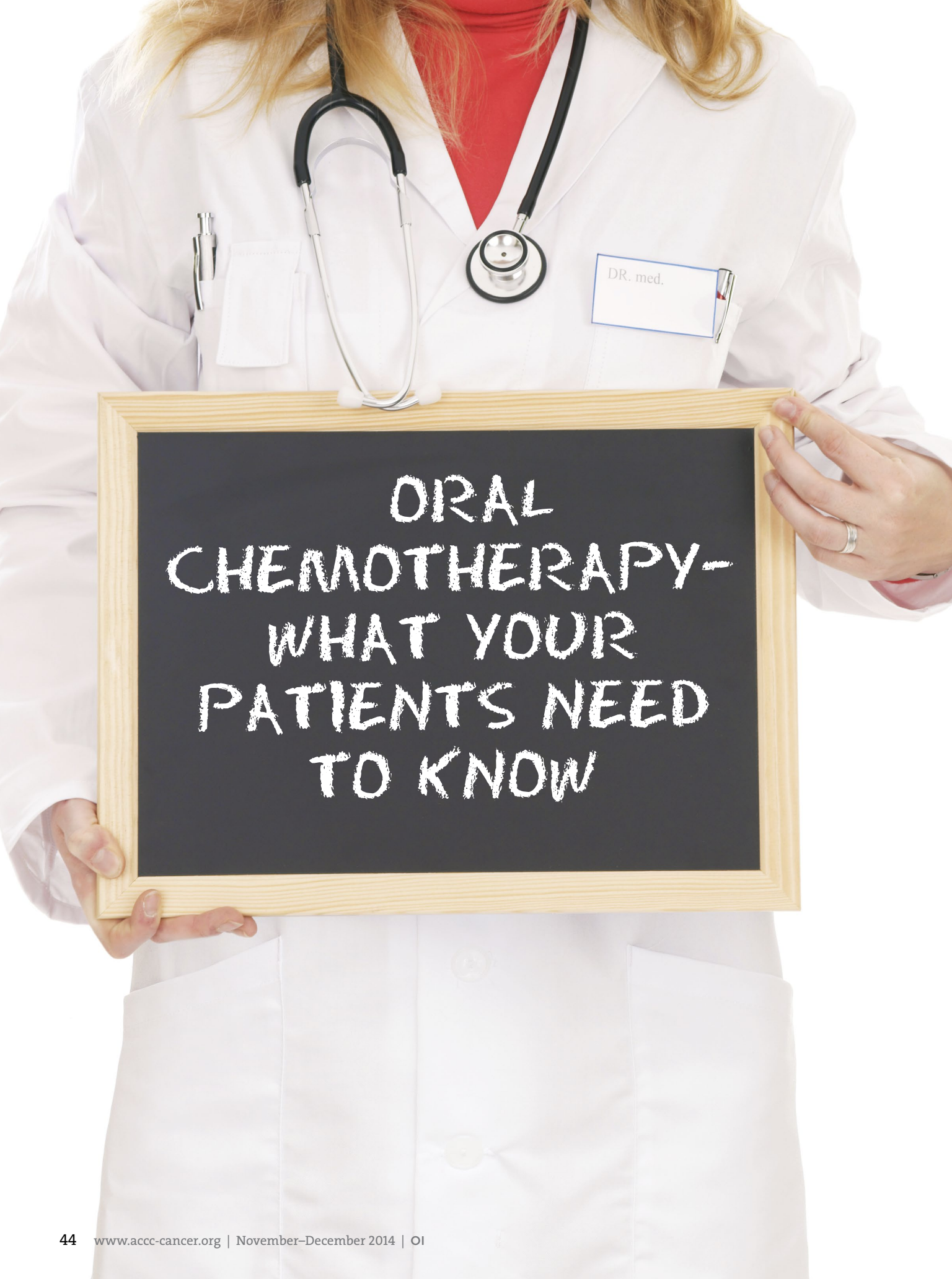
DR. med.
ORAL CHEMOTHERAPY- WHAT YOUR PATIENTS NEED TO KNOW

BY ELIZABETH BETTENCOURT, RN, MSN, OCN

Cancer treatment delivery is undergoing a shift from intravenous to oral treatment. In fact, it is projected that the use of oral chemotherapy will more than double in the next several years.[1] One estimate puts 25 percent of anticancer agents in the research pipeline as "designated for oral administration."[2] This increased use of oral chemotherapy agents is moving the administration of cancer treatment from a medical facility to a patient's home. While more convenient for patients, this loss of direct medical supervision during cancer treatment administration can lead to adherence and safety issues for patients. The patient and their caregivers are now responsible for ensuring that the patient receives the right drug and the right dose, at the right time.

