ANTINEOPLASTIC DRUG ADMINISTRATION: ORAL (ONCOLOGY) - CE

ALERT

Don appropriate personal protective equipment (PPE) based on the patient’s signs and symptoms and indications for isolation precautions.

Refer to Oncology Nursing Society (ONS) interim guidelines for PPE recommendations during an emergent shortage of PPE (e.g., pandemic).

Ensure that a licensed independent practitioner is on site and immediately available during all antineoplastic drug administration.

Only qualified physicians, physician assistants, advanced practice registered nurses (APRNs), or nurses with demonstrated competency administer antineoplastic therapies. Refer to the professional’s regulatory scope of practice and the organization’s practice.

Institute special precautions to prevent exposure to hazardous medications when handling and administering antineoplastic agents and caring for patients receiving them. Exposure to hazardous medications, including antineoplastic drugs, poses health risks for practitioners, including carcinogenicity, teratogenicity, genotoxicity, and impaired fertility.

Take steps to eliminate interruptions and distractions during medication preparation.

OVERVIEW

In general, antineoplastic drug therapy is the use of chemical and biologic agents to destroy cancer cells. The use of these drugs is based on cellular kinetics, including the cell cycle, cell-cycle time, growth fraction, and tumor burden. Antineoplastic therapies are classified according to the phase of action during the cell cycle, mechanism of action, biochemical structure, or physiologic action.

Antineoplastic agents can be systemic treatments for malignancies such as solid tumors, including those that have metastasized regionally or distantly as well as malignancies of the hematopoietic system. These agents can also be administered regionally to provide a higher local dose to an area of the body that is impacted by cancer. Antineoplastic agents can be administered as adjuvant (primary) or neoadjuvant therapy and as single agents, in combination with other agents, or concurrently with radiation therapy. Treatment decisions are individualized based on patient-specific factors including age, comorbidities, cancer cell-specific factors (e.g., hormone or protein expression, molecular targets), tumor location, tumor burden, and potential toxicities or adverse reactions.

Depending on the disease state and the goal of therapy, antineoplastic agents are administered via a variety of routes (e.g., oral, intramuscular, intrahepatic, intraperitoneal, intrathecal, intravenous, and subcutaneous). Regardless of the route or setting, hazardous antineoplastic drugs present a danger and must be handled differently than other medications.
Oral antineoplastic therapy can be administered in capsule, liquid, or tablet form. The overall efficacy of these agents (Table 1), often called oral agents for cancer, is similar to that of intravenous antineoplastic agents.

Table 1: Common Oral Antineoplastic Agents

<table>
<thead>
<tr>
<th>Category</th>
<th>Drugs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alkylating agents</td>
<td>Busulfan, Chlorambucil, Cyclophosphamide, Melphalan, Temozolomide</td>
</tr>
<tr>
<td>Antimetabolites</td>
<td>Capecitabine, Fludarabine, Methotrexate</td>
</tr>
<tr>
<td>Camptothecins</td>
<td>Topotecan</td>
</tr>
<tr>
<td>Camptothecins</td>
<td>Topotecan</td>
</tr>
<tr>
<td>Epipodophyllotoxins</td>
<td>Etoposide</td>
</tr>
<tr>
<td>Immunotherapeutic agents</td>
<td>Lenalidomide, Pomalidomide, Thalidomide</td>
</tr>
<tr>
<td>Miscellaneous</td>
<td>Hydroxyurea, Procarbazine</td>
</tr>
<tr>
<td>Nitrosoureas</td>
<td>Lomustine</td>
</tr>
<tr>
<td>Targeted therapies</td>
<td>Abemaciclib, Acalabrutinib, Afatinib, Alectinib, Bosutinib, Certinib, Crizotinib, Dasatinib, Erlotinib, Everolimus, Gefinitib, Ibrutinib, Imatinib, Lapatinib, Neratinib, Nilotinib, Olaparib, Osimetinib, Palbociclib, Pazopanib, Ribociclib, Rucaparib, Ruxolitinib, Sorafenib, Sunitinib, Vorinostat</td>
</tr>
</tbody>
</table>

