July 2012

Impact of Community Pharmacists on Management of Cancer Chemotherapy and the Resulting Side Effects

Jacqueline M. Nunner  
*Ohio Northern University*

Jessica Stemen  
*Ohio Northern University*

Courtney Porter  
*Ohio Northern University*

Ellen Hazelet  
*Ohio Northern University*

Mark E. Olah  
*Ohio Northern University, m-olah@onu.edu*

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Impact of Community Pharmacists on Management of Cancer Chemotherapy and the Resulting Side Effects

Jacqueline M. Nunner, fourth-year pharmacy student from Dayton, Ohio; Jessica Stemen, fourth-year pharmacy student from Gahanna, Ohio; Courtney Porter, fifth-year pharmacy student from Canfield, Ohio; Ellen Hazelet, fifth-year pharmacy student from Columbia City, Ind.; Mark Olah, R.Ph., Ph.D., associate professor of pharmacology

This knowledge-based activity is targeted for all pharmacists and is acceptable for 1.0 hour (0.1 CEU) of continuing education credit. This course requires completion of the program evaluation and at least a 70 percent grade on the program assessment questions.

ACPE Universal Activity Number (UAN): 0048-0000-12-032-H01-P

Objectives
1. Identify the most common chemotherapy-induced side effects and associated signs and symptoms.
2. Identify commonly dispensed oral chemotherapy agents associated with chemotherapy-induced side effects.
3. State possible pharmacologic treatments for the most common chemotherapy-induced side effects.
4. Recognize non-pharmacologic ways in which community pharmacists can help manage chemotherapy-induced side effects.
5. Identify resources available to community pharmacists to help manage chemotherapy-induced side effects.
6. Recognize common limitations prohibiting community pharmacists from being able to manage chemotherapy-induced side effects.

Most Common Oral Chemotherapy Side Effects
Debilitating as the disease itself may be, the difficulties faced by patients with cancer are often compounded by the harsh side effects of CINV, diarrhea, constipation, neutropenia, anemia and neuropathy. Despite advances in antiemetic agents, CINV deters many cancer patients from completing otherwise beneficial treatment regimens, and thus remains a paramount concern when antineoplastic treatment is initiated. In addition to causing withdrawal from treatment, nausea and vomiting can have detrimental effects such as serious metabolic disorders, nutritional depletion and anorexia, deterioration of patients’ physical and mental status, esophageal tears, fractures and wound dehiscence. CINV has variable onset, ranging from anticipatory (prior to chemotherapy administration), acute (within 24 hours of initial chemotherapy administration) or delayed (occurring 24 hours to days following treatment). Methotrexate (Rhematrex®), temozolomide (Temodar®) and capecitabine (Xeloda®) are commonly dispensed oral chemotherapy agents associated with CINV. Figure 1 outlines an algorithm for the treatment of CINV in an acute care setting. Options for the non-pharmacological management of CINV, as seen in Table 1, include wearing loose-fitting clothing and eating small, frequent meals. Patients may consider eating toast, crackers, and yogurt; eating ice cubes before meals may also reduce symptoms of CINV. Patients should also drink water throughout chemotherapy to prevent dehydration. Simple hygiene in keeping the oral cavity clean can also help in the management of CINV. Eating before a session of chemotherapy and lying flat after meals are not recommended.

Antiemetic agents are commonly prescribed to help treat CINV pharmacologically. Table 2 lists several chemotherapy agents at various risk categories for CINV and further offers

Abstract
The severe side effects of chemotherapy negatively affect quality of life and may limit the amount of life-saving drug delivered to patients with cancer. These adverse events can be difficult to manage and evidence-based guidelines are lacking. Insufficient supportive care can amplify common side effects, such as chemotherapy-induced nausea and vomiting (CINV), myelosuppression, alopecia, gastrointestinal effects and neuropathy. Therefore, it is important to recognize the most commonly dispensed chemotherapy agents and the side effects that accompany them. Community pharmacists, as easily accessible health care professionals, can provide valuable supportive care to help manage potentially debilitating side effects. However, a major limitation when managing side effects secondary to chemotherapy is the limited access to patient information in most community pharmacies. By allowing community pharmacists increased access to patient health records using technology, limitations experienced in practice can be minimized to improve the community pharmacist’s ability to provide quality care.