Many barriers can affect a patient's adherence to an oral chemotherapy regimen, including:

- Cost
- Dosing complexity
- Forgetfulness
- Distractions of everyday life
- Side effects
- Misinterpretation of the instructions.

Several studies show that patients on long-term medications geared towards decreasing mortality, such as oral chemotherapy, have a low adherence rate of 42 percent.[3] Nurses are on the front line of the medical team and must take steps to prevent or minimize non-adherence, adverse effects, and toxicities.[4] Comprehensive patient education can provide patients with the tools they need to adhere to their prescribed oral chemotherapy regimen. This article presents vital information for patients starting oral chemotherapy.

The Oral Chemotherapy Nurse Navigator Role

As the only oral chemotherapy nurse navigator (OCNN) at the Palo Alto Medical Foundation, (PAMF) Sunnyvale and Mountain View, Calif., I have implemented a process to ensure that patients on oral chemotherapy are thoroughly educated and monitored throughout the course of therapy. In brief, here is how our process works.

Comprehensive patient education can provide patients with the tools they need to adhere to their prescribed oral chemotherapy regimen.

I am notified by the physician when an oral chemotherapy agent is prescribed, and I make the initial contact with patients to discuss the prescription and begin the education process. The actual time from prescription writing to delivery of the drug to the patient can vary anywhere from two days up to as long as three weeks. Prior authorization is required for most oral chemotherapy. As copayments are unaffordable for many, additional time is often necessary to help patients obtain grants from copayment assistance organizations or financial assistance from drug manufacturers.

Once the prescription is ready for pick up at the pharmacy or ready for delivery to the patient, I meet with each patient for a teaching session specifically tailored to the patient's prescribed treatment. This teaching session can be as short as 30 minutes, but can take longer, depending on the patient needs. Education is thorough, patient and drug specific, and continuous throughout the patient's course of therapy. Three to five days after the start of treatment, I contact the patient (usually by phone) to assess side effects, reinforce education, answer questions, and provide emotional support. After that period, patients are contacted once a week for the next six to eight weeks, then monthly as needed for the length of their treatment.

Adjustments to this monitoring schedule are made based on individual patient needs. For example, patients on multiple medications for varied conditions or with complicated oral chemotherapy dosing schedules may need more frequent contact to assist with adherence to the oral chemotherapy. Patients on long-term treatment, such as imatinib (Gleevec®) and dasatinib (Sprycel®), may require less frequent monitoring, especially if no changes in the treatment plan occur.

Patient education prior to the start and during oral chemotherapy treatment is an essential part of assisting patients with adherence and should include education about:[5]

1. Storing, handling, and disposing of oral chemotherapy
2. Concurrent cancer treatment and supportive care medications and/or measures (if applicable)
3. Possible drug/drug and drug/food interactions
4. The plan for missed doses.

Other areas specific to oral chemotherapy that patients should be educated about include:

- Dosing requirements
- Monitoring parameters
- Blood testing requirements
- Side effects and management
- Drug access, which includes helping patients identify and access resources to help pay for their drug(s)
- The refill process.

Oral Chemotherapy Storage

Based on information from the FDA-approved package inserts, I educate patients and caregivers on the proper storage of their oral chemotherapy medication(s). Most oral chemotherapy agents should be stored at room temperature (68° to 77°F). Some drugs can be exposed to higher temperatures up to 86° F for a limited amount of time. Refer to the drug manufacturer for specific information about temperature exposure. Chlorambucil (Leukeran®) and trametinib (Mekinist®) require refrigeration. Regorafenib (Stivarga®) expires 28 days after the bottle is opened and requires the desiccant package to remain in the bottle. Some oral agents require protection from light. Patients must be aware of these temperature and storage requirements to ensure that these medications—some of which are delivered via specialty pharmacies directly to the patient—are not left unattended in extreme temperatures. In my education session, I tell patients to always follow the storage requirements recommended by the drug manufacturer.

