff (particularly those in professional training programs) to complete chemotherapy medication-error awareness programs.[30] Educational programs should be discipline specific. Program content should include medication-error case scenarios, problem-solving to prevent and mitigate medication errors, and discussion about the effects that medication errors have on patients' quality of life and the health system.[11,31]

Standardized Drug Procurement and Storage. Pharmacists who select and procure drugs should strive to minimize or eliminate look-alike drug product containers and limit the availability of different vial sizes for parenteral medications whenever possible.[12] Frequent additions to the variety of available drug products and changes among alternative manufacturers' drug products can contribute to medication-use errors and should be avoided. If it is necessary to change manufacturers, healthcare organizations should develop a process to ensure staff are educated about the new product and that computer systems have the appropriate manufacturer's information. When practical, drug products with similar names and packaging should not be stored next to each other. Medication-use systems that involve a formulary should separate nonformulary products from those that are on the formulary. Healthcare providers should familiarize themselves with chemotherapy drugs that are not on formulary before prescribing, preparing, and administering them.

Standardized Medication Preparation and Dispensing. Chemotherapy medications should be dispensed in ready-to-administer dosage forms whenever possible. Generally, chemotherapy for intermittent parenteral administration should be prepared so that each medication container has only one dose. The risk of incorrect medication use is increased when the amount of drug dispensed in a single container exceeds the amount to be administered during a 24-hour period. It is essential that individuals and committees responsible for developing and overseeing medication-use systems establish guidelines on whether prescribers may order chemotherapy preparations to be administered from a single container for more than 24 hours. In all practices where parenteral drugs with extended stability (more than 24 hours) are sanctioned, it is imperative that the duration of their use is clearly labeled and that healthcare providers are trained to correctly prescribe, prepare, and administer them.[20]

When preparing a chemotherapy admixture, a quantity of medication that most closely approximates the prescribed dose should be segregated from other drug supplies. For treatment regimens that include two or more drugs, especially when medications are to be administered by different routes, the medications should be physically segregated during preparation and when administered. Compounded medications should be prepared one at a time, using standardized techniques whenever possible.

The chemotherapy preparation process should include an independent double check by two separate individuals of the correct drug, diluents, administration containers, and volume measurements before the solutions are transferred to the final administration container. A person other than the individual who selected the components of the prepa-

ration (drug and diluent) and measured the volume of diluent solutions used to reconstitute the medications should visually confirm the correct product(s) and measurement(s) before the solutions are transferred from the measuring device to the drug vial for reconstituted drugs and to the final administration container. Post hoc or proxy methods for checking medication preparation, including pulling back syringe plungers to demonstrate the volume of fluid that was injected into the secondary container, should not be used as the sole method for verifying chemotherapy product preparation. Verification may be accomplished by direct visual inspection; remote monitoring through telepharmacy applications (with pictures); or by weighing syringes, other transfer devices, and intermediate product containers before fluid transfer is completed. Whenever possible, methods that allow direct observation of product preparation should be used. The actual original medication vials and diluents that were used during preparation must be present for inspection during the verification process.

Technologies to automate the preparation of sterile products, including chemotherapy, are emerging. Some robotic technologies enclose and automate the entire production process, and these products may provide a variety of benefits to institutions with a sufficient volume of chemotherapy to justify their substantial cost. A more common technology organizes information, manages workflow, adds new checks, and documents parenteral drug therapy preparation through a combination of computer software, barcodes, and cameras. In these systems, the components of a chemotherapy preparation are verified with bar code technology and pictures before preparation, and pictures of the preparation are stored. These systems add additional double checks with the barcode technology and improve documentation of the preparation and other relevant information such as product lot number. In some settings, the photos taken through this technology enable the pharmacist to check chemotherapy preparation outside the sterile area. Like other technologies, automation for parenteral therapies must be carefully implemented to be certain the new technology is not eliminating checks in the process. For example, bar coding the components of a chemotherapy dose does not eliminate the need to check the components of the chemotherapy before they are admixed.

Standardized Medication Labeling. Strict procedures should be established for standardizing medication labeling. A uniform, systematic labeling method should be used, especially when multiple drugs are prepared for a single patient. Medication labels should be mechanically printed (not handwritten). Chemotherapy medications should be labeled immediately after preparation. Oral medications should also be sealed with child-resistant or poisoning-prevention closures.

Chemotherapy agents are administered parenterally by many routes other than the intravenous route (e.g., intrathecally, intrahepatically, intrapleurally, intraarterially). Inadvertent administration by the wrong route can result in serious or fatal consequences (e.g., administering vincristine intrathecally is fatal). Medication-use systems should include policies and procedures that clearly distinguish medications administered by the intravenous route from those intended for administration by other routes. Auxiliary labels may facilitate distinguishing among medications that are administered by particular delivery methods.