Introduction
Hardships endured by cancer patients are often worsened by the severe side effects of chemotherapy. As health care professionals who are easily accessible to patients, community pharmacists can provide valuable supportive care to help manage potentially debilitating side effects in individuals undergoing chemotherapy. This is especially true when dispensing oral agents that do not require administration within an outpatient clinic. While the chemotherapy regimens are often determined by strict evidence-based guidelines, the supportive care offered to patients is not as well-controlled. Insufficient supportive care can amplify the side effects of chemotherapy endured by patients such as chemotherapy-induced nausea and vomiting (CINV), myelosuppression, alopecia, gastrointestinal effects and neuropathy. A major obstacle to pharmacist involvement in managing side effects secondary to chemotherapy is the lack of access to patient information in most community pharmacies. By increasing pharmacists’ access to patient health records using technology, limitations experienced in practice can be minimized to improve the community pharmacist’s ability to provide quality care.
an antiemetic schedule for consideration. Current CINV recommendations include a combination of a neurokinin 1 (NK1) receptor antagonist, a 5-HT3 receptor antagonist and dexamethasone, depending on the emetic risk (mild, moderate or severe) of the chemotherapeutic agent. However, breakthrough CINV can occur and it is necessary for clinicians to monitor a patient's response to antiemetic agents throughout chemotherapy to maintain optimal treatment. Non-pharmacologic treatments such as dietary alterations or acupuncture have also been explored.

Diarrhea is consistently poorly monitored and underreported despite being one of the most prevalent side effects of chemotherapeutic agents, especially those regimens containing Adrucil® (5-fluorouracil or 5-FU) and irinotecan (Camptosar®). Complications can range from suboptimal

Table 1: Non-pharmacological Management of CINV\textsuperscript{19}

<table>
<thead>
<tr>
<th>Non-pharmacological Interventions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wear loose fitting clothing</td>
</tr>
<tr>
<td>Eat small, frequent meals</td>
</tr>
<tr>
<td>Avoid sweet, fatty, high-salt, or spicy foods</td>
</tr>
<tr>
<td>Eat toast, crackers, and yogurt; drink lemon, grapefruit, and ginger teas</td>
</tr>
<tr>
<td>Eat ice cubes before meals and chemotherapy sessions</td>
</tr>
<tr>
<td>Do not lie flat after meals</td>
</tr>
<tr>
<td>Keep the oral cavity clean</td>
</tr>
<tr>
<td>Take deep breaths through the mouth, and place cold towels on head and neck</td>
</tr>
<tr>
<td>Discuss uncontrolled symptoms with health care professionals</td>
</tr>
</tbody>
</table>
therapy to fatality. Prior to treatment, clinicians may evaluate risk factors for diarrhea, including age, gender, bowel pathology, and chemotherapy schedule. Should the patient experience chemotherapy-induced diarrhea, assessment of possible contributing factors such as diet, infection, disease states implicated in malabsorption or inflammation and confounding medications is necessary. Because of the variation in onset, it is recommended that patients at risk or who have developed treatment-induced diarrhea are monitored throughout therapy. Intervention consists of both pharmacologic and non-pharmacologic measures, depending on the severity and duration of the diarrhea. Some oral agents known to cause diarrhea include lopatinib (Tykerb®), erlotinib (Tarceva®) and sorafenib (Nexavar®).6,7 The National Cancer Institute (NCI) classifies the stages of diarrhea as shown in Table 3.6 Table 4 offers appropriate options for the management of each of these stages according to the American Society of Clinical Oncology (ASCO). First-line treatment of uncomplicated diarrhea consists of loperamide at a standard dose (initially 4 mg, then 2 mg every four hours or after every unformed stool; maximum of 16 mg per day) or an increased dose for persistent symptoms if physician recommended. The drug octreotide is indicated in loparena refractory diarrhea and as a preliminary treatment in complicated diarrhea. Fluoroquinolone antibiotics or vancomycin are recommended for prophylaxis or if infectious diarrhea is suspected. Other treatments such as atropine, budesonide, diphenoxylate, activated charcoal or probiotics are less commonly used.9

Like diarrhea, constipation is also a common side effect of numerous chemotherapy treatments that is underreported and undertreated. Patients undergoing chemotherapy may suffer from constipation due to a number of reasons including dehydration, neuropathy, decreased exercise tolerance, electrolyte imbalances, antiemetic agents and use of analge-