(Data from M.M. Olsen, K.B. LeFebvre, K.J. Brassil [Eds.], [2019]. Chemotherapy and immunotherapy guidelines and recommendations for practice. Pittsburgh: Oncology Nursing Society.)
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They can, however, be affected by the absence or presence of food and digestive enzymes in the stomach and glycoproteins in the gastrointestinal tract that may reduce their bioavailability.\(^1\) Drug metabolism also can be affected by mechanisms such as the cytochrome P450 pathway, which can lead to decreased effectiveness or resistance.\(^1\) Patients with physiologic conditions, such as dysphagia or malabsorption, may require a different mode of treatment or modification in therapy.

Patients being considered for oral antineoplastic therapy should receive a general pretreatment assessment as well as an assessment of their ability to swallow and retain the agent, read and interpret written instructions, open packaging, understand and follow directions for dosing and safe handling, and be aware of possible food-medication or drug-drug interactions \((\text{Box 1}).\)^3\(^3\) Because oral antineoplastic agents can be expensive, the patient’s financial situation (including insurance coverage) should be assessed, and, if appropriate, the patient should be referred to drug assistance programs or social services.

**Box 1: Interactions: Oral Agents and Foods**

**Oral Agents That Interact with Foods**
- Acid-suppressing drugs (e.g., antacids, proton pump inhibitors)
- Antibiotics
- Anticonvulsants
- Antidepressants
- Anxiolytics
- Antifungals
- Antihypertensives
- Anticoagulants (e.g., warfarin)
- Non-steroidal anti-inflammatories
- Vitamin and herbal supplements (e.g., St. John’s wort, ginseng, ginkgo biloba, milk thistle)

**Foods That Interact with Oral Agents**
- Alcohol
- High-fat foods
- Grapefruit juice
- Dairy products
- Tyramine rich foods (e.g., wine, aged cheese, yogurt)


In many cases, patients self-administer antineoplastic agents without supervision by oncology health care professionals.\(^9\)^10\(^13\) Though convenient for patients and caregivers, self-administration may increase the risk of medication errors, compromise therapeutic efficacy and the patient’s safety, and inadvertently expose family members or caregivers to hazardous substances. Because these agents are administered orally, they are incorrectly thought of as less hazardous than antineoplastic agents administered intravenously.\(^12\)
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Oral antineoplastic agents are metabolized much like IV antineoplastic agents; thus, drug metabolites are present in body fluids, and safety precautions should be observed. In addition, oral agents are often taken continually for months or years, necessitating observance of safe handling precautions. Because patients who take oral antineoplastic agents at home may not be seen by a practitioner as frequently as those receiving IV therapy, they need more detailed information on how to manage adverse reactions and when to contact their practitioners for urgent care.

Most oral antineoplastic agents have a narrow therapeutic index; thus, a small increase in dose is associated with a large increase in the likelihood or severity of adverse reactions, and a small decrease in dose may result in therapeutic failure. Missed doses, one of the most common errors in oral antineoplastic therapy, negatively impact the therapeutic effect. The dosing regimens, including dose, timing with respect to meals or other medications, dosing frequency, and duration of therapy, are often very complex. Agents may be dosed based on body surface area or other patient-specific factors (e.g., laboratory test results), may be given intermittently (e.g., 2 weeks of an every-3-week cycle), may require multiple pills, or may have different doses at different times of the day. Many patients receive multiple medications, increasing the risk of drug interactions. Patients may be accustomed to crushing other medications and mixing them with food or fluid, but oral antineoplastic agents should not be manipulated in this way. Whenever possible, the nurse should engage a motivated caretaker to double-check doses and ensure safe handling to decrease the risk of a medication error.