Labels for oral dosage forms, rectal suppositories, and topically applied unit-dose products should include *all* of the following information:

1. Patient's name, unique identifying code or number, and location within a treatment facility (when applicable).
2. Date (with or without specifying time) the medication was dispensed.
3. Generic drug name.
4. Dosage form and strength.
5. Amount of medication per dose (when the container dispensed holds more than one dose).
6. Administration route.
7. Detailed instructions to the patient for self-administering the medication (including a dosing calendar when appropriate).
8. Supplemental administration instructions (e.g., starting and completion dates and times; number of doses to administer; cautionary information about when medications are to be taken in relation to food ingestion and other medications; and instructions and warnings regarding administration route, handling precautions, storage conditions, and container closures).
9. The quantity dispensed within each container (the number of tablets, capsules, or suppositories, packaged in a single container).

Labels for injectable dosage form containers should include *all* of the following information:

1. Patient's name, unique identifying code or number, and location within a treatment facility (when applicable).
2. Generic drug name.
3. The amount of medication per container and, when a product container holds more than one dose (e.g., multiple doses for intermittent administration), the amount of medication per dose).[20]
4. How much overfill is added to a container when excess medication and fluid volumes are added to displace air from the tubing lumen ("dead space") in administration sets.
5. Route of administration (for example, medications prescribed for administration other than by the intravenous route—especially those for intrathecal administration— should bear ancillary labels that distinctively identify the intended administration route).
6. The name and amount of all drug additives in a chemotherapy admixture.
7. Diluent (vehicle fluid) name.
8. The volume of fluid to be administered. Adding overfill to the container should be discouraged, but when unavoidable, both the volume to administer and the overfill volume should be specified. Proper education for nurses administering these products is essential to ensure that patients do not receive additional drug.
9. Administration rate and duration. Ideally, both administration rate and duration should be specified. Because administration rates can be calculated from the volume to be administered and duration of administration, duration is the essential component.

10. Supplemental administration instructions, such as starting and completion dates and times; prohibitions about when medications are not to be administered in relation to other medications; and instructions and warnings regarding administration (e.g., information about special requirements for administration sets, including inline filtration, warnings to avoid intrathecal administration with vinca alkaloid drugs, and hazardous-drug warning labels).
11. When it is necessary to prepare more than one medication intended for sequential administration, the container labels should be numbered. The sequence in which each container is to be used and the total number of containers (e.g., bag 1 of 3, bottle 3 of 7) should be indicated.
12. Date (with or without specifying time) the medication was ordered or prepared. Investigational compounds, in particular, should be labeled with the date and time they were prepared.
13. Expiration date and time after which a medication should no longer be used (i.e., beyond-use date and time).
14. Cautionary warnings as required for hazardous drug products.[45]
15. Storage specifications.
16. The name (with or without specifying location or telephone number) of the institution, pharmacy, or practice from which a medication was dispensed and the prescriber's identity.

Credentialing Pharmacists for Chemotherapy Medication-Use Programs. Pharmacy managers and supervisors should require pharmacist employees to complete training and demonstrate competencies related to chemotherapy medication use, evaluating medication orders, preparing chemotherapy medications, safe handling procedures, error surveillance and reporting programs, and local policies as a prerequisite to pharmacist credentialing. Healthcare organizations should periodically reassess pharmacist employees' competencies related to their responsibilities, increasing the frequency of reassessment if performance problems occur.[14]

Roles for Pharmacists. Among primary healthcare providers, pharmacists generally are best positioned to ensure that medications are used rationally and safely and increase others' awareness about medication errors and how to prevent them. Pharmacists should participate in all aspects of patient care related to chemotherapy treatment, including developing policies for safe and appropriate medication use and other services consistent with pharmacist patient care.[11,30] Pharmacists should participate with other primary healthcare providers in multidisciplinary groups that develop, implement, and periodically reevaluate practice-specific procedures and processes for verifying chemotherapy medication orders, resolving procedural questions related to confirming and processing medication orders, and evaluating and resolving disputes among healthcare providers.

Each organization should establish a minimum acceptable level of pharmacist participation in the error-prevention elements of patient care, such as proactively reviewing medication orders, screening laboratory results, providing drug information and patient counseling, and reviewing drug storage conditions.[11,46]

The following roles are recommended for pharmacist participation:

1. Educating healthcare providers about medication errors.
2. Independently verifying medication dosages, routes of administration, and schedules.
3. Participating in multidisciplinary efforts to establish drug-specific utilization constraints that limit maximum doses, administration rates, and administration schedules for chemotherapy medications.
4. Participating in multidisciplinary efforts to standardize the prescribing vocabulary and the development, implementation, and maintenance of standardized order sets.
5. Participating in multidisciplinary efforts to educate patients, their families, and personal caregivers.
6. Participating in multidisciplinary efforts to develop adherence programs and monitor patient adherence to prescribed regimens, including recommendations for supportive care to treat and or mitigate adverse events associated with chemotherapy agents.
7. Participating in multidisciplinary efforts to assist patients with accessing medications (e.g., prior authorization, manufacturer assistance programs, copay assistance programs, coping with drug shortages).
8. Improving communication among healthcare providers and among healthcare providers, patients, and caregivers.
9. Working with pharmaceutical or equipment manufacturers on medication-specific safety strategies.