### Table 2: Emesis Risk of Various Chemotherapy Agents and Proposed CINV Treatment4

<table>
<thead>
<tr>
<th>Emetic Risk</th>
<th>Chemotherapeutic drug</th>
<th>Antiemetic schedule</th>
</tr>
</thead>
<tbody>
<tr>
<td>High (&gt;90%)</td>
<td>Cisplatin, Mechlorethamine, Streptozocin, Dacarbazine, Carmustine, Dactinomycin, Cyclophosphamide (&gt;1500 mg/m²)</td>
<td>5-HT3 serotonin receptor antagonist: Day 1 Dexamethasone: Days 1-4 Aprepitant: Days 1-3</td>
</tr>
<tr>
<td>Moderate (30 to 90%)</td>
<td>Oxaliplatin, Cytarabine (&gt;1000 mg/m²), Carboplatin, Ifosfamide, Cyclophosphamide (&lt;1500 mg/m²), Doxorubicin, Daunorubicin, Epirubicin, Idarubicin, Idarubicin, Iriotecan</td>
<td>5-HT3 serotonin receptor antagonist: Day 1 Dexamethasone: Day 1(2,3)a Aprepitant: Days 1,2,3</td>
</tr>
<tr>
<td>Low (10 to 30%)</td>
<td>Paclitaxel, Docetaxel, Mitoxantrone, Topotecan, Etoposide, Pemetrexed, Methotrexate, Mitomycin, Gemcitabine, Cytarabine (&lt;1000 mg/m²), Fluorouracil, Bortezomib, Cetuximab, Trastuzumab</td>
<td>Dexamethasone: Day 1</td>
</tr>
<tr>
<td>Minimal (&lt;10%)</td>
<td>Bevacizumab, Bleomycin, Busulfan, Fludarabine, Vincreistine, Vinorelbine, Vinblastine, 2-Chlorodeoxyadenosine, Rituximab</td>
<td>Prescribe as needed</td>
</tr>
</tbody>
</table>

*aMay omit days 2 and 3 if aprepitant is given; for patients receiving a combination of anthracycline and cyclophosphamide

### Table 3: NCI Classification of Stages of Diarrhea

<table>
<thead>
<tr>
<th>Toxicity Grade</th>
<th>Diarrhea</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Increase of &lt;4 stools/day over baseline</td>
</tr>
<tr>
<td></td>
<td>Mild increase in ostomy output compared with baseline</td>
</tr>
<tr>
<td>2</td>
<td>Increase of 4-6 stools/day over baseline</td>
</tr>
<tr>
<td></td>
<td>Intravenous fluids &gt;24 hours</td>
</tr>
<tr>
<td></td>
<td>Moderate increase in ostomy output compared with baseline</td>
</tr>
<tr>
<td></td>
<td>Not interfering with daily living</td>
</tr>
<tr>
<td>3</td>
<td>Increase of &gt;7 stools/day over baseline</td>
</tr>
<tr>
<td></td>
<td>Incontinence</td>
</tr>
<tr>
<td></td>
<td>Intravenous fluids</td>
</tr>
<tr>
<td></td>
<td>Severe increase in ostomy output compared with baseline</td>
</tr>
<tr>
<td></td>
<td>Interfering with daily living activities</td>
</tr>
<tr>
<td>4</td>
<td>Life-threatening consequences (e.g., hemodynamic collapse)</td>
</tr>
<tr>
<td>5</td>
<td>Death</td>
</tr>
</tbody>
</table>
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Table 4: ASCO Recommended Guidelines for the Management of Treatment-induced Diarrhea

<table>
<thead>
<tr>
<th>Diarrhea CTC grade</th>
<th>Management</th>
</tr>
</thead>
<tbody>
<tr>
<td>Uncomplicated grade 1-2</td>
<td>Stop all lactose containing products Drink 8 to 10 large glasses of liquid/day Eat frequent small meals</td>
</tr>
<tr>
<td>Grade 2</td>
<td>Hold cytotoxic chemotherapy and consider lapatinib dose reduction Administer standard dose of loperamide (consider continuation of loperamide until diarrhea-free for 12 hours)</td>
</tr>
<tr>
<td>Grade 3 or 4 diarrhea or grade 1 or 2 with complicating featuresa</td>
<td>Consider hospital admission Administer octreotide Use intravenous fluids if appropriate Use prophylactic antibiotics as needed (especially if diarrhea is persistent beyond 24 hours or there is fever or grade 3-4 neutropenia) Hold both cytotoxic chemotherapy and lapatinib</td>
</tr>
</tbody>
</table>

aGrade 3 cramping, nausea/vomiting, decreased performance status from baseline; >grade 2 fever, any sepsis, grade 3 or 4 neutropenia, grade 3 bleeding, grade 2 dehydration.