The increased use of oral antineoplastic drugs has resulted in a number of challenges. Systematic education about adherence to oral drug regimens and self-monitoring for adverse reactions are necessary for patient safety. Patient education should include proper storage, handling, preparation, administration, and disposal of oral antineoplastic agents; concurrent cancer treatment and supportive care medications and measures, when applicable; possible drug-drug and drug-food interactions; safe management of body fluids; and a plan for missed doses. A plan for assessment of a patient’s adherence should be implemented.

If the patient expresses concern regarding the accuracy of a medication, the medication should not be given. The concern should be explored, the practitioner notified, and the order verified.

EDUCATION

- Provide developmentally and culturally appropriate education based on the desire for knowledge, readiness to learn, and overall neurologic and psychosocial state.
- Explain the rationale for oral antineoplastic therapy.
- Teach the patient and caregiver the names of the prescribed agent as well as the route, dose, and frequency of the regimen.
- Provide the patient and caregiver with verbal and written information on the route, rationale, dose, frequency, side effects, and self-care measures to minimize or prevent adverse reactions.
- Provide medical contact information, including when to notify the practitioner of adverse reactions or changes in dosing.
- Instruct the patient and caregiver on the administration, storage, and safe handling of oral antineoplastic agents, including the importance of taking them as scheduled,
swallowing oral drugs whole, avoiding medications and foods that interact with the oral antineoplastic agents, and taking unused medication to the clinic or pharmacy for proper disposal.

- Instruct the patient and caregiver on how and when to take the patient’s temperature.
- Instruct the patient and caregiver regarding the potential side effects and adverse reactions to the medication.
- Instruct the patient and caregiver to alert the practitioner or to go to the emergency department if adverse reactions or signs and symptoms of infection occur.
  - Fever of 38°C (100.4°F) or higher
  - Persistent nausea and vomiting
  - Diarrhea or constipation
  - Intolerance to food
  - Decreased urine output
  - Change in mental status
  - New bleeding or bruising
- Teach the patient and caregiver how to manage short-term and long-term side effects.
- Instruct the patient on protective measures to avoid infection.
- Explain critical safety guidelines the patient should follow after receiving antineoplastic therapy. Note that safety precautions should be observed for at least 48 hours after therapy and that in some cases, precautions must be ongoing.
- Instruct the patient and caregiver on the importance of keeping appointments for laboratory tests and clinical examinations.
- Discuss the goals of therapy and the measurement of the response to therapy.
- Discuss fertility issues with patients of childbearing age before, during, and after drug therapy.
- Encourage the patient to discuss with the practitioner whether resuming or maintaining a sexual relationship while taking oral antineoplastic medication is safe. Agents can be considered hazardous, teratogenic, or both.
- Discuss adherence strategies with the patient and caregiver and determine what will work for the patient.
- Encourage questions and answer them as they arise.

**ASSESSMENT AND PREPARATION**

**Assessment**

1. Perform hand hygiene and don PPE as indicated for needed isolation precautions.
2. Introduce yourself to the patient.
3. Verify the correct patient using two identifiers.
4. Obtain the patient’s history.

a. Type of cancer
b. Previous therapy, including dates

Rationale: Careful assessment and documentation of previous therapies allow the practitioner to calculate cumulative doses of agents that have lifetime limits.

c. Toxicities of previous therapy and severity (including radiotherapy)
d. Self-care measures used to minimize toxicities and effectiveness of measures
e. Nutritional status and intake
f. Use of complementary and alternative medicine
g. Previous and concurrent medical and surgical problems
h. List of current medications and supplements (including complementary and alternative therapies)
i. Allergies, including food, drug, and environmental (including latex)
j. Reproductive history
k. Presence of pain, including location, intensity, quality, and factors that make it better or worse
l. Presence of fatigue

5. Assess the patient for specific contraindications to the prescribed medications and advise the practitioner accordingly.