Drug Information Resources and Education for Providers. Pharmacists should help ensure the availability of up-to-date references on the appropriate use of chemotherapy drugs for all healthcare providers involved in medication use.[11,31] Drug information resources should provide information about:

- Drug products' FDA-approved labeling, compendia-supported indications, and investigational uses.
- Drug-specific precautionary warnings and information about adverse effects, particularly dosage- and schedule-limiting effects.
- Potential interactions with other drugs, disease states, and foods.
- Administration methods, including drug admixture stability and compatibility data.
- Usual adult and pediatric dosages.
- Dosage recommendations for single- and multiple-treatment courses.
- Treatment modifications for persons with concurrent pathologies or end-organ impairment.
- Safety Data Sheets.
- Pharmacokinetically based dosing and monitoring guidelines.

Information and guidelines for handling chemotherapy extravasations and hypersensitivity reactions, including the use of antidotes, should be developed by a multidisciplinary team and be readily available.

Pharmacists should develop and provide discipline-specific educational materials about chemotherapy medication use to healthcare providers who prescribe, prepare,

and administer chemotherapy medications. The instructional tools developed for each professional healthcare discipline should complement the materials developed for the other disciplines.[11]

When new chemotherapies, treatment regimens, or treatment protocols are introduced, pharmacists should assume a continuous, proactive leadership role in developing educational programs and materials for healthcare providers, patients, and caregivers.[11,31] Pharmacists should assess the competency of individuals assigned primary responsibility for chemotherapy education to confirm their ability to effectively communicate medication-related information.

For patients whose care is transferred from oncologists to nonspecialist practitioners, oncology pharmacy specialists should develop and provide drug monographs, medication-use summaries, and other treatment-related materials describing how oral and parenteral chemotherapy medications and treatment regimens are to be accomplished.[12,30] The need is especially acute among organizations and practitioners who provide local care for patients enrolled in clinical trials or receiving investigational chemotherapy treatments.

Treatment Protocols. Oncology pharmacy specialists should participate in developing treatment protocols for standard treatments and clinical investigations. In practice settings where chemotherapy medications and treatment regimens are used routinely, pharmacists should initiate the development of tools that standardize the way medications are ordered, thereby facilitating accurate and appropriate prescribing, order interpretation and verification, and medication processing and dispensing.[31,47] Pharmacists should lead initiatives to standardize drug preparation procedures, including reconstitution, dilution, and drug admixture methods for commonly used parenteral chemotherapy medications.[12]

CPOE. Pharmacists should work with information systems personnel, computer programmers, and software vendors to develop CPOE systems. System requirements should include mechanisms for standardizing medication orders, decreasing opportunities for error by minimizing data entry, and screening orders for medication doses and administration schedules that exceed established limits. Pharmacists should advocate for and participate in establishing maximum safe chemotherapy dosage and scheduling limits with physicians, nurses, and other primary healthcare providers. Pharmacists should guide the appropriate use of clinical decision support in CPOE systems for chemotherapy and the medication management process.

Vocabulary and Nomenclature. Pharmacists are uniquely qualified to lead multidisciplinary efforts to develop and implement clear, detailed, standardized vocabulary and nomenclature for chemotherapy treatment regimens, medication orders, and administration instructions. Pharmacists should participate in the early stages of protocol development for standard treatments and clinical investigations to ensure that pharmacotherapeutic regimens are clearly described, easily understood, and incorporate standardized language, content, abbreviations, and units of measure.[11,20,30]

Patient Education and Counseling. Pharmacists should ensure that educational materials used for patient education are comprehensive and routinely updated. When meeting or interviewing patients, their family members, or other home-based caregivers (e.g., completing medication-use and allergy histories, screening blood pressure, performing ongoing treatment response assessment, dispensing medications), pharmacists should provide medication education and counseling. They should verify that patients and their caregivers understand the following:

1. The purpose of the medication and its intended use.
2. The appropriate use and safe handling of medications (e.g., don't place oral chemotherapy agents in a pill box, keep away from children) and administration devices.
3. Appropriate temperature and safe storage conditions.
4. Special precautions to prevent exposure to hazardous materials that may be present in patients' clothing, linens, body fluids, and excreta during and after treatment.
5. The potential interactions with other medications and foods.
6. The critical need for good medication adherence practices.
7. What to do if a dose is missed.
8. Dosing calendars or other supplemental information to improve adherence.
9. Common and possible adverse effects associated with the medication.
10. Methods for preventing, managing, and reporting adverse effects.
11. What to do if potentially serious adverse effects occur, including when to contact a provider, who to contact, and how to reach them.[11,36]
12. How to properly dispose of the medication, container, and supplies.
13. Access and cost issues (specialty pharmacies, prior authorization, out-of-pocket costs, options for pharmaceutical manufacturer or copay assistance, drug shortages).

Pharmacists should provide educational materials to patients and suggest supplemental and alternative information resources, such as the National Cancer Institute information services department (1-800-4-CANCER and www.cancer.gov), the American Cancer Society, libraries, and bookstores.[11] If pharmacists are not available to provide chemotherapy patient education, they should assist in competency assessment of those assigned primary responsibility for that education.

