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NCCN Task Force Report: Oral Chemotherapy

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After completion of this CME activity, health care providers should be able to:

- Outline how oral chemotherapy is financed and how payment issues for oral chemotherapy may differ from those of parenteral chemotherapy
- Recognize the common misperceptions about oral chemotherapy and discuss these with patients
- Utilize patient selection criteria for oral chemotherapy regimens
- Summarize the impact that widespread use of oral chemotherapies may have on oncology practice

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NCCN Task Force Report

NCCN Task Force Report: Oral Chemotherapy

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Abstract

Oral chemotherapy is emerging as a new option for well-selected patients who can manage potentially complex oral regimens and self-monitor for potential complications. If a choice between oral and parenteral therapy is available, patients may opt for oral chemotherapy because it is more convenient to administer, allows them to avoid multiple office visits, and gives them a sense of control over their own cancer care. Whether these potential advantages are maintained in regimens that combine oral and parenteral drugs is less clear. The use of oral chemotherapeutic agents profoundly affects all aspects of oncology, including creating significant safety and adherence issues, shifting some traditional roles and responsibilities of oncologists, nurses, and pharmacists to patients and caregivers. The financing of chemotherapy is also affected. To address these issues, the NCCN convened a multidisciplinary task force consisting of oncologists, nurses, pharmacists, and payor representatives to discuss the impact of the increasing use of oral chemotherapy. (*JNCCN* 2008;6[Suppl 3]:S1–S14)

Oral chemotherapeutic drugs have been available for decades and include the familiar agents chlorambucil, cyclophosphamide, methotrexate, and 6-mercaptopurine (6-MP). However, the past 4 years has seen an accelerating expansion of the development of oral anticancer drugs, including oral cytotoxic agents, small molecule inhibitors directed at cell surface receptors and other proteins, and other agents targeted at the tumor microenvironment.

Capecitabine received FDA approval in April 1998, ushering in a new era of oral chemotherapy. Capecitabine approval was followed by FDA approval of a number of oral small molecule inhibitors of a variety of defined targets, including imatinib in 2001, gefitinib in 2003, and erlotinib in 2004. Five more new oral agents were then approved in the 7 months between December 2005 and July 2006. Lapitinib and nilotinib were approved in 2007. Experts anticipate that this trend will continue in the coming years. They further estimate that more than one quarter of the 400 antineoplastic agents now in the pipeline are planned as oral drugs.

Compared with the oral chemotherapy drugs available before 1996, these newer drugs, consistent with their parenteral contemporaries, are considered costly. For example, the estimated yearly cost of lenalidomide for a patient with multiple myeloma is $74,000, and, depending on dosage, the yearly cost of imatinib for patients with chronic myelogenous leukemia (CML) ranges from $29,000 to $57,000. Imatinib accounts for the largest percentage of spending on oral chemotherapy, ranging from 29% to 39%, depending on whether pharmacy benefits are provided by an insured health plan or self-insured employer. The availability of these new drugs has had an immediate impact on pharmacy budgets. Spending on oral chemotherapy drugs, while still a small proportion of total pharmacy benefit costs, has more than doubled between 2002 and 2006, from 0.3% to 0.7%.[1]

Anticancer agents, including oral drugs, can be broadly categorized as chemotherapy, which in the past generally referred to cytotoxic agents, and biologic therapy, which generally referred to therapy targeted specifically at cell surface proteins or pathways that are relatively specific to cancer biologic pathways. Biologic therapy is also often referred to as *targeted therapy*. However, *chemotherapy* has also been used as an inclusive term encompassing all antineoplastic therapies, and the distinctions between targeted and non-targeted and biologic therapy versus chemotherapy would, at this time, appear to be somewhat artificial. In this discussion, the term *chemotherapy* is used generally to describe both cytotoxic and biologic therapy.

Drivers of Oral Chemotherapy

In the past, developers of new anti-cancer therapies focused primarily on parenteral drug delivery, in part because this route bypassed the variable absorption patterns of the gastrointestinal tract. For example, oral drugs must be stable in the low pH environment of the stomach but also must dissolve in the small intestine where the drug is absorbed. Additionally interaction with other substances in the gastrointestinal tract, such as food or other drugs, must be considered, as must the first pass effect on the liver.

In contrast, parenteral administration was considered relatively straightforward and compatible with the cytotoxic action of most chemotherapies. Cytotoxic chemotherapy regimens are designed to deliver the maximal tolerated dose of chemotherapy to optimize cell kill in a single episode, followed by a several week period to allow bone marrow recovery. This episodic administration lends itself to the parenteral route. In fact, the operational and financial infrastructure of oncology practice has been based on the parenteral administration of chemotherapy. Oncology office visits and the configuration of office space have been centered on chemotherapy infusion, and oncologists derive a substantial portion of their income from supplying and administering parenteral chemotherapy.

Oral chemotherapy is changing this model. Many current anti-cancer therapies are primarily cytostatic in nature and thus are optimally effective when given chronically, so both tumor cells and the tumor microenvironment are continually exposed. This mechanism of action virtually requires oral daily therapy. Furthermore, the daily low-dose schedules often do not have the same dose-limiting side effects as high-dose intermittent schedules, making the cycling of regimens to allow for marrow recovery unnecessary.

Older paradigms used anticancer therapy for a limited number of cycles and then stopped. In contrast, many current therapies require prolonged treatment. For example, life-long imatinib therapy has revolutionized the treatment of CML and is an alternative to allogeneic stem cell transplantation.

New monitoring techniques for residual disease have also prolonged the duration of therapy. Before the availability of molecular monitoring of disease recurrence, the duration of treatment of some leukemias was based on the normalization of the peripheral blood or marrow. Now therapy may be continued if sensitive monitoring techniques detect minimal residual disease. These factors have prompted oncologists to reframe some cancers as chronic diseases requiring chronic therapy.

Imatinib therapy for CML is perhaps the best example yet of the promise of targeted therapies; the target is well defined and exquisitely sensitive to imatinib monotherapy. However, it is becoming apparent that this elegant simplicity is not typical of the more common epithelial malignancies. The complexity of the underlying pathobiology in colon cancer, for example, suggests that multiple different targeted therapies will be needed, both directed at the tumor cells themselves and the underlying tumor microenvironment. This suggests that there will be a growing market for the simultaneous use of multiple different targeted therapies.