Neutropenia is a significant side effect because toxicity related to neutropenia limits the dose of chemotherapy that can be tolerated. Neutropenia is defined as an absolute neutrophil count (ANC) of less than 500 cells/mm³ or an ANC that is expected to decrease to less than 500 cells/mm³ during the next 48 hours of monitoring.11 The degree and duration of neutropenia predispose the chemotherapy patient to infection due to suppression of the production of neutrophils, a key component of innate immunity and a significant sign of infection.12 Although all chemotherapy patients are at risk of developing neutropenia, challenges still exist in determining those populations at a greater risk, and presentation of chemotherapy-induced neutropenia may be limited to a fever alone. Prevention of infection is key, and antibiotic, antiviral or antifungal prophylactic therapy is based on patient characteristics.11 It is important for pharmacists to stress the increased risk of infection to patients and educate them on the signs and symptoms. While it is difficult to recommend pharmacologic treatment from a community pharmacist’s setting, non-pharmacologic suggestions can be made, including limiting exposure to infection by practicing good hygiene and avoiding crowded public areas.

Anemia may originate from decreased production of red blood cells (RBCs), increased destruction of RBCs or blood loss, and is characterized by a decrease in normal hemoglobin concentration or RBC count. In patients undergoing cancer treatment, this may result from the myelosuppressive nature of cytotoxic chemotherapy such as Sutent® (sunitinib), or from the disease itself. Patients suffering from anemia can experience dizziness, fatigue and shortness of breath. In addition to significantly altering quality of life, anemia may further complicate treatment due to delays associated with therapy. Typically anemia is treated using erythropoiesis-stimulating agents (ESAs), blood transfusions or iron supplementation to maintain hemoglobin levels and patients should be directed to their physician for treatment.13 Educating patients on the signs and symptoms of anemia and quickly re-
ferring them back to their physician is the best non-pharmacologic way to care for this side effect from a community pharmacist’s standpoint.

Neuropathy presents as a difficult side effect of many chemotherapeutic agents, both in terms of diagnosis and treatment. Unlike anemia, which can be diagnosed based on lab values and symptoms, neurologists managing cancer patients must rely largely on the pattern of neuropathy associated with specific agents. Neurotoxicity is often dependent on the cumulative dose of the treatment; severity of neuropathy increases with the duration of treatment and progression is halted with termination of treatment. Loss of sensations, paresthesia, pain and loss of motor function all vary depending on schedule of treatment and the agent used. Common chemotherapeutic agents implicated in neuropathy include platinum compounds, vinca alkaloids and taxanes. Because treatment of chemotherapy-induced neuropathy is typically symptomatic, prevention and management of risk factors, such as pre-existing neuropathy upon initiation of treatment, is key in this patient population.¹⁴

**Oncology Resources**

When patients inquire about other side effects not addressed above, there are a few educational resources for further information. These include The NCCN Clinical Practice Guidelines in Oncology website (http://www.nccn.org) which separates treatment guidelines by site and often includes a section on supportive care specific to each cancer type. Additionally, access to relevant literature and case reports in oncology can be found at the American Society of Clinical Oncology website (http://www.asco.org). Lastly, but perhaps most importantly, contacting a board certified clinical oncology pharmacist who deals with these drugs on a daily basis would most likely provide the information necessary to inform the patient. When used together, these resources can help community pharmacists not entirely familiar with chemotherapeutic drugs provide excellent, continuous care to patients undergoing chemotherapy.

**Clinical Trials**

*Chauvelot et al. 2010*¹⁵

Community pharmacists currently aid in the management of multiple chronic disease states such as heart failure. Many of the principle strategies and services employed in heart failure care are applicable to the management of cancer chemotherapy as well. Chauvelot and colleagues used two sets of surveys to determine the role of the pharmacist in heart failure management from the viewpoints of both patients and pharmacists.¹⁵ Patients viewed community pharmacists as a medication therapy specialist, but less than 40 percent of survey participants felt the pharmacist should take on larger roles in therapy management such as disease explanation and medical follow-up. Pharmacists felt they were knowledgeable about the disease state and could educate the heart failure patient in 68 percent of cases. Community pharmacists are ideally placed to educate patients about their disease states and improve medication adherence, in addition to traditional roles as drug dispensing experts. The difficulty arises in overcoming current perceptions about the role of the community pharmacist from both patients and other healthcare providers. Pharmacists must also be empowered to play a larger role in disease state management through continuing education.