Advocates for Patients' Rights. Pharmacists should encourage patients and their caregivers to participate in their own care and advise patients how to protect themselves from medication errors. Pharmacists should advise patients that they are entitled to satisfactory answers from their healthcare providers. Pharmacists should encourage patients to double-check the details of their treatment, including drug names and dosages, and to request dosage recalculation if their biological measurements change. Pharmacists who participate in developing treatment plans and protocols should ensure that consent-for-treatment forms contain accurate, complete information to secure patients' informed consent. Pharmacists should help to prepare treatment consent forms; provide patients with an accurate and detailed description

of their treatment plan in clear, unambiguous, and easily understood language and answers to their questions about the treatment and alternative treatment options; and assess patients' understanding of expected and possible outcomes. Pharmacists should also describe their role as primary care providers and the care they provide.[11,12]

Clinical Intervention, Analysis, and Performance Improvement. In addition to dispensing medications, pharmacists can help improve the quality of patient care by implementing a proactive clinical intervention program and documenting healthcare providers' deviations from planned chemotherapy treatments. Longitudinal data collection, analysis, and reporting can reveal system flaws that contributed to (or failed to prevent) prescribing errors, suggest targets for quality improvement, and validate pharmacists' interventions.

Pharmacists should proactively work with other primary care providers to establish medication-use reporting and surveillance programs. Committees established for this purpose should include representatives from medical, nursing, pharmacy, and risk-management disciplines. Programs should continually evaluate local medication-use systems to identify potential problems and solutions related to medication use and prevent medication errors.[11,43] Such programs in institutions should seek endorsement from appropriate local multidisciplinary committees (e.g., pharmacy and therapeutics, medical executive, and clinical practice committees).

Feedback for Pharmaceutical Manufacturers and Regulators. Pharmacists should work with pharmaceutical manufacturers and the FDA to eliminate ambiguous, confusing, and potentially misleading drug product and treatment information from published resources (e.g., product packaging, package inserts, official compendia, and promotional information). Pharmacists working in the pharmaceutical manufacturing industry should proactively identify preventable causes of product-user errors and adverse effects associated with product labeling, packaging, and promotion.[48] Pharmacists' voluntary participation in national reporting programs can increase the awareness of medication errors and promote error prevention throughout the healthcare system. These aggregate data promote changes in product identity, packaging, labeling, commercial information, and marketing practices that are subject to manufacturers' control and governmental regulation.[11,41]

Recommendations for Medication Administration Systems and Roles for Nurses

Nurses are often the last link in the chain of healthcare providers who provide treatment with chemotherapy medications. To safeguard patients from mistakes that have potentially lethal consequences, evidence-based systems have evolved that promote safety and include[4]:

- Requirements for credentialing persons who administer chemotherapy medications.
- Tools and methods to facilitate documentation and identification of correct medication use.
- Independent verification of medication orders.
- Independent double check of the final product and infusion pump settings.
- Accurate documentation of medication use and effects on patient care.
- Strict compliance with regulations and practice standards.
- Patient education regarding medication safety.

Credentialing Nurses for Chemotherapy Medication-Use Programs. Organizational policies and procedures should require nurse employees to complete training and demonstrate nursing care-related competencies, such as administering chemotherapy medications, caring for patients who have received chemotherapy medications, and knowledge of local policies. Specialty certification (e.g., ONS Oncology Certified Nurse credential, ONS Chemotherapy and Biotherapy Provider Card) is highly encouraged. Nurses may be required to complete additional training and competency assessments before they are permitted to administer experimental medications. Training usually combines didactic and supervised practical instruction. Didactic instruction generally includes training about specific chemotherapy agents, appropriate dosages and dosage ranges, adverse effects and clinical toxicities, administration techniques, and safe handling. Technical experience in administering chemotherapy medications requires demonstrating competence with administering intravenous medications. Healthcare organizations should periodically (at least annually, but more frequently if performance problems occur) reassess nurses' competencies related to their responsibilities.

Standardized Medication Administration Practices. In collaboration with the multidisciplinary team, nurses within an organization should standardize chemotherapy administration practices. It should be determined whether intravenous chemotherapy agents should be infused as a primary or secondary infusion across the organization. Institutions should establish cut-off times to initiate nonurgent chemotherapy administration in relation to the need for adequate staffing.

Medication safety technologies should be implemented to enhance the chemotherapy administration process. ASHP encourages health systems to adopt bar-code-enabled medication administration (BCMA) technology to improve patient safety and the accuracy of medication administration and documentation.[39] Infusion pumps that provide dose and infusion-rate warnings (often called "smart pumps") should also be implemented. Because of unique challenges from chemotherapy (e.g., BSA-based dosing), some organizations' pumps may not immediately provide warnings for chemotherapy, and care must be taken to make enhancements to the technology to accommodate chemotherapy. Appropriate use of both of these technologies provides new checks in the chemotherapy administration process.