   Rationale: Some antineoplastic agents and some radiotherapy locations may cause late or long-term side effects or have dose limitations that may contraindicate further treatment.

6. Assess the patient’s knowledge regarding health, medication use, and the medication schedule and his or her ability to prepare medications.
7. Assess the patient’s preference for fluids and determine whether he or she must avoid certain foods or fluids (e.g., grapefruit juice) when taking the medication. Explain fluid restrictions, if prescribed.
8. Perform a physical examination.

   a. Hematologic: color of skin and mucous membranes; presence of bruising or petechiae; signs of infection, including fever, cough, erythema, or throat exudate; activity intolerance

      Rationale: Assume that fever in the neutropenic patient is infectious and take steps to manage it accordingly.

      Fever response may be diminished in older patients, those with multiple comorbidities, and those taking certain medications (e.g., acetaminophen, nonsteroidal antiinflammatory drugs, steroid medications).

   b. Neurologic: preexisting motor and sensory deficits; cognitive and behavioral functioning; peripheral neuropathies
   c. Pulmonary: rate, rhythm, and depth of respirations; use of accessory muscles; cough; dyspnea
   d. Cardiovascular: heart sounds, pulses, rate, rhythm
   e. Gastrointestinal: integrity of lips, gums, teeth, mucosa, and tongue; moisture of oral cavity; ability to swallow, presence of bowel sounds; pattern of bowel movements; hemorrhoids; pain; bleeding
   f. Renal: pattern of urinary elimination, including frequency; color and amount of urine
   g. General: body temperature, blood pressure

9. Obtain the patient’s psychosocial history.

   a. Ability to perform self-care and activities of daily living
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10. Determine the patient’s performance status using a standard measurement tool (e.g., Eastern Cooperative Oncology Group system, Karnofsky score).

11. Obtain laboratory test results and diagnostic data.
   a. Complete blood count (CBC) with differential
   b. Serum electrolytes, calcium, liver function tests, serum creatinine, blood urea nitrogen (BUN)
   c. Miscellaneous tests as warranted (e.g., a pregnancy test for a woman of childbearing age who has not had a complete surgical or chemical hysterectomy)

12. Review current laboratory results. Document abnormal values and notify the practitioner before continuing therapy.

13. Verify that informed consent has been obtained.

**Preparation**

1. Verify the patient’s actual height and weight in kilograms. Reweigh the patient if appropriate. Stated, estimated, or historical weight should not be used.

2. Recalculate drug doses based on weight before each new cycle of antineoplastic therapy.

   **Rationale:** Doses of some oral antineoplastic agents are based on body surface area (BSA). Accurate measurement of the patient’s height and weight is needed to perform this calculation. Patients may understate or overstate their height and weight, so measurements must be performed.

3. Obtain and review orders for other medications (e.g., antiemetics, antipyretics, steroids).

4. Verify the sequence of antineoplastic agents to be administered.

5. Obtain safe-handling supplies (e.g., hazardous waste container, PPE).

6. Obtain the medications, check the practitioner’s order, and verify the expiration dates and inspect the medication for discoloration or other loss of integrity.

7. Review medication reference information pertinent to the medication’s action, purpose, onset of action and peak action, normal dose, and common side effects and implications.

**PROCEDURE**

1. Perform hand hygiene and don gloves and appropriate PPE based on the patient’s signs and symptoms and indications for isolation precautions. Use the ONS interim guidelines for PPE recommendations during an emergent shortage of PPE (e.g., pandemic) (Table 2).