The very terms *targeted* and *biologic* therapy suggest that toxicity will be less than that encountered using traditional cytotoxic therapies (although to what degree toxicities are lower, versus different, is debatable). This perception and the perceived ease of oral administration may lead clinicians to add targeted therapies to other cytotoxic regimens or to use them as monotherapies in situations in which minimal validated treatment options are available.

The perception also exists that the standards for efficacy may be lower for targeted therapies. In fact, the standards for efficacy have been progressively lowering over the past several decades, but this process has more to do with the date of application than the mechanism of action of the agent involved. This difference in acceptable outcomes may also be related to the fact that targeted therapies are assumed to be less toxic, although the side effects of some biologic therapies can be quite significant.

For a number of reasons, pharmaceutical companies have invested heavily in the development of oral cancer drugs. One strong incentive is the introduction of Medicare Part D, which provides coverage for many oral chemotherapies for the first time. Research has been invested in both novel oral agents and also oral counterparts to existing cytotoxic therapies. For example, oral versions of docetaxel and topotecan are under development.[2] Experts suggest a market will exist for both oral and intravenous versions of many drugs. For example, in the new histone deacetylase inhibitors class of drugs (e.g., the recently approved vorinostat), both oral and intravenous agents are

under development. For agents such as these, the choice between oral and intravenous administration may depend on physician and patient preferences and type of insurance coverage.

Common Misconceptions About Oral Chemotherapy

As the previous discussion shows, oral chemotherapy suggests a number of benefits. However, growing experience in administering these therapies suggests that a cautious approach is warranted. Clinicians should also understand the common misconceptions that may be contributing inappropriately to the enthusiasm for oral chemotherapy.

Patient Preference

Patient preference for oral chemotherapy has been one of the main drivers for its current popularity. Oral administration would seem to avoid many of the more objectionable aspects of parenteral therapy: the office visit and associated inconvenience of transportation and parking, time spent waiting in the office, and time lost during intravenous set up and infusion.

In 1997 Liu et al.[4] reported on the results of a questionnaire addressing patient preference for oral versus intravenous palliative chemotherapy. Preference for route of administration was evaluated against diminishing treatment response. Of 102 assessable patients, 92 preferred oral chemotherapy and 10 preferred intravenous therapy. Not unexpectedly, the major reason given for preferring oral chemotherapy was convenience. However, although patients expressed a clear preference for oral chemotherapy, they were unwilling to sacrifice efficacy for this preference.

Although these results seem to support convenience as a driving factor for patient preference, at least in the palliative setting, this survey may have presented oral chemotherapy in an overly simplistic fashion. For example, the convenience of oral chemotherapy will only be realized if the patient is on an exclusively oral regimen. Patients on combination regimens will need to make office infusion visits anyway; for these patients, it may actually be more convenient to receive the entire regimen parenterally. Capecitabine, for example, is an oral alternative to 5-fluorouracil (5FU) that is often administered with other parenteral agents.

Additionally, patients may not realize that choosing an oral therapy over an intravenous equivalent will shift many of the responsibilities of managing the regimen and monitoring for doses and toxicity from the oncology team more directly to the patient. Although, some patients may appreciate a sense of empowerment from oral chemotherapy and get a sense of satisfaction from having direct responsibility for managing their chemotherapy, this same responsibility could become overwhelming, particularly for sick patients simultaneous dealing with complicated dosing regimens and schedules or for patients without reliable assistance from family or friends. The reliable administration of oral chemotherapy in the pediatric population is also challenging, even among well-intentioned families.[5]

These advantages and disadvantages of oral chemotherapy must be carefully discussed with the patient. Only well-motivated and health-literate patients and families may be able to manage complex oral chemotherapy regimens, and only patients with good oral food intake, good gut function, and minimal nausea and vomiting will be good potential candidates.

Fewer Side Effects and Easier Administration

Patient preference for oral chemotherapy may be based on the incorrect assumption that oral therapy is associated with minimal side effects; some patients may incorrectly assume that oral chemotherapy is not "real" chemotherapy and is more akin to taking a vitamin or antibiotic. This dangerous misconception may also be the rationale for the preference of oral chemotherapy in frail elderly patients.

Patients must understand that oral equivalents of cytotoxic therapies, such as capecitabine, have side effects that are similar to their parenteral counterparts (in this case, fluorouracil). The need to monitor for side effects and titrate dosages increases the complexity of oral chemotherapy regimens. For example, many oncologists can relate examples of patients who began to experience toxicity from capecitabine on a Friday but who did not consult a physician over the weekend. If these patients continue on the same dosage, either because they do not recognize the incipient side effects or because they do not want to compromise the effectiveness of their chemotherapy, they may have a life-threatening level of toxicity by Monday.

Furthermore, from the patient's perspective, an oral regimen may not be simple to administer. Instructions for capecitabine may include:

- Take with water within 30 minutes of a meal.
- If a dose is missed, do not take the drug when remembered and do not take a double dose.
- Stop taking capecitabine and contact the doctor if experiencing 4 or more bowel movements than usual per day, diarrhea at night, loss of appetite or large reduction in fluid intake, more than 1 vomiting episode in 24 hours, mouth sores, temperature greater than 100.5 °F, or pain, redness, or swelling of hands or feet that prevents normal activity.[6]

Oral regimens must also be integrated with noncancer drug therapies taken for comorbidities. Oral chemotherapy regimens may be particularly difficult to manage in assisted living situations where drugs are dispensed by staff with limited experience in monitoring the side effects of chemotherapy.

Furthermore, supportive care agents such as the 5-hydroxytyptamine3 (5-HT3) antagonist antiemetic drugs are best used parenterally and intermittently. Reimbursement for these agents on a daily oral basis is often limited when pharmacy benefit management programs base reimbursement on the FDA-labeled indications. When all these requirements are considered, a periodic office visit to receive chemotherapy may be more attractive to patients.