Handling Oral Chemotherapy

While many of the oral chemotherapy agents currently in use and in research are targeted agents and not considered cytotoxic, there is not much known regarding the risks of handling these agents.[6] Patients and caregivers must be educated in measures to ensure their safety, as well as the safety of the environment. During my education session, I use several resources that offer guidelines for the handling of oral chemotherapy by patients and their caregivers, such as:[7,8]

- Oral chemotherapy should always be kept away from children and pets.
- Oral chemotherapy should not be chewed, crushed, cut, or dissolved.
- It is recommended that patients administer the chemotherapy agent to themselves. However, if a caregiver is preparing the medication, it is encouraged that gloves be worn. An alternative for those who may have limited financial resources would be to pour the oral chemotherapy agent into a bowl, or the lid of the pill bottle, and then pour the pills into the patient's hand or mouth. The bowl should be cleaned with soap and water. The patient does not need to avoid contact with the chemotherapy agent by wearing gloves. However, both the patient and the caregiver should wash their hands after handling the oral chemotherapy drug.
- Many patients store their oral medications in pill boxes. This can help improve patient adherence to the dosing schedule. The pill box should be used only for the oral chemotherapy, and washed with soap and water when treatment has been completed. Pill boxes are not to be used for Stivarga. Several oral chemotherapy drugs are dispensed in blister packs, eliminating the need for pill boxes.
- Patients, caregivers, pharmacists, and nurses should always wash their hands with soap and water any time contact with an oral chemotherapy agent occurs.
- Common side effects of oral chemotherapy are nausea, vomiting, and diarrhea. If a patient on oral chemotherapy soils linens with bodily fluids, launder soiled linen separately from non-soiled linen.

Patient education is key to ensuring the safe handling of oral chemotherapy agents.

Disposal of Oral Chemotherapy

Proper disposal of oral chemotherapy agents can help keep people safe and protect the environment. Oral chemotherapy agents, while not cytotoxic, are still considered hazardous and therefore must be disposed of properly. Most cities have a hazardous waste disposal policy that patients can follow, but most fire stations and retail pharmacies will *not* dispose of oral chemotherapy.

(continued on page 48)

Proper disposal of oral chemotherapy agents can help keep people safe and protect the environment.

Figure 1. Sample Calendar for Patients on Intravenous Carfilzomib (Kyprolis®) and Oral Lenalidomide (Revlimid®)

SUN	MON	TUE	WED	THU	FRI	SAT
					1 Revlimid*	2 Revlimid
3 Revlimid	4 Revlimid	5 Revlimid	6	7	8	9
10	11 Labs: CBC (complete blood count) and CMP (comprehensive metabolic panel)	12 MD Visit	13 C3D1 Kyprolis Dexamethasone IV Revlimid	14 C3D2 Kyprolis Dexamethasone IV Revlimid	15 Revlimid	16 Revlimid
17 Revlimid	18 Revlimid	19 Revlimid Labs: CBC	20 C3D8 Kyprolis Dexamethasone IV Revlimid	21 C3D9 Kyprolis Dexamethasone IV Revlimid	22 Revlimid	23 Revlimid
24 Revlimid	25 Revlimid	26 Revlimid Labs: CBC	27 C3D15 Kyprolis Dexamethasone IV Revlimid	28 C3D16 Kyprolis Dexamethasone IV Revlimid	29 Revlimid	30 Revlimid
31 Revlimid						

* Notes: Revlimid 15 mg daily for 21 days, then one week off.

Patients should be contacted within the first week of starting oral chemotherapy, and then weekly for the next few weeks.

In addition, only a few drug manufacturers provide instructions on oral chemotherapy disposal. Celgene, the maker of lenalidomide, thalidomide, and pomalidomide, provides patients with packaging material to return unused medications. Hospitals and practices must ensure that their patients are provided proper disposal instructions for these medications.