Standardized Tools for Recording Medication Administration. Nurses with a variety of experiences have devised and contributed to designing tools to facilitate the prevention of drug administration errors, such as standardized work sheets used to calculate medication dosages and administration rates and checklists of pertinent laboratory results and physiological measurements. Treatment flow sheets provide easily interpretable information about when a patient's previous treatments were administered, whether dosages

and medication delivery deviated from planned treatment, and the cumulative amount of medication administered. Thoughtfully designed treatment flow sheets may become part of a patient's permanent medical record and can be an invaluable resource for patient care.

Checking Orders and Equipment for Administering Chemotherapy Medications. Medication orders for chemotherapy require documentation of independent double-checks by two individuals prior to administration.[4] These individuals should be different than the individual who prepared the product. In addition, nurses should evaluate and confirm the functional integrity of vascular access devices (and devices for other administration routes), medication pumps, and other devices that control medication delivery. For adjustable and programmable mechanical and electronic devices, mechanical adjustments or electronic programming for delivering the correct dose at the appropriate rate should be independently verified with another healthcare provider who is knowledgeable about the delivery device before it is used to administer medications.

Recording and Tracking Chemotherapy Use. After medications have been administered, it is a nurse's responsibility to manually or electronically record the activity. The documentation should be in a standardized format and include the patient's name, the names of all medications administered, dosages, administration routes, rates of administration, the date and time administration began, the duration of administration or time that treatment was completed, and whether adverse effects were observed or reported by the patient during or after administration. Communications with patients, other healthcare providers, and personal caregivers should be documented in an objective, chronological narrative style, reporting the dates and times the events occurred, the names of involved persons, and how questions and problems were resolved.

Clinical Intervention, Analysis, and Performance Improvement. Nurses and other personnel should immediately report to medically responsible personnel and their supervisors any instance in which medications were used incorrectly and the events attributable to the error. In response to discovering a medication-use error, a provider's primary responsibility is to ensure the patient's safety. Subsequently, the error and related circumstances should be recorded in accordance with specific policies and procedures. Medication-use error reports (also called occurrence, safety, or incident reports) should be written in an objective, chronological, narrative style without editorial remarks and speculative comments. Comprehensive occurrence reports are useful in discovering and evaluating system flaws and may provide the impetus for improving medication-use systems.

To prevent medication errors, nurses and other personnel who administer chemotherapy medications must comply with policies and procedures that define standards of practice. It is important, however, to periodically reevaluate practice standards in order to assess how well a medication-use system functions, make appropriate changes, and, ultimately, improve patient safety and the quality of care.

Healthcare providers administering chemotherapy medications should not deviate from guidelines for ordering, preparing, and administering chemotherapy agents. Examples of inappropriate practice include borrowing medications from a patient's drug supply to give to another patient and preparing agents without the proper facilities or staff. Medication administration schedules should be followed as closely as possible; providers and caregivers should strive to comply with treatment plans. Drug administration should be documented promptly after it is completed, and providers administering chemotherapy medications should rigorously comply with local requirements for documenting treatment. To prevent the inadvertent duplication of treatment, it is recommended that one individual assume the primary responsibility for each patient during a work period (shift or tour of duty). When one individual cannot assume primary responsibility for each patient during a work period, appropriate hand-off communication is essential.

Nurses and Patient Education. Nurses who administer chemotherapy medications have a prominent role in educating patients about their chemotherapy. Nurses should encourage patients and their personal caregivers to ask questions about their treatment. Patient education guidelines may be included in treatment maps and clinical care plans.

Recommendations for Patient Education

Well-informed patients (and their authorized caregivers) are the vital last link in the safety chain to prevent errors related to chemotherapy medications. Patients are entitled to know all pertinent facts about the medications they receive during their treatment. Healthcare providers charged with educating patients should have demonstrated competency to accurately perform this function. Healthcare providers have an obligation to encourage patients to ask questions and to provide answers.

The following suggestions are offered to help patients and their caregivers ensure optimal outcomes from the cancer therapy medications.

Multifocal Medication Education. Patients need multifocal education about the purpose, adverse effects, schedules, routes of administration, and descriptions (e.g., colors, shapes) for all the medications they will receive during their treatment. This includes the chemotherapy regimen, including both oral and intravenous therapy, and all ancillary and supportive medications, such as antiemetics and medications that hasten bone marrow recovery. In order to ensure patients receive the appropriate education to manage their therapy or its side effects, it is imperative that roles of the various healthcare professionals are defined and that responsibility for primary patient education versus reinforcement of key information is clearly delineated. When patients are well informed and the information they receive is reinforced by nurses, pharmacists, and other caregivers, they are better prepared to detect a misinterpreted medication order and assertively question conflicting information.[49] Healthcare professionals should be sensitive to the emotional aspects of patients with cancer when planning medication education. Education should take place at a time when a patient is able to listen and understand. Medication education should not be attempted when patients are sedated or confused as a result of medications or immediately after receiving their cancer diagnosis.

Patients should participate in their care by asking questions about their cancer treatment and related medications and by confirming the regimen with their nurse before receiving treatment. Healthcare providers should make educational materials available in counseling and treatment areas to encourage patients to learn more about their cancer therapies.