Another common perception is that oral drugs have a broader therapeutic index and thus are safer than parenteral drugs. The therapeutic index is based on the class of drug and its mechanism of action, not the route of administration. Thus, the therapeutic index of oral agents versus intravenous counterparts is generally the same. Nevertheless, clinicians should note that although biologic agents are not cytotoxic in nature, the adverse effects associated with them can still be significant. For example, the skin rash and diarrhea associated with epidermal growth factor inhibitors can be debilitating.

In summary, the assumption that all patients will prefer oral agents or that all patients are appropriate candidates for oral therapies is overly simplistic. Furthermore, that oral chemotherapy is routinely preferable for frail, elderly, and less motivated patients is also a commonly held misconception. Generally, highly motivated, capable patients who want and can actively participate in their care are better suited to assume the increased responsibility that comes with chronic home oral administration of chemotherapy.

Certainly, for some regimens, oral chemotherapy is the only alternative. However, the example of imatinib monotherapy, a simple regimen with minimal side effects, may be the exception rather than the rule. An entirely oral chemotherapy regimen may offer significant advantages over traditional infusion therapy in carefully selected patients, but patients must understand that the decision to use oral chemotherapy requires detailed consultation with the oncologist and oncology team, as well as ongoing support over the course of therapy.

Cost of Oral Chemotherapy: Offset by Decreased Need for Support Staff or Infusion Centers?

Some have argued that the high cost of oral chemotherapy drugs may be offset by the decreased need for ancillary services, particularly oncology nursing staff and infusion centers. Experience, however, has not uniformly borne this out. Oral chemotherapy requires a significant amount of nursing time for patient education when starting an oral chemotherapy regimen and extensive telephone consultation thereafter. Furthermore, in most practices, no time is built in for counseling patients on oral chemotherapy, and most offices do not have any dedicated space or personnel for this counseling. Thurs, education and counseling have been improvised in hallways and other less private settings. Some oncologists offer written material, video material, or group educational sessions, but the bottom line is that the extensive and ongoing patient education required to ensure safe and effective oral chemotherapy is uncompensated and perhaps underappreciated. In contrast, prolonged infusion sessions provide many built-in opportunities for education.

Patient Selection Criteria for Oral Chemotherapy

Adherence

Although many patients may be eligible for oral chemotherapy, only a subset will both want to take oral agents and be considered appropriate candidates based on their ability to adhere to the regimen. One of the key factors in assessing candidacy for oral chemotherapy is adherence. Adherence can be a challenging commitment for many patients, and the decision to take oral chemotherapy must be based on a collaborative discussion between the patient and physician, with appropriate support from oncology staff.

In clinical trials of oral agents, adherence has generally been excellent[7] except for selected populations (e.g., adolescents). However, in contrast with the clinical trial experience, adherence to chronic medication therapy in adult ambulatory care is generally fair to poor. Unfortunately, there is currently no well established mechanism to prospectively assess adherence. For example, approximately 50% of patients taking statin drugs will discontinue taking the medication within 6 months.[8]

Patients with cancer are believed to be particularly motivated to adhere to chemotherapy regimens. In fact, occasional overadherence can pose health risks. Nevertheless, studies have shown that nonadherence to oral chemotherapy is still an issue.

For example, imatinib is a very effective oral agent; it has an uncomplicated daily regimen and few major side effects. The drug is considered life-saving for patients with CML, converting a universally fatal disease into a manageable chronic one. Given these factors, one might expect a near 100% adherence rate. However, studies have not borne this out. Tsang et al.[9] analyzed pharmacy claims data to determine prescription adherence and persistency of 4043 patients receiving imatinib over 24 months. Overall compliance (defined as apparent mg taken/mg prescribed) was 75%, and only 50% of patients were 100% compliant. Persistency (time on therapy without significant gaps in refills) averaged 255 days over 24 months. Although adherence and persistency in this study may be superior to those seen with nononcology medications, suboptimal adherence with daily imatinib may compromise treatment effectiveness.

Partridge et al.[7] reviewed the literature regarding adherence to oral chemotherapy. Most studies examined adherence in the context of a clinical trial, which probably represents the optimal situation of highly motivated and supervised patients. However, even in this setting, adherence was variable, ranging from less than 20% to almost 100%.

Assessing adherence to parenteral therapy is straightforward; physicians know exactly how much chemotherapy was given over what period of time and on which day. This level of control is not possible with oral chemotherapy, where there is shared responsibility for ensuring that prescriptions will be filled, that the patient will promptly initiate the drug therapy at the correct time of day at the correct dosage, or that the patient will alert the clinician of adverse symptoms in a timely way. Payor information systems can capture whether or not the prescription is filled, but anecdotes abound of patients who have shoeboxes full of unused prescriptions. In addition, few innovations have been developed in oncology care to help support safe and reliable administration of oral chemotherapy. Lessons for disease management programs in asthma and depression management may offer helpful lessons for oncology.

Studies have shown that adherence is related to sociodemographic characteristics, type of regimen (i.e., side effects and duration), and characteristics of the illness (i.e., symptoms and seriousness). However, predicting how these parameters interact with each other and determining how they can be used to predict adherence is difficult.[7]

Table 1 summarizes factors often associated with nonadherence to oral regimens and lists factors that may help oncologists identify patients who need specialized or targeted interventions to support the reliable use of oral chemotherapies.

Monitoring Adherence

Predicting adherence is an issue in selecting appropriate patients for oral chemotherapy. However, after therapy is started, techniques to monitor adherence are important to determine treatment effectiveness, assess toxicity, and assure safety. Adherence-monitoring techniques can be broadly categorized into direct and indirect methods. The simplest direct method is to directly observe therapy, which is, of course, possible with parenteral therapy. Pharmacokinetic measurement

Table 1 Factors Associated With Nonadherence to Oral Regimens

Complex treatment regimens
Substantial behavior change required
Inconvenient or inefficient clinics
Inadequate supervision
Poor communication with health care providers
Patient dissatisfaction with care
Patient health beliefs in favor of nonadherence
Inadequate social support
History of nonadherence
History of mental illness

From Partridge AH, Avorn J, Wong PS, Winer EP. Adherence to therapy with oral antineoplastic agents. J Natl Cancer Inst 2002;94:652–661; with permission.

is another, more-cumbersome example of a direct method. However, this measurememt can also be manipulated by the patient who becomes adherent just before an office visit. Additionally, requiring a blood sample to monitor oral therapy shows a certain irony.