Concurrent Cancer Treatment

Oral chemotherapy can be prescribed as a single agent or as part of a multi-drug regimen for the treatment of cancer, so patients must be instructed in all aspects of the chemotherapy regimen. Many single agent regimens require the concomitant use of steroids, such as dexamethasone or prednisone. Patients receiving oral chemotherapy as part of a multi-drug intravenous chemotherapy regimen will need specific instructions about how the oral chemotherapy dosing correlates with the intravenous chemotherapy.

Patients have many different learning styles so educational tools should be tailored to support them. Also, some patients will benefit from a calendar that indicates the actual days and times to take oral chemotherapy (Figure 1, page 47). Several apps are now available for patients to use on their smartphones to help remind them to take their oral chemotherapy medications.

At PAMF, I give each patient a one-page summary of the important issues related to his or her specific drug regimen (see Figure 2 and Figure 3, right). I identify the best mechanism to educate each patient to ensure the correct dosing of oral chemotherapy.

Supportive Care Medications & Measures

Oral chemotherapy agents have side effects unique to each drug category. Hypertension, QT interval prolongation of the heart, and lab abnormalities are common side effects for many oral chemotherapy agents. Hypertension and hypertensive crises are not uncommon with pazopanib and regorafenib in the first one to three weeks of therapy. Patients may require blood pressure monitoring either daily or weekly, depending on their personal health history. Antihypertensive medications may be required.

The use of EKG monitoring of the QT interval may be required for patients receiving some oral chemotherapy (i.e., sunitinib, sorafenib, and crizotinib), with or without concomitant use of cardiac medications.

To ensure patient safety, hospitals and practices must monitor continually for potentially serious side effects. Further, patients require frequent reminders to follow through with monitoring requirements. At PAMF, I also educate patients about the prescribed drugs that treat these conditions.

Many oral chemotherapy treatments require frequent laboratory monitoring of blood counts, blood glucose, and liver enzymes. Patients need to know:

1. What testing is required
2. When to have the blood work done
3. If fasting is required.

For example, some oral chemotherapy (i.e., dasatinib, lenalidomide) can cause myelosuppression (a condition in which bone marrow activity is decreased, resulting in fewer red blood cells, white blood cells, and platelets) in the first few weeks of therapy and complete blood counts may be required weekly.

Hepatotoxicity (chemical-driven liver damage) is a potential serious side effect of many oral chemotherapy agents. Patients may require monitoring of the liver enzymes at least every two weeks for the first two to three months of treatment.

Hyperglycemia (high blood glucose) is also a common side effect of some oral chemotherapy agents.

Other common side effects of oral chemotherapy include nausea and vomiting, diarrhea, mouth sores, and skin rash, so patients must be educated on how to manage these side effects as well. An important component of this education is to discuss with the patient the need to inform the practice or hospital if these side effects occur. Many times, patients on oral chemotherapy accept these side effects as a normal part of treatment and continue on with therapy. This can result in over-adherence, a condition that can worsen the side effects and possibly result in hospitalization. At PAMF, I provide patients with their providers' contact information—not only for regular business hours, but for afterhours as well. I encourage patients to use the afterhours support if needed, since waiting over a weekend can result in severe toxicity and declining health.

Because it is not unusual for a patient to be prescribed an oral chemotherapy agent and not contact or return to see the provider for several months—especially if side effects have not occurred—follow-up care with these patients is essential. Patients should be contacted within the first week of starting oral chemotherapy, and then weekly for the next few weeks.

(continued on page 50)

Figure 2. Sample of a Patient-Specific One-Page Summary for Daily Pazopanib (Votrient®)

VOTRIENT (PAZOPANIB) PATIENT INSTRUCTIONS

MEDICATIONS
- Votrient _____ tablets (_____ mg) once a day every day.
- Take Votrient on an empty stomach, at least 1 hour before or 2 hours after food.

BLOOD MONITORING
- CMP (comprehensive metabolic panel) performed every 2 weeks for 2 months, then every month.
- CBC (complete blood counts) performed once a month.
- BP (blood pressure) performed once a week for 6 weeks, then every month.