Health-System Procedures Education. Patients should understand the health system's plan for chemotherapy medication-error prevention. They should become familiar with their providers' routine procedures for checking medication orders so that they can understand the safeguards that have been established and why delays may occur before their treatment can be started. For example, patients can remind the person administering chemotherapy to compare medication labels with a patient's identity and can verify their height and weight each time they are measured.

Patient Participation in a Medication-Use System. Patients (or their caregivers) should be knowledgeable about their medications and the ways in which the medications are to be administered according to their treatment plan. In some circumstances, patients should be encouraged to take responsibility for some of their care to help improve their quality of life. Examples include self-administering medications, maintaining the patency of vascular access devices, giving themselves a subcutaneous injection, and troubleshooting a problem with the portable infusion pump. Patients should demonstrate their ability to perform these functions if they are included in the therapy plan. Competency and readiness for self-administration should be assessed for patients prescribed oral chemotherapy.

Each patient should be given a detailed treatment calendar that clearly identifies his or her treatment plan. They should be encouraged to keep their calendar with them to compare the expected treatment with what is being dispensed and administered.

Patients' Responsibilities. Patients should be taught and empowered to detect and to seek help in managing adverse effects that may occur during their cancer treatment. Healthcare providers should be promptly informed about adverse effects experienced during a chemotherapy cycle before the next cycle commences. Patients should keep a list of the medications that they may self-administer to treat these adverse effects. Patients should be encouraged and taught how to report medication errors and near misses that occur as a result of self-administration. Safe handling, storage, and disposal of oral chemotherapy should be taught to the patient or their caregiver.

It is important for healthcare providers to be able to determine potential interactions between a patient's nonchemotherapy medications and the chemotherapy they are to receive. Therefore, patients should be requested to provide to their healthcare team members a list of all medications they are using, including over-the-counter preparations, dietary supplements, and other complementary and alternative medicines. In general, use of any medication should be discussed with their healthcare providers before initiating therapy.

Recommendations for Manufacturers and Regulatory Agencies

Pharmaceutical manufacturers have a responsibility to exercise care in designing product packaging and labeling, determining dosage strengths and dosage forms, and in promoting their products, as these features may contribute to errors in prescribing, product selection, preparation, and administration. Companies that market chemotherapy agents should develop and support educational programs that encourage safe and accurate prescribing, preparation, administration, handling, storage, and disposal of their products. The following guidelines address some of the major areas.

Product Naming, Packaging, Labeling, and Drug Dosage Strengths/Forms. Companies should avoid trademarking drug names that look or sound similar to those of other drug products. Proprietary drug names for new products and product formulations should not be similar to existing generic and proprietary names. Manufacturers should avoid appending letters and numbers to drug names, as this practice can result in potential confusion with dosage strengths, medication quantities, and the amount of medication to be administered.

Product packaging and labeling should provide clear, easily distinguished features to identify a drug and the amount of drug per dosage unit (e.g., tablet, capsule, wafer) and within a product container (e.g., vials, bags, bottles, prefilled syringes). It is particularly important that a drug product's USAN-approved generic name appear more prominently than other information on the product label. Drug names should be printed on both the front and back of the containers and packaging of parenteral drugs; "Tall Man" characters should be used to distinguish between similar drug names. Container labels for drugs that are in solution and for those that require reconstitution or dilution before they are used should identify the total drug content in mass units (or biological activity units) rather than concentration.[49] Product packaging and labeling that include both mass and concentration values should be designed to display mass units more prominently. Product packaging should include a bar code on inner and outer packaging.

Labels should be unique and well designed. Distinguishing colors and contrasting hues facilitate identifying and distinguishing drug products and products in different strengths and concentrations. Warnings and special or unique instructions should be prominently displayed on product packaging and labeling. Unique labeling and packaging techniques should be used to prevent product misidentification and to warn about dosing errors and unique characteristics that predispose medication users to potentially serious or life-threatening toxicities. Examples include the unique way that the Platinol-AQ brand of cisplatin injection (Bristol-Myers Squibb, Princeton, NJ) is packaged to prevent misidentification with carboplatin and the cautionary statements on vials containing vincristine sulfate injection that warn against using the entire contents of a vial for a single patient (on bulk packages) and that intrathecal administration may be fatal.

A statement that declares a drug's approved routes of administration is optional and may or may not appear on product packaging. If the agent is approved for administration by only one route, it must be clearly indicated.

Appropriate storage temperatures or conditions should be clearly visible on drug labeling and packaging.

Drug labeling and packaging must identify the manufacturer's product lot or control number.

Drugs that must be reconstituted and diluted before clinical use should include reconstitution instructions that identify appropriate diluents and volumes.

A manufacturer's drug product preparation date (for experimental drugs) or an expiration date should be clearly visible on the product label.

Special instructions (e.g., "Shake Well," "Do Not Shake," "Albumin Required") and instructions for dilution should appear on product labeling. In cases where important information will not fit on a product label, a package insert, or "pull-away" label may be required as part of the labeling and packaging.

In the case of oral chemotherapy agents, careful consideration should be given to dosage forms and strengths provided. Often patients must combine multiple strengths of a medication to receive their prescribed dosage, thereby increasing the opportunity for a medication error. Many oncology patients have difficulty swallowing and cannot take solid dosage forms. Manufacturers should be responsive to dosing practice patterns and other patient-specific needs of oncology patients that become apparent after medications are released into the market.