A wide variety of indirect methods have been investigated, including, most obviously, questioning the patient about adherence. However, patient self-report may sometimes be unreliable because of either inaccurate recall or shame in admitting nonadherence. Other indirect methods include patient diaries, pill counts, rates of prescription refills, and electronic medication monitors.[10] Of course, relatively simple methods as pill counts and prescription refills do not confirm adherence to the dosing schedule. A microelectronic monitoring system consisting of an "intelligent" tablet bottle can record the date and time of bottle openings. This approach has been used primarily in clinical trials, in which measuring adherence is critical. The expense of this approach limits its applicability to large scale use. Regardless of the technique used to assess adherence, clinicians must realize that lack of adherence typically reflects the complexity of the regimen rather than willful or manipulative behavior from the patient.

Uncertainty about patients' ability to adhere to recommended treatments can create a therapeutic dilemma for the physician who is faced with a patient who appears to be nonresponsive to an oral drug. The physician cannot be certain if the lack of response represents true chemotherapy resistance or nonadherence. Similar to oral therapy in general, the inability to accurately confirm adherence has significant implications for investigating effectiveness and adverse events. Oncologists may need to contract explicitly with patients about oral chemotherapy adherence and to create a more elaborate infrastructure to support safe and reliable administration of oral chemotherapy.

Safety Issues

Medication Errors

Medication errors are a significant source of concern regarding the administration of chemotherapy. In recent years, a robust infrastructure of checks and balances has been implemented for the administration of parenteral chemotherapy, including templated orders, electronic order-entry systems with decision support, and clinician double-checks, In many academic institutions, every dose of chemotherapy is reviewed by at least 3 or 4 licensed health care providers. Key safety measures include checking calculations of such common parameters as dose per meter squared and estimate of body surface area. Written consent forms are used in some organizations for parenteral chemotherapy. Many comprehensive cancer centers have also developed standard order forms for a variety of chemotherapy regimens.

To date, however, fewer controls are built in for oral chemotherapy, so any presumed safety can only be characterized as hypothetical at present. For example, standard order forms generally do not exist for oral chemotherapy. Weingart et al.[11] reported the results of a survey of 42 cancer centers in the United States regarding current safety practices for oral chemotherapy. The information required on a prescription, such as diagnosis, cycle number, any prescription double check by other clinicians, calculation of body surface area or dose per meter squared per body surface area, was variable. Ten of 42 responding cancer centers had no formal process for monitoring adherence, and 10 centers reported at least 1 serious adverse event in the prior year. The authors concluded that few of the safeguards routinely used for infusion chemotherapy had been adopted for oral chemotherapy at U.S. cancer centers.

Given these gaps in safeguards, the potential exists for a physician to write a prescription for an oral antineoplastic agent that is then filled at a local community pharmacy unfamiliar with oral chemotherapy or dosing schedules. In this possible scenario, the patient may not be given adequate instructions or understand the instructions for taking the chemotherapy, which may involve complicated cycles. The consequences of this scenario are potentially serious if, for example, a patient takes a drug that is intended to be taken weekly on a daily basis instead.

Drug interactions are another issue for all oral drugs. Pharmacy systems have built-in alerts to detect potential drug interactions, but the alerts are often perceived to be too sensitive and are overridden. Some systems may allow some alerts to be overridden, but in cases of serious potential risk, insist that the order/prescription be stopped until the pharmacist consults with the physician.

Specialty pharmacies (discussed further in a later section) may provide an additional level of safety checks, but the number of pills that a patient may receive with 1 prescription is still an issue. Capecitabine

is one of the most common oral antineoplastic agents, and the policy in some academic centers is to limit a prescription to a maximum of 4 to 6 weeks of therapy. However, this safeguard is unlikely for drugs supplied by a mail order pharmacy. In addition, prescribing physicians may also lose patient contact if an extended supply of medication is given with a single prescription. This issue may be further aggravated if the patient is from out of town and does not routinely see the prescribing physician. Large employers have financial incentives to provide pharmacy benefits through mail-order pharmacies. The growing numbers of oral chemotherapeutics with potential serious side effects may prompt employers to rethink the balance between costs and potential safety issues when mail order pharmacies are used across the board.

Communication Issues

To prescribe oral chemotherapy safely, the clinician must take a comprehensive medication history. This can be challenging if clinicians do not elicit this information reliably or keep the medication list up to date by reconciling information about medications from various sources. The situation is improving under the Joint Commission requirement for "medication reconciliation" and with the use of electronic medical records and computerized order entry systems. In some organizations, clinicians can access information on drugs dispensed by pharmacies. Some payers can provide up-to-date dispensing histories, but these systems are not widely available or accessible. Other institutions' dispensing information systems capture prescriptions filled within the particular hospital network, but do not provide information on drugs received through mail order or community pharmacies.

Adequate communication of side effects and toxicities is another key factor that may affect patient safety. Parenteral therapy provides opportunities for communication, particularly with nursing staff during therapy. Patients may be more comfortable detailing side effects and other concerns to support staff, but this kind of key interaction with nurses and other clinicians may not be available for patients receiving an entirely oral regimen. Therefore, additional communication channels and mechanisms may be necessary. These communication issues are similar to those associated with other complicated oral regimens for such common medical conditions as diabetes or asthma, although the potential for adverse events may be higher with oral chemotherapies.

The ability to monitor symptoms in real-time would help identify toxicities that may resolve by the next physician visit and consequently not be adequately recalled by the patient. Internet systems may improve communication for all patients. For example, patient-friendly web-based programs have been developed that allow patients to communicate chemotherapy toxicities in real-time either from home or in the oncologist's office.

One such program is called the STAR program, which has been investigated in patients with lung cancer and gynecologic malignancies.[12,13] Patients were encouraged to log in and report symptoms at each follow up or to access the system from home. In one study involving 80 patients with gynecologic cancer, 42 severe toxicities (grade 3–4) entered from home prompted 7 clinician interventions. Additionally, online self reporting of toxicity symptoms was shown to be feasible in 107 patients with lung cancer. Patients reported high satisfaction with the program, and the nurses who received the symptom reports felt that the information was useful for clinical decisions, documentation, and discussions.