*Dohler et al. 2011*¹⁶

The objective of a study by Dohler et al. was to identify responsibilities of health care professionals in the management of cancer chemotherapy by using focus group discussions consisting of clinical pharmacists with a background in cancer care.¹⁶ Clinical pharmacists, physicians and nurses used a two-round Delphi process to allocate the identified responsibilities specifically to the aforementioned professionals. Members of the DKG, Germany’s largest multiprofessional association in oncology, completed a survey to rate their acceptance of the proposed tasks and their allocation to various professions. The study identified areas for pharmacist involvement in patient education and counseling in addition to the prevention of drug related problems. Results showed that the pharmacist’s role included eight of 11 proposed patient education tasks focused on increasing medication compliance. Pharmacists were also pertinent to seven of 20 proposed tasks in preventing medication issues, including screening for interactions. With up to 75 percent of cancer patients using oral, complementary chemotherapy treatments, the role of the pharmacist is crucial. Unfortunately, according to additional surveys, pharmacists are not yet able to perform their allocated tasks. The primary issue is that pharmacists do not feel as though they are an integral part of the health care team. However, as evidenced by the allocation of tasks, physicians, nurses and pharmacists are all necessary to effectively manage a patient’s cancer chemotherapy regimen.

Community pharmacists can practice some of the roles proposed for clinical pharmacists in this study. Patient education, improving medication adherence and screening for drug-drug interactions are all tasks that are performed on a regular basis in the community pharmacy. Pharmacists currently use these services to manage heart failure; the same strategy can be applied to cancer chemotherapy.

*Simons et al. 2011*¹⁷

Additionally, in a study assessing intensified pharmaceutical care, Simons et al. conducted a prospective, multi-centered, observational cohort study with control group.¹⁷ The intervention group in the study received intensified pharmaceutical care. Subjects were recruited from three hospitals. Fifty subjects were enrolled in the study and divided evenly between the control group and intervention group. The intensified pharmaceutical care included education about the drug capecitabine, details on the treatment regimen, risks of noncompliance and information on other current medications all from a registered pharmacist. Later, subjects received a medication dosing schedule and information on possible adverse events including preventative methods. A pharmacist contacted each subject in the intervention group once during each cycle of chemotherapy via telephone to answer questions and provide further counseling.
Adherence to medication therapy was monitored using a Micro Electronic Monitoring (MEMS™) vial that registered every time the subject opened the container. Limitations of the MEMS™ system include the inability to determine if the patient actually swallowed the medication and how many pills the patient took out of the container each time it was opened. The primary endpoint was daily adherence. The intervention group had a mean daily adherence of 96.8 percent which was significantly higher than 87.2 percent mean daily adherence in the control group. However, overall adherence between the two groups was not statistically significant though the intervention group was higher than the control group (97.9 percent and 90.5 percent, respectively). None of the subjects in the intervention group had a daily or overall adherence below 80 percent. Five subjects in the control group (21 percent) had an overall adherence below 80 percent, and six subjects (25 percent) showed daily adherence less than 80 percent.

This study shows that intense, individualized pharmaceutical care, including patient education, has the potential to improve daily adherence to medications. With many oral chemotherapeutic agents available today, pharmacists have the ability to maximize patient therapy while minimizing compliance-related treatment failure.

**Improvement of Pharmacists’ Management of Chemotherapy Side Effects**

Limitations must be overcome to optimize pharmacists’ management of chemotherapy side effects. Due to underuse of health information technology (HIT), fragmented health care is a common concern for all patients and can be especially troublesome for oncology patients. HIT consists of a variety of ways to transmit health information electronically among patients, health care professionals, payers and insurers. Promoting national use of electronic health records (EHR), personal health records (PHR) and clinical data exchanges would create a continuum of care for patients allowing health care professionals nationwide to have access to a patient’s entire health record when needed. When dispensing medications to patients in a community setting, pharmacists could be sure a complete drug utilization review is conducted and all aspects of a patient’s chemotherapy regimen, including side effects and drug-drug interactions are addressed. Ensuring pharmacists who directly interact with patients are properly informed of patients’ medical history creates an opportunity for increased patient education regarding treatment side effects and improvement in chemotherapy adherence.