Product changes should be widely communicated to prescribers, pharmacists, nurses, and other healthcare providers involved in drug prescribing, preparation, and administration.

Package inserts and product information that describe medical indications, medication doses, administration schedules, safe handling, disposal, and product use should not include abbreviations. This is especially important for drugs used in complex treatment regimens.

Educational Materials and Programs. Pharmaceutical manufacturers and drug product sponsors should be encouraged to provide educational materials and programs that promote and encourage safe use of their drug products. Programs should clearly explain the indications appearing on FDA-approved labeling, dosages, methods for preparation, administration routes and schedules, and safe handling and disposal. Treatment descriptions should be standardized and consistent with guidelines designed to prevent medication-use errors.[20] Medication names and administration information should not be abbreviated in educational and promotional materials.

Restricted Drug Distribution. Chemotherapy agents, particularly newer oral chemotherapy agents, may be subject to restricted distribution. Restricted drug distribution products are available only through a select distribution program in which only prescribers and patients registered with the program are able to prescribe, administer, and receive the product.[50] Restricted distribution can occur due to decisions made by pharmaceutical manufacturers or as a result of Risk Evaluation and Mitigation Strategies (REMS).[51] There are circumstances in which properly implemented constraints on the traditional drug distribution system are appropriate.[52] The primary safety concern is that restricted distribution may adversely affect continuity of care. For example, when patients receive medications from various sources (clinic, local pharmacy, specialty pharmacy), it is difficult to establish a comprehensive medication list for screening of drug interactions, therapeutic duplications, and other important aspects of medication management. Delays in therapy could result when patients must wait for medications to be shipped to their home from a specialty pharmacy. Receiving prescriptions by mail does not allow for a face-to-face interaction between the patient and the pharmacist, where patient concerns and educational deficits may be identified. In addition, specialty pharmacies may not have access to the patient's complete health record and this may compromise the specialty pharmacist's ability to properly verify the order. Given these challenges, when patients can only obtain chemotherapy through a restricted drug distribution system, pharmacists and other providers should proactively provide relevant information to patients and specialty pharmacies to coordinate care. Follow up, such as phone calls, should be conducted to verify that the patient receives the chemotherapy and understands proper use. The ASHP Task Force on Caring for Patients Served by Specialty Suppliers provided recommendations for effectively managing restricted-distribution drugs and other aspects of working with specialty suppliers.[50] The National Comprehensive Cancer Network (NCCN) has also commented on specialty pharmacies and their effects on patient care and medication safety regarding chemotherapy.[53]

Regulatory Oversight. Regulatory agencies have a responsibility to review product packaging, labeling, and advertising to ensure that their content accurately reflects safety and efficacy data and conforms with language that has been approved by the FDA. A key component in those reviews should be that the product packaging and labeling facilitate safe and appropriate use and prevent users from making errors in selecting, preparing, and administering a drug product. Pharmacists should be consulted in screening proprietary drug names, product packaging, and labeling before drug products are approved for commercial use.

Recommendations for Identifying and Managing Medication Errors

Medication-use errors with chemotherapy are distinguished from errors with other types of drugs in two important ways, both of which relate to the inherent toxicity of chemotherapy agents. Individually and categorically, the therapeutic index for chemotherapy drugs is less than that for any other class of drugs. Adverse effects are an expected pharmacodynamic consequence attendant with chemotherapy use, and clinical toxicities may occur and persist at substantially lower dosages and schedules than are therapeutically used. The second characteristic that distinguishes chemotherapy from many other types of drugs is that subtherapeutic doses ("underdoses") of chemotherapy can severely complicate further treatment. Subtherapeutic doses of chemotherapy medications may not only fail to provide a therapeutic benefit but may also compromise patients' ultimate response to therapy by delaying effective treatment until adverse effects are resolved or contributing to cumulative, long-term patient harm from adverse effects. It should be noted that chemotherapy treatments are almost always repeated, and the effect of a medication-use error may not be apparent until long after

the error occurs. Consequently, if treatment plans and medication orders are not verified during each treatment cycle, errors may be compounded during repeated cycles and go undetected throughout an entire treatment course. With the increased responsibility placed upon patients to manage oral therapies, it is likely that medication errors will occur with self-administration. Patients should be educated and encouraged to report medication errors to their healthcare providers, who in turn should report the error through the institutional reporting system. Patient reported errors should be handled with the same concern and diligence as an error that occurred in the hospital, clinic, or physician's office.