Biohazard

Some 20 to 30 years ago, biohazards of chemotherapy were not appropriately recognized. Residents and interns could be found mixing doxorubicin solutions in a back office sink. Since that time, various workplace regulations have addressed the issue of occupational biohazards of parenteral chemotherapy; however, no such systems are in place for oral chemotherapy. Issues include whether or not oral chemotherapy should be placed in automatic pill counting machines and, if they are manually counted by the pharmacists, whether a dedicated counting tray should be used. Tablets will leave residue in the bottle and on the patient's hand, an issue which may be most relevant for parents treating their children at home. These issues have not been well investigated for oral chemotherapy.

Oral Chemotherapy: Factors Affecting the Practice of Oncology

The large number of oral chemotherapies in the pharmaceutical pipeline prompts consideration of how the practice of oncology could change in the future.

Process of Care

The transition to oral chemotherapy may lead to a diffusion of direct patient care from the oncologist to a variety of individuals that the oncologist has no personal or financial relationship with or no direct supervisory role for. For example, specialty pharmacies participate in safety monitoring and some monitoring of chemotherapy side effects. Free-standing outpatient clinics, some run by pharmacists, may evolve to provide monitoring services for oncology patients. However, the oncologist still retains the ultimate responsibility for the patient's care, and the expanding number of entities involved in cancer care management can make coordinating this care more challenging.

Oncology Offices and Infusion Centers

As noted, many oncology offices are set up to deliver parenteral chemotherapy, and the growing number of oral alternatives raises the potential problem of overcapacity. For the foreseeable future, however, this does not seem to be an issue. Cancer is primarily a disease of an older population, and given the aging of the U.S. population, the incidence of cancer is likely to grow. Although many novel cancer therapies provide only an incremental survival benefit, these new drug therapies may cumulatively result in a greater number of patients living for a longer period of time.

Even if the percentage of chemotherapy given as oral chemotherapy grows to 20% to 25% over the next decade, the most likely scenario is that oral chemotherapy will primarily be complementary to parenteral therapy. Whether oral therapy precedes, follows, or is used in combination with parenteral therapy, most patients will probably be treated parenterally at some point in their care. Thus, the bottom line is that oral chemotherapy is unlikely to substantially replace parenteral therapy at least for the next decade.

Oral chemotherapy may present a particular problem if a patient receiving oral therapy is admitted. The hospital must determine how to continue the oral chemotherapy while the patient is hospitalized: should patients bring the drugs to the hospital or should the hospital bear the uncompensated cost of providing the drugs? Continuing oral chemotherapy during an acute inpatient hospitalization has emerged as a complicated financial, ethical, and emotional issue.

Financial Impact

Oncology revenues in private practice have been largely based on the delivery of parenteral agents. In contrast, oncologists do not derive any revenue from oral chemotherapy independent of the fees received from office visits needed to monitor care. In addition, although oncologists generally receive payment for administering parenteral chemotherapy, no similar reimbursement is provided for administering oral chemotherapy.

Not surprisingly, research has suggested that financial constraints may play a role when a choice between oral and parenteral drugs is possible. For example, Jacobsen et al.[14] analyzed the prescribing practices for chemotherapy according to type of physician reimbursement for treatment of Medicare beneficiaries with metastatic lung, breast, or colorectal cancers treated between 1995 and 1998. The study focused on the treatment of metastatic disease because a wide variety of chemotherapies are available in this setting without definitive evidence of one regimen's superiority.

The authors found that providers who were more generously reimbursed prescribed more costly chemotherapy regimens. Frequently, the financial incentives of providers align with those of patients, who are trying to cope with a burdensome co-pay for oral therapy.

Other specialties face these same choices between oral and parenteral drugs. Rheumatologists and their patients, for example, must choose between 2 tumor necrosis factor inhibitors for the treatment of rheumatoid arthritis; infliximab (Remicade), which requires an IV infusion, and etanercept (Enbrel), which is self administered subcutaneously.

Distribution of Oral Chemotherapy

Prescriptions for oral chemotherapy can be filled in several ways: community pharmacies, mail order pharmacies, specialty pharmacies, hospital pharmacies, through the physician's office as part of competitive acquisition programs (CAP), or through an office-based pharmacy that is legal in a number of states. Each of these distribution channels has different implications for the patient and physician.

Mail Order Pharmacies

Mail order pharmacies typically provide a minimum 90 day drug supply, which may represent thousands of dollars for oral cancer chemotherapeutics. The rationale behind a 90 day supply is that cost savings are available related to volume discounts and to eliminating

multiple dispensing fees. However, oral chemotherapy does not easily fit into the model of mail order pharmacy. For example, for safety reasons, hospital pharmacies frequently limit oral chemotherapies to a 30 day supply. Additionally, some oral chemotherapies require dose alterations, but these cannot be easily accommodated because mail orders typically include only 1 dosage. Additionally, patients do not have any opportunity to interact with a pharmacist, and this lost educational opportunity could impact the safety of oral chemotherapy.

Specialty Pharmacies

Specialty pharmacies were specifically designed to address the limitations of mail order pharmacies by focusing on a specific class of therapeutic drug that involved more complex management issues, a greater potential for harm, and more significant expense. Most often, patients take their prescriptions to their regular pharmacy, where the prescription is routed to a single vendor staffed by oncology pharmacists. The specialty pharmacist then calls the patient and discusses the therapy before shipping the drug.

In some programs, the specialty pharmacist will have access to the patients' prescription medication records through payor information systems so that potential drug interactions can be anticipated. The oncology pharmacist can then call the physician for further discussion. Each drug may also have its own monitoring program, which notifies the pharmacist to call the patient within the time frame when common toxicities are expected. For example, the side effects of capecitabine therapy may be most severe in the first 4 days of therapy. Although these side effects will be identified by the specialty pharmacist, oncologists may not be informed by the monitoring program.