FREQUENCY OF MD/NP VISITS
- You will see the doctor (MD) or nurse practitioner (NP) 2 weeks after starting therapy, and then every month.
- You will have blood work done 1 to 3 days prior to each MD/NP visit(s).

OTHER PRECAUTIONS
- Do not eat or drink grapefruit or star fruit juices or products while on Votrient.
- Inform your oncologist if you are prescribed an antibiotic as some antibiotics can interfere with Votrient.

DISPENSING PHARMACY

Name _____

Address _____

Phone number _____

Figure 3. Sample of a Patient-specific One-Page Summary for the V-BIRD Regimen

V-BIRD PATIENT INSTRUCTIONS ONE CYCLE = 21 DAYS

MEDICATIONS
- Revlimid _____ mg (_____ capsule) once a day for 14 days, then 7 days off.
- Dexamethasone _____ 4 mg tablets by mouth all at once on days 1, 8, and 15 (same day, every week).
- Velcade infusion on days 1, 8, and 15.
- Aspirin, 81 mg (1 tablet) every day.
- Acyclovir, 1 tablet, twice a day, every day.
- Bactrim (Septra), 1 tablet, twice a day on Saturdays and Sundays only.

BLOOD MONITORING
- CBC (complete blood counts) every week for 8 weeks, and then every 3 weeks, a few days before the cycle starts.
- CMP (comprehensive metabolic panel) every three weeks, a few days before the cycle starts.
- Pregnancy test every week for the first 4 weeks, and then 7 days prior to each cycle.

FREQUENCY OF MD/NP VISITS:
- You will see the doctor (MD) or nurse practitioner (NP) every 3 weeks prior to the start of each cycle.
- You will have blood work done prior to each MD/NP visit(s).

OTHER PRECAUTIONS
- You will take the Celgene phone and/or Internet survey every 3 weeks, 7-10 days prior to each cycle.
- The pharmacy should call every 3 weeks to arrange delivery of Revlimid to your home.

DISPENSING PHARMACY

Name _____

Address _____

Phone number _____

This follow-up lets providers:

- Assess for side effects
- Reinforce side-effect management and obtain the required laboratory monitoring
- Ensure adherence to the dosing regimen
- Answer any questions that patients and caregivers may have.

Proactively connecting with patients receiving oral medications can lead to early intervention after side effects develop, resulting in better adherence to the treatment regimen.

Drug/Drug & Drug/Food Interactions

Patient education about oral chemotherapy must include a discussion about drug and food interactions. Oral chemotherapy can be affected by prescription and over-the-counter medications, as well as supplements and food. A common group of medications that can affect the blood levels of many oral chemotherapy agents are CYP3A inducers and inhibitors. Inducers can reduce blood levels of oral chemotherapy while inhibitors can increase the blood level. CYP2D6 and CYP2C9 inducers and inhibitors are another group of medications that interact with several oral chemotherapy agents. Patients on any of these medications may require adjustment of the oral chemotherapy dose, or discontinuation of the interacting medication.

Patients on anticoagulants require close monitoring. INR (international normalized ratio) levels can be affected by some oral chemotherapy (i.e., capecitabine) and should be monitored more frequently in the first few weeks of treatment, if warranted.

Patients must be educated to inform their oncologist when they are prescribed antibiotics by another provider. Erythromycin, ciprofloxacin, and clarithromycin are not recommended or require close monitoring when taken while on some oral chemotherapy. Sometimes, it is necessary to interrupt the oral chemotherapy agent while on a course of antibiotics.

Antacids and proton pump inhibitors can interfere with the absorption of oral chemotherapy. While on capecitabine, antacids must be avoided for two hours before and after the capecitabine dose. Some oral chemotherapy agents require that proton pump inhibitors be taken at a different time of the day than the oral chemotherapy agent.

Likewise, patients must be educated on what foods should be avoided while on oral chemotherapy. Grapefruit, grapefruit juice, and grapefruit products, as well as star fruit and Seville oranges are CYP3A inhibitors and should be avoided while patients are on an oral chemotherapy agent that interacts with them. I let patients know that Seville oranges are commonly used to make orange marmalade. Patients should stop eating these fruits prior to the start of oral chemotherapy and for a few weeks after the discontinuation of the oral chemotherapy.