In addition to the actions already set forth in the ASHP Guidelines on Preventing Medication Errors in Hospitals,[1] the following actions are recommended after detecting a medication error[6]:

1. Implement monitoring and interventions for controlling injurious effects and ensuring patient safety.
2. Determine whether an error could have previously occurred during prior treatment in the same patient and in other patients. Medication preparation work sheets or logs and drug administration records should be evaluated. Unexpected toxicities and an apparent or unaccountable lack of therapeutic and adverse effects should be investigated when it is suspected that a medication error has occurred.
3. Seek the advice of healthcare professionals from various disciplines. The diverse perspective of providers in other disciplines may facilitate discovering and understanding the circumstances that allowed a medication error to occur.
4. Determine whether an immediate temporary or stopgap change in policy or procedure is necessary to prevent recurrence of an error while the proximal cause is being analyzed.
5. Provide immediate professional counseling and support for employees implicated in causing or contributing to an error that results in serious patient harm. Counseling and support should be offered to all personnel who learn that they have been involved in a medication error without regard for how recently the error occurred.
6. Establish procedures to inform and follow up with patients and their families about a medication error.
7. Understand that reporting medication errors and adverse drug reactions is a responsibility that should be shared by all healthcare providers. However, health systems may designate a person or committee to be specifically responsible for reporting and investigating medication errors and adverse drug reactions. In investigational drug studies, a study's principal investigator must report serious adverse events to the trial's sponsors (the drug manufacturer and the investigational new drug application holder) and to the institutional review board that oversees study conduct. Investigational drug sponsors are required to report to the FDA serious adverse effects associated with investigational agents, even if they are caused by a medication-use error. While reporting of medication errors in investigational studies to the institutional review board and the FDA occur, it is imperative they also be reported through the institutional reporting system or committee so that system and process improvement can occur in the setting of investigational studies.
8. Encourage practitioners to report medication errors to a national medication-error tracking program. This allows other providers to learn how medication errors occur and how they can be prevented. Reporting mechanisms for medication-use systems should be standardized by policy. Mechanisms must be developed for ongoing, interprofessional analysis and use of information that is reported to medication-error databases.[54]

Categorizing Medication Errors. In practice settings where a variety of disciplines provide patient care, serious potential and actual errors should be reported to an oversight committee composed of representatives of all the disciplines that provide care. By standardizing the way medication errors are reported, comparisons between reports and databases are facilitated, error trends are more easily identified, and system-based solutions can be developed.[55] Continuous oversight by a multidisciplinary quality-assurance committee promotes continuity and permits all primary patient-care providers to evaluate system flaws and develop and improve the quality of processes and systems that safeguard patient care.[43] Medication-use oversight committees are advised to review medication-error reports from systems other than their own and evaluate their local medication-use system for design characteristics that may permit similar errors.[30,38]

The ASHP Guidelines on Preventing Medication Errors in Hospitals[1] recommend adopting a system for categorizing medication-error severity, such as the one developed by Myers and Hartwig, et al.[54,55] Although this system is generally applicable to errors of occurrence with chemotherapy drugs, it categorizes errors by severity and prioritizes them without consideration for the frequency at which repeated errors occur. Accordingly, errors with the highest severity ranking receive the greatest efforts toward remediation. In contrast, potential errors are assigned a "zero" ranking, the lowest severity level, as they do not reach patients. By relegating potential errors to the lowest priority category, this outcome severity-based system risks trivializing system-design flaws. Errors discovered before they reach patients could cause devastating consequences, yet serious nascent errors are often transformed into potential errors only by serendipitous discovery. Therefore, potential errors should be distinguished from errors of occurrence and subcategorized based on their potential to cause harm.[54,55] However, potential errors should not be taken less seriously than errors of occurrence. When serious potential errors are discovered, the systems and processes that contributed to the errors should be evaluated and their proximal causes identified. The greatest efforts toward remediation of potential errors and errors of occurrence should be concentrated on eliminating the causes of errors that could have and had, respectively, the greatest adverse effects on patients' health.

NCC MERP's definition for medication errors includes any event that may cause or lead to inappropriate medication use.[2] The definition is complemented by the NCC MERP Taxonomy of Medication Errors, a comprehensive expandable tool intended for use in developing databases and analyzing medication-error reports.[56] The Taxonomy provides standardized language and structure for recording and tracking medication-error-related data for errors of occurrence

and potential errors. NCC MERP permits interested persons to adopt it as it is presented or adapt it for use in a particular practice setting.

Conclusion

The use of chemotherapy and biotherapy agents presents healthcare organizations with distinct safety challenges that require additional precautions to prevent medication errors. These guidelines provide best practices for the safe use of chemotherapy and biotherapy agents to help practitioners improve their medication-use systems to prevent medication errors and patient harm from these agents. The guidelines describe the medication-use responsibilities shared by and unique to specific professional healthcare disciplines, progressing from general to specific applications. Although the guidelines focus on the safe use of chemotherapy in treatment of cancer patients, in general the recommendations apply for all uses of a chemotherapy agent, regardless of indication. These wide-ranging recommendations focus on preventing errors with chemotherapy agents in hospitals and ambulatory care clinics that offer direct pharmacy services, but the guidance may also be useful in other settings. Because of the complexity of and differences between practice settings and organizational arrangements, aspects of these guidelines may be more applicable to some practice settings than others. Healthcare providers should use their professional judgment in assessing and adapting the recommendations to their own circumstances, keeping in mind that these guidelines address a specific aspect of the medication-use process and should be augmented as appropriate by other clinical and practice guidance.

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