Specialty pharmacies are also more flexible in both the number and dosages of pills provided. Unlike mail order pharmacies, many impose 30 day limits on oral chemotherapies for safety reasons, but also to ensure that a subsequent refill is needed, thus avoiding waste. In addition, many can also provide a variety of dosages to accommodate needed dose alterations.

One potential source of confusion for patients is that they may receive drugs and information about appropriate use of those drugs from multiple sources. For example, drugs for hypertension may come from a mail order pharmacy, drugs for treatment of acute illness may come from a community pharmacy, and the oral chemotherapy may come from the specialty pharmacy.

Another challenge of specialty pharmacies is the insertion of an additional health care professional into the medical care of the patient, creating the need for further coordination. For example, patients can be confused if the information provided by the pharmacist is not consistent with that from the oncologist. Additionally, if the patient tells the pharmacist about adverse reactions, the pharmacist must then ensure that the information is relayed correctly to the oncologist and placed in the patient's medical record. Few programs have robust mechanisms in place to ensure that information is communicated to (and received by) the appropriate parties. This can be a particular vexing challenge.

From the oncologist's perspective, adding the pharmacist is an asset to the patient's overall care as long as the pharmacy team is well integrated into overall care. Specialty pharmacies may be superfluous in a dedicated cancer center with large and active clinical pharmacy departments that already have sophisticated support strategies in place. In contrast, a specialty pharmacy system may be particularly helpful to smaller community practices with no other access to an oncology pharmacist.

Hospital Pharmacies

Hospital pharmacies associated with comprehensive cancer centers most often have similar capabilities to specialty pharmacies. For example, oncology pharmacists and nurses are often part of the health care team that reviews all medications and interacts with the patients. The comprehensive cancer center also interacts with satellite community pharmacies to provide the same services. In addition, an information system that records all the medications the patient receives through the parent hospital pharmacy is typically in place. However, the sophistication of the information systems is variable. Furthermore, information may be incomplete if some prescriptions are filled through specialty pharmacies or pharmacies outside the center network. In some institutions, almost half of the oral prescriptions are filled outside the network.

One exception is investigational therapies that are only provided through a hospital pharmacy. These oral drugs have a higher risk of adverse events and typically have a prescribing and tracking system that is independent of other routine oral agents.

Community Pharmacies

Depending on insurance coverage and set-up of the local hospital-based pharmacy, patients may access oral chemotherapy through a community pharmacy. For example, some hospitals may limit the availability of oral chemotherapy to investigational agents or patients with inadequate coverage, and mail order or specialty pharmacies may not be an option in some insurance plans. In this situation, the community pharmacy may order the drug for the patient, but the pharmacy staff may not have adequate experience to provide appropriate counseling. Some pharmacy chains may require counseling for some oral chemotherapy agents, but the quality and value of these consultations may be variable.

CAP

CAPs are a component of the Medicare Modernization Act (MMA) in which physician-owned clinics were offered the opportunity to acquire drugs for their Medicare patients from a CAP vendor. The CAP vendor assumes the risk of purchasing the drug, including the 20% co-pay from the beneficiary. The limitation of the CAP program is that the physician must acquire all drugs from the single vendor. Because of problems in administering the program and aligning economic incentives, very few physicians signed up, and CAP has not emerged as a major supplier of oral chemotherapy.

Financing Oral Chemotherapy

Medicare Part D

Medicare Part D, part of the MMA, profoundly changed the landscape of reimbursement for oral chemotherapy. Before Part D, the only oral chemotherapies covered by Medicare were a limited number of oral drugs with injectable counterparts covered under Medicare Part B, such as capecitabine. With Part D, cancer chemotherapy is now covered by 2 different components of Medicare: Part B for parenteral therapies and Part D for oral chemotherapies. This dual system can be very confusing to both patients and physicians.

In Medicare Part D, oral drugs are provided through either a prescription drug plan offering drug-only coverage or a Medicare Advantage Prescription Drug Plan (MA-PD), which offers both medical and drug coverage. Most patients have opted for a prescription drug plan, since it does not require them to change their existing medical coverage.

Both of these programs may use formulary and other management tools. The Centers for Medicare and Medicaid Services (CMS) review Part D plans' formularies to ensure that they do not discriminate against beneficiaries with certain health conditions. One stipulation was the requirement that any Part D formulary include "substantially all members" of certain therapeutic classes of drugs, including anti-neoplastic drugs. The rationale for this policy was that a choice of therapies was more important in cancer treatment than in other illnesses; therefore virtually all oral cancer chemotherapies are included on formularies.

As originally set up, Part D has a $250 deductible and a 25% co-pay for the next $2000 in oral drug costs. Unfortunately, Part D also has a gap in coverage, referred to as the "donut hole," and the patient is responsible for the next $2850 in drug costs. The particular levels that establish the 25% co-pay and the donut hole are indexed to inflation and adjusted on an annual basis. After the $2850 has been fully paid, the beneficiary is responsible for 5% of the remaining costs. This cycle starts again at the beginning of every calendar year.

Hundreds of different private insurance companies offer Part D plans with different co-pay rates and different deductibles. For example, some plans offer a version of the standard benefit that features a reduced deductible or flat co-payments instead of co-insurance. A 2006 analysis of Part D formularies found that both prescription drug plans and local MA-PDs cover 75% of cancer drugs, whereas regional MA-PDs cover 85%. No plans applied step therapy restrictions to cancer drugs.[3]

Although Medicare Part D does provide relief from catastrophic drug costs, the co-pays can still be burdensome, particularly given the high cost of oral chemotherapy. Medicare beneficiaries may qualify for a low income subsidy that reduces the cost-sharing burden, but this program is underused, perhaps because it adds one more form to an already complex process. Patients who cannot afford either the donut hole or co-pays may take their drugs intermittently or not at all.

These factors may affect the choice of oral versus parenteral chemotherapy. For example, patients starting chemotherapy toward the end of the year will promptly experience the large "donut hole" expense,

only to be faced with the same expense during the next year. Therefore, one could envision some patients choosing to start parenteral therapy and transition to oral therapy at the beginning of the next year.