**Conclusion**

Through increased management of supportive care, community pharmacists can decrease patient incidence of debilitating side effects. Recognizing these side effects, recommending drug therapy and educating patients on proper management allows for optimal anticancer therapy. While limitations to patient information exist, pharmacist involvement not only improves patients’ quality of life, it allows for the best chance possible to fight their disease.

**References**


Assessment Questions

1. Which is NOT a common chemotherapy-induced side effect?
   a. Nausea
   b. Constipation
   c. Loss of sight
   d. Anemia

2. Which is NOT a common sign or symptom of anemia?
   a. Dizziness
   b. Fatigue
   c. Shortness of breath
   d. Clubbing of fingers

3. All of the following are typical in patients suffering from neuropathy associated with chemotherapy EXCEPT:
   a. Neurotoxicity is often dependent on the cumulative dose of the treatment
   b. Severity of neuropathy increases with the duration of treatment
   c. Progression of neuropathy is halted with termination of treatment
   d. A diagnosis of neuropathy is made using clinical lab values

4. Which oral chemotherapy agent is mismatched with one of its common side effects?
   a. Methotrexate; CINV
   b. Erlotinib; neuropathy
   c. Lapatinib; diarrhea
   d. Sunitinib; anemia

5. What are the antiemetic medications required for a patient receiving highly emetogenic chemotherapy?
   a. S-HT3 serotonin receptor antagonist, dexamethasone, and aprepitant
   b. S-HT3 serotonin receptor antagonist and dexamethasone
   c. Only non-pharmacologic treatment is warranted at this time
   d. S-HT3 serotonin receptor antagonist

6. What pharmacologic intervention is appropriate for a patient suffering from grade 2 diarrhea?
   a. Administer octreotide
   b. Administer standard dose of loperamide
   c. Use of prophylactic antibiotics
   d. Increase of lactulose containing products

7. What non-pharmacologic suggestions should NOT be made to patients suffering from CINV?
   a. Wear loose fitting clothing
   b. Eat small, frequent meals
   c. Increase intake of sweet, fatty, high-salt, or spicy foods
   d. Eat ice cubes before meals

8. What non-pharmacologic suggestions should be made to patients taking chemotherapy agents prone to causing neutropenia?
   a. Explain the signs and symptoms of infection
   b. Instruct patients to practice good hygiene
   c. Instruct patients to avoid large crowded areas
   d. All of the above

9. What resources are available to aid in patient education and monitoring of chemotherapy agents?
   a. NCCN Clinical Practice Guidelines in Oncology
   b. ASCO website
   c. Board certified clinical oncology pharmacist
   d. All of the above

10. A common limitation of community pharmacists' management of patient side effects is:
    a. The underuse of HIT
    b. Too much patient information
    c. Limited access to patients
    d. Easy access to patient lab values
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Program Title: Impact of Community Pharmacists on Management of Cancer Chemotherapy and the Resulting Side Effects
UAN: 0048-0000-12-032-H01-P  CEUs: 0.1

All information must be printed CLEARLY to ensure accurate record keeping for attendance and the awarding of continuing education credit. Certificates will be distributed as a PDF document to a valid email address.

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Pharmacy License #: State: ONU Alumni? Y N

Program Content:

<table>
<thead>
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<th>The program objectives were clear.</th>
<th>Strongly Disagree</th>
<th>Strongly Agree</th>
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<td>1 2 3 4 5</td>
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<tr>
<td>Identify the most common chemotherapy-induced side effects and associated signs and symptoms.</td>
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<td>Recognize non-pharmacologic ways in which community pharmacists can help manage chemotherapy-induced side effects.</td>
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<td>Material presented was relevant to my practice.</td>
<td>1 2 3 4 5</td>
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</tbody>
</table>

Comment/Suggestions for future programs:

Thank you!

Answers to Assessment Questions—Please Circle Your Answer


Any questions/comments regarding this continuing education program can be directed to Lynn Bedford, Advanced Administrative Assistant for the Office of Continuing Education (email: l-bedford@onu.edu, phone 419-772-1871).

Ohio Northern University is accredited by the Accreditation Council for Pharmacy Education as a provider of continuing pharmacy education. This program is eligible for credit until 05/08/15.