> Continued follow up with the patient allows nurses the opportunities to reinforce concepts previously discussed, educate about symptom management, and assess for adherence.

St. John's Wort is also a CYP3A inducer and should be avoided when on oral chemotherapy.

Food can also affect the absorption rates of chemotherapy. For example, since abiraterone (Zytiga®) taken with food can result in an increased systemic exposure to the drug, food should be avoided for two hours before and two hours after taking this oral medication. Conversely, some oral drugs must be taken *with* food, such as regorafenib (Stivarga®), which should be taken with a low-fat breakfast.

As you can see, there are many unique requirements for the safe administration of oral chemotherapy agents, so comprehensive education is essential to ensure the safety of patients taking oral chemotherapy.

Missed Doses

Patients need to know what to do if they forget a dose. In general, for oral chemotherapy taken once or twice a day, the missed dose can be taken if it is within six hours of the normal dosing time. If it is more than six hours, then the medication should be skipped. Most drug package inserts provide specific information for the patient about what to do if a dose is missed. The important factor is to avoid over-dosage.

Refill Process

Hospitals and practices that dispense oral chemotherapy should have a process for refilling these medications. Those that rely on outside pharmacies must ensure that patients are informed of the dispensing process for each particular pharmacy. Most oral chemotherapy is now dispensed by specialty pharmacies and mailed directly to the patient's home or to the physician's office. It is important that patients using specialty pharmacies plan ahead and order the refills early enough to ensure that the refill is received before they run out of their medication. At PAMF, many of our patients experienced delivery delays as a result of last year's severe winter weather. Most specialty pharmacies have plans in place to ensure that drug delivery is not affected by outside issues.

Educate, Educate, Educate

Oncology nurses have an important role in educating patients about the many facets of the oral chemotherapy treatment regimen. Education about oral chemotherapy is not a one-time event, but must be continued throughout the course of treatment. Continued follow up with the patient allows nurses the opportunities to reinforce concepts previously discussed, educate about symptom management, and assess for adherence. The end result is the safe administration of oral chemotherapy, resulting in the best clinical outcome for the patient. OI

Elizabeth Bettencourt, RN, MSN, OCN, is the oral chemotherapy nurse navigator at Palo Alto Medical Foundation, Sunnyvale and Mountain View, Calif.

References

1. Moody M, Jackowski11 J. Are patients on oral chemotherapy in your practice setting safe? *Clin J Oncol Nurs*. 2010;14(3): 339-346.

2. Moore S, Brandt ML. Adherence to Oral Therapies for Cancer: Helping Your Patients Stay on Course Toolkit. Available online at: www2.ons.org/ClinicalResources/OralTherapies/Toolkit. Last accessed Sept. 16, 2014.

3. Wood L. A review on adherence management in patients on oral cancer therapies. *Eur J Oncol Nurs*. 2012;16(4):432-438.

4. Kav S, Johnson J, Rittenberg C, Fernandez-Ortega, P, et al. Role of the nurse in patient education and follow-up of people receiving oral chemotherapy treatment: an international survey. *Support Cancer Care*. 2008;16(9):1075-1083.

5. Neuss M, Polovich M, McNiff K, Esper P, et al. 2013 updated American Society of Clinical Oncology/Oncology Nursing Society chemotherapy administration safety standards including standards for the safe administration and management of oral chemotherapy. *Oncol Nurs Forum*. 2013;40(3):225-233.

6. Reeves D, Kam T, Storey S. Oral antineoplastic handling at health care institutions in the United States: survey of nurses and pharmacists. *Hosp Pharm*. 2013;48(4):303-3013.

7. Goodin S, Griffith N, Chen B, Clark K, et al. Safe handling of oral chemotherapeutic agents in clinical practice: recommendations from an international pharmacy panel. *J Oncol Pract*. 2011;7(1):7-12.

8. Lester J. Safe handling and administration considerations of oral anticancer agents in the clinical and home setting. *Clin J Oncol Nurs*. 2012;16(6):E92-E197.