Co-pays and co-insurance, although familiar aspects of medical care, are relatively new concepts for cancer chemotherapy. The idea of cost sharing is to expose the patient to the cost of therapy so that he or she can judge whether a treatment is worth the cost. Traditionally, patients with cancer have been shielded from this type of decision-making, and pharmacy benefits, at least for large employers, have not yet required high co-pays or co-insurance for cancer care. However, smaller employers may be considering these strategies as one way to make health insurance affordable for their employees.

Additionally, consumer-directed health plans and health savings accounts are other strategies to offer affordable insurance. Consumer-directed health plans typically combine a health plan with a high deductible and a health reimbursement arrangement (HRA) or health savings account (HSA). HRAs and HSAs are tax-advantaged accounts used to pay health care expenses. Balances can be used for future health use, potentially creating the incentive for enrollees to control their medical expenses.

High co-pays, co-insurance, or deductibles have an uncertain impact on chemotherapy use. Whether patients would choose to undergo additional chemotherapy for metastatic disease if the drug offered is associated with only an incremental benefit but a very high cost is unknown. This is a frequent situation in the use of biologic therapies to treat metastatic epithelial tumors.

Studies in non-oncology settings suggest that out-of-pocket expenses will affect therapy decisions. For example, Schneeweiss et al.[15] studied adherence to statin therapy after myocardial infarction during 3 different time periods: when the statins were fully covered, with a co-pay, and with co-insurance. Although initiating therapy was not affected by coverage, the authors found that adherence was greatest with full coverage policies and that sudden changes to full out-of-pocket spending, similar to Medicare's Part D donut hole, almost doubled the risk of patients stopping. Similar studies have not been done in the oncology setting, for either primary or adjuvant therapy. However, given the gravity of a cancer diagnosis, many oncologists report that patients are unlikely to interrupt primary therapy if at all possible, and seek other funding, such as second mortgages on their homes.

Avoiding co-pays can affect prescribing practices in other ways. For example, sunitinib comes in 3 strengths, 12.5, 25, and 50 mg tablets. The starting dose is typically 50 mg, and dose reductions are not unusual. Therefore, physicians may prescribe the 12.5 mg tablets so that if dose adjustments are required, patients can avoid a separate prescription with a new co-pay. In this scenario, the patient must take 4 tablets instead of one to reach the starting dose of 50 mg. This type of maneuvering adds to the complexity of oral chemotherapy.

The array of Part D plans is confusing to patients and physicians alike, and physicians typically do not know what type of coverage patients have when planning treatment. Thus, they cannot anticipate the economic consequences. The assumption that most patients over age 65 have some sort of Medicare coverage is tempting, but many patients in that age range are covered by commercial plans based on prior employment. Conversely, patients under age 65 may have Medicare coverage based on other disabilities.

No easy mechanism is currently in place in the physician's office to determine what type of coverage a patient has for oral chemotherapy. Making this determination can be time consuming, and further cost is added to the health care system when staff must make sure that the correct payment and co-payment have been received.

The Medicare donut hole also affects the revenue streams at hospital pharmacies. At the beginning of the year, hospitals may accumulate bad debt as patients are working their way through the donut hole. In contrast, revenue is more secure in subsequent months as Medicare Part D assumes coverage for most of the costs. To compensate for this shortfall, hospital pharmacies must increase their charges in subsequent years, thus creating a vicious cycle. Some hospitals have adopted the policy of continuing treatment for patients even if insurance coverage runs out. In this situation, the hospital could end up buying oral chemotherapy for some patients.

Trends in Financing and Managing Oral Chemotherapy

Formulary Management: The high cost of many new oral chemotherapies has set the stage for new management cost control strategies. Payers have limited ways of monitoring parenteral therapy; frequently the

therapy has already been administered when the payor receives an initial claim. However, oral therapy can be more tightly monitored and controlled through pharmacy benefits because the patient will present a prescription to a community or cancer center pharmacy or have the drug provided by specialty pharmacies contracted for by insurance companies.

One common strategy for pharmacy benefit management is the tiered drug formulary. Whether this strategy could be applied to oral chemotherapies is unclear, however, at least for the foreseeable future. For example, states have variable regulations regarding what drugs must be included in a formulary. Oncology drugs often must be included despite minimal data in the published literature, making it difficult to exclude even a few drugs.

Furthermore, formulary management is based on the preferential selection of one member from a class of drugs. Currently, no oral chemotherapy drug classes including multiple agents, making it impossible to apply formulary management. Additionally, head-to-head trials investigating the equivalence or potential superiority of 2 related drugs have not been done and are unlikely, because manufacturers have no financial incentive to do such studies. Sunitinib and sorafenib or cetuximab and panitumumab are examples of related agents; however, the differences among the multiple targets of these agents prevent them from being considered bioequivalent. The class of multikinase inhibitors that includes imatinib, nilotinib, sunitinib, dasatinib, sorafenib, and lapatinib is an example of a pharmacologic class that might lend itself to formulary management. In addition, gaps in the clinical data limit the ability to create a formulary system, be it simple or tiered.

Finally, the business premise of formularies is that the manufacturer will provide a pricing discount if their drug is favorably listed on the formulary. This may not apply to biologic therapies, however, because negotiating discounts are only possible when a different manufacturer makes 2 similar compounds for the same indication. Dasatinib and nilotinib are both tyrosine kinase inhibitors used to treat CML, and they are made by different manufacturers. However, a manufacturer will only be receptive to providing a discount if the payor can prove that usage of the drug will increase if it is preferentially placed on the formulary. This can be more difficult to prove for oral chemotherapy than for drugs in non-cancer therapeutic classes. In summary, the lack of a cogent argument for a managed care company to favor a particular agent or agents impairs the availability of market forces (e.g. discounts) to limit the costs of these compounds via the implementation of formularies for oral chemotherapy.

Preference for generic drugs is another basic formulary management strategy, but creating generic versions of bioengineered therapies will be very difficult. For example, for a pharmaceutical drug, generic manufacturers need only demonstrate that the generic has the same chemical formula and bioavailability. This cannot be done with bioengineered drugs, however, and regulators are considering whether generic versions of bioengineered therapies must reach the same standards of research and testing as their predecessor.[16] The issue of FDA regulation of generic versions or "biosimilars" of bioengineered drugs has been a hotly debated issue for years.