<table>
<thead>
<tr>
<th>PPE</th>
<th>ONS recommendations*</th>
<th>Pandemic interim guidelines (in descending order)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gown</td>
<td>Disposable poly-coated gown</td>
<td>• Regular disposable gown (water resistant)</td>
</tr>
</tbody>
</table>
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<table>
<thead>
<tr>
<th>PPE Item</th>
<th>Description</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mask</td>
<td>Mask with face and eye protection required only if splashing likely and for spill cleanup</td>
<td>• Cloth gown (facility laundered) for infection control and nonhazardous drugs</td>
</tr>
<tr>
<td>Eye protection</td>
<td>Mask with eye protection or goggles if splashing likely or spill cleanup</td>
<td>• N95 mask for symptomatic or patients with COVID-19 and hazardous drug spills and cleanup</td>
</tr>
<tr>
<td>Gloves</td>
<td>Double chemotherapy-tested gloves</td>
<td>• Single chemotherapy-tested gloves</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Double standard examination gloves</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Single standard examination gloves</td>
</tr>
<tr>
<td>Shoe covers</td>
<td>Only in area for compounding hazardous drugs</td>
<td>• Work-only, washable shoes</td>
</tr>
</tbody>
</table>

COVID, coronavirus; PAPR, powered air purifying respirator; PPE, personal protective equipment
*Highest-level recommended practice based on supplies of available PPE

2. When no PPE shortage exists, don one pair of disposable, powder-free gloves that have been tested for use with hazardous drugs and, if inhalation exposure is possible, a National Institute for Occupational Safety and Health (NIOSH)-approved respirator (N95).

   Rationale: PPE must be used for the safe administration of hazardous medications. For the administration of an intact tablet or capsule provided in a unit-dose package, a single pair of chemotherapy-tested gloves is sufficient with an N95 respirator when inhalation exposure is possible.11,14

3. Two practitioners or personnel approved to prepare or administer antineoplastic therapies verify the patient using two identifiers, confirm with the patient the planned treatment, and verify the drug name, dose, and route of administration, expiration dates and times, and appearance and integrity of the drugs.

4. Explain the procedure to the patient and ensure that he or she agrees to treatment. Be specific if the patient is to self-administer medications.

5. Administer pretreatment medications (e.g., antiemetics, antipyretics, steroids) per the practitioner’s order.

6. Ensure the six rights of medication safety: right medication, right dose, right time, right route, right patient, and right documentation. Use a bar code system or compare the medication administration record to the patient’s identification band.

7. Ensure that independent double-checks of dose calculations are completed by the two practitioners for any variances between the ordered dose and the recalculated or rounded dose, per the organization’s practice.

8. Assist the patient to a comfortable position for taking oral medications.

9. Administer the oral antineoplastic agent per the practitioner’s order.

10. Discard supplies, remove PPE and discard it in an appropriate hazardous drug waste receptacle, and perform hand hygiene.

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MONITORING AND CARE
1. Monitor the patient for adverse and allergic reactions to the oral antineoplastic drugs. Recognize and immediately treat respiratory distress and circulatory collapse, which are signs of a severe anaphylactic reaction. Follow the organization’s practice for emergency response.
2. Obtain vital signs before therapy.
3. Monitor laboratory test results, including the CBC with differential, electrolytes, BUN, and creatinine before therapy and as ordered by the practitioner depending on the specific drugs given.
4. Assess the patient for acute toxicities associated with the type of drugs administered, such as anaphylaxis.
5. Assess, treat, and reassess pain.

EXPECTED OUTCOMES
- Patient and caregiver describe administration procedure, including names of agents, routes, schedule of administration, schedules for laboratory testing, and clinical examinations.
- Antineoplastic therapy is delivered safely, and all hazardous waste is disposed of properly.
- Patient and caregiver describe potential complications and short-term and long-term side effects of chemotherapy.
- Patient and caregiver describe self-care measures to prevent or minimize side effects of therapy.
- Patient and caregiver understand the side effects that should be reported immediately to the practitioner.
- Patient and caregiver can name appropriate community resources.
- Patient demonstrates self-care skills.
- Patient understands how oral antineoplastic therapy may impact fertility and participates in options to preserve reproductive function and pregnancy prevention.
- Medication is administered per the six rights of medication safety.
- On-time rate is greater than 90%.
- Caregivers and other family members are not exposed to antineoplastic therapy or its byproducts.
- Patient reports adverse reactions in a timely manner.