Value-Based Co-Insurance: Value based co-insurance is essentially a form of health care rationing controlled by the patient in which incentives are put into place to promote the use of high-value interventions.[17,18] This concept is similar to current pharmacy formularies, but applied on a broader scale to the comparative effectiveness of procedures, diagnostic services, and medical devices. In the context of oral chemotherapy, a drug that has been shown to have a very minimal incremental benefit on progression-free survival would have a high rate of co-insurance. In contrast, a drug such as imatinib, which may be considered curative or at least associated with a long progression-free survival, would have minimal co-insurance.

Objections to value-based plans include the inequity of a tiered benefit. However, other experts point out the inequity of the current situation of millions of uninsured Americans who lack access to essential health benefits. The values applied to different chemotherapy scenarios will obviously be controversial and will require additional data on clinical and comparative effectiveness.

Annual and Life Time Maximums for Cancer Care: Annual and lifetime maximum covered amounts are another strategy used by employers, particularly smaller ones, to limit their financial exposure with beneficiaries with serious or life-threatening illnesses. However, this type of coverage often creates an underinsured population of patients, especially in cancer care. Although coverage amounts may seem adequate to

average consumers, patient undergoing extensive treatments may find the inadequacy of these coverage maximums readily and tragically apparent.

Conclusions

Oral chemotherapy is emerging as an alternative for appropriately selected patients who, with support from

Table 2 Advantages and Disadvantages of Oral Compared With Parenteral Chemotherapies

	Patient	Physician/Health Care Team	Health Care System
Safety/Adherence			
Oral	Patients assume greater responsibility and control	Difficult for clinicians to monitor adherence and toxicity Lack of safety checks may lead to medication errors	Poor adherence or overadherence can lead to acute inpatient admissions and diminished effectiveness
Parenteral	Adherence based on controlled administration in clinic or office	Tight control of adherence; robust system of checks and balances to reduce medication errors Busy cancer centers may have hazards related to high-volume, high-intensity setting	
Convenience			
Oral	Convenience gain only if oral chemotherapy is NOT given with parenteral therapy	Convenience of oral therapy is over simplified for some regimens; patient appropriateness must be carefully considered	
Parenteral	Often has shorter duration of therapy than oral		
Drug Supply and Distribution			
Oral	Can receive from hospital pharmacy, mail order, or specialty pharmacy	Specialty pharmacy may be required	Oral drugs can be tightly controlled through pharmacy benefit May be cost savings with 90 day supply Drug waste may be an issue
Parenteral	Requires office visit	Direct control by oncologist	Payors have limited ability to directly manage parenteral therapy
Communication Issues			
Oral	Requires new patient education	Expanding role for mid-level providers in patient education	Patient education time not compensated
Parenteral	Infusion sessions allow for prolonged contact of the patient with the health care team.		
Oncology Infrastructure			
Oral	Potentially fewer office visits; follow up may occur at specialty monitoring clinics	Adequate space for patient counseling not always available	Improved information systems and integrated electronic medical record may improve safety
Parenteral	Office set up specifically for parenteral therapy	Infusion centers must be maintained; most patients receive parenteral therapy at some point	
Financing			
Oral	May face significant cost sharing, including Medicare Part D "donut hole"	No revenue for dispensing/administering oral therapy	Both oral and parenteral biologic or targeted therapies are considered costly; consideration of new benefit designs may be needed
Parenteral	May have better coverage compared with oral	Approximately 80% of community oncologists' revenue is from dispensing/administering parenteral chemotherapy	

their clinicians, can adequately manage the challenges. Some patients may respond to an increased sense of control associated with the self-management of some of their care, others may prefer to avoid the multiple office visits and intravenous infusions required in parenteral chemotherapy. Additionally, some oral chemotherapies may be associated with fewer side effects than parenteral alternatives. However, the promise of oral chemotherapies will only be realized with careful attention to the safety and monitoring requirements.

The growing number of oral chemotherapies, either currently marketed or in the development pipeline, will significantly impact all aspects of oncology care. From the oncologist's perspective, oral chemotherapies may have a major impact on office practice, reducing the traditional revenues derived from the administration of parenteral therapy and requiring heightened attention to the selection of patients who are appropriate candidates for oral chemotherapy, with subsequent monitoring and support for adherence. The patient–physician relationship may be altered, with fewer oncology office visits and an increased need to coordinate cancer care with other entities, such as specialty pharmacies or clinics.

For older patients, the advent of Medicare Part D ensures that they will not be subject to catastrophic medical costs related to oral chemotherapy, but significant gaps in drug reimbursement still exist. In addition, in response to the growing cost of pharmaceuticals, employers are contemplating other benefit designs, such as lifetime caps on cancer care coverage, higher deductibles, co-pays, or co-insurance.

Oral chemotherapy has been conceptualized as a convenient, less toxic form of therapy that will be driven by patient preference. However, many of the safety issues related to oral chemotherapy are underappreciated, and many patients will not be appropriate candidates. Safety issues include the lack of checks and balances to avoid medication errors, possible lack of patient adherence, and a shift in the responsibility for managing a potentially complicated oral regimen to the patient. The risks and benefits of oral chemotherapy from the patient, physician and health care system perspective shown in Table 2. Clinicians should note that many of the disadvantages listed are not inherent to oral chemotherapy, but reflect the fact that adequate safety and support systems have not evolved as quickly as oral chemotherapy agents.

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Post-test Please circle the correct answer on the enclosed answer sheet.

1. Which of the following drugs is/are available in an oral formulation?
   a. Imatinib
   b. Laptinib
   c. Capecitabine
   d. Lenalidomide
   e. All of the above

2. Which of the following is/are considered drivers of oral chemotherapy?
   a. New oral biologic therapies are primarily cytostatic in nature and require daily therapy.
   b. Molecular monitoring of disease has prolonged duration of treatment, favoring oral therapy.
   c. The perception exists that patients clearly prefer oral therapy.
   d. Biologic agents have predictable absorption.
   e. Only a and c above
   f. Only a, b, and c above

3. Which of the following is/are TRUE about patient preference for oral therapy