UNEXPECTED OUTCOMES
- Patient and caregiver unable to describe drug protocol, including names of agents, routes, schedule of administration, schedules for laboratory testing, and clinical examinations
- Medication error
- Patient and caregiver unable to describe potential short-term and long-term side effects of drugs
- Patient and caregiver unable to describe self-care measures to prevent or minimize side effects of therapy
- Patient and caregiver unable to list side effects that should be reported immediately to the practitioner
- Patient and caregiver unable to name appropriate community resources
- Patient unable to demonstrate self-care skills
- Patient hospitalized because of adverse reactions
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- Patient unable to state how therapy may affect fertility and the options available to preserve reproductive function or prevent pregnancy
- Full dose of antineoplastic therapy not taken correctly or as ordered
- Caregivers or other family members exposed to antineoplastic therapy or its byproducts
- Adverse reactions not reported in a timely manner
- Medication not administered per the six rights of medication safety

**DOCUMENTATION**
- Verification of chemotherapy with practitioners involved
  - Name of patient
  - Name of drug
  - Schedule
  - Route
  - Volume
  - Expiration date and time
  - Rate
  - Dose
- Laboratory results
- Name of individual administering antineoplastic agents
- Education and response to education
- Patient’s response to the medication, including any adverse reactions
- Unexpected outcomes and related interventions
- Psychosocial support provided
- Patient’s weight in kilograms per the organization’s practice

**SPECIAL CONSIDERATIONS**
- Older adults may have comorbidities that predispose them to more severe adverse reactions of oral antineoplastic therapy.
- Older adults may metabolize oral antineoplastic agents differently than younger adults.
- Older adults and patients with neurologic problems may have difficulty opening containers or counting pills. Additional measures may be needed to ascertain that the correct medication is available when needed.
- A patient who takes medications for comorbid conditions may experience a drug-drug interaction with antineoplastic agents; a thorough understanding of other drugs being taken, including over-the-counter medications and complementary and alternative medications, is critical to prevent underdosing or overdosing of the antineoplastic agents.
- Most antineoplastic therapy administered to pediatric patients is given IV in the inpatient or outpatient setting. However, some agents (e.g., etoposide, imatinib, mercaptopurine, methotrexate, steroids, thioguanine) are administered via the oral route; thus, parents or caregivers must assist with administration.
- If antineoplastic therapy is administered during pregnancy:
  - The fetus’s gestational age should be established.10
  - Multidisciplinary management with involvement by an oncologist, neonatologist, perinatologist, and obstetrician should occur to optimize outcomes.2
  - Antineoplastic agents are generally avoided during the first trimester of pregnancy and near the time of anticipated delivery.2
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REFERENCES

ADDITIONAL READINGS
Elsevier Skills Levels of Evidence

- Level I - Systematic review of all relevant randomized controlled trials
- Level II - At least one well-designed randomized controlled trial
- Level III - Well-designed controlled trials without randomization
- Level IV - Well-designed case-controlled or cohort studies
- Level V - Descriptive or qualitative studies
- Level VI - Single descriptive or qualitative study
- Level VII - Authority opinion or expert committee reports

Supplies

- Agents for the treatment of extravasation
- Emergency equipment (e.g., oxygen)
- Emergency medications (e.g., epinephrine)
- Hazardous medication disposal container
- Closed IV tubing and connectors with appropriate filters as indicated in the drug package insert
- PPE
  - For isolation precautions: gloves and PPE, as indicated
  - For antineoplastic administration: chemotherapy-tested gloves; disposable, lint-free gown; one pair of disposable, powder-free gloves appropriate for use with hazardous drugs; eye protection and face mask, when splashing is possible; and a NIOSH-approved respirator, when inhalation exposure is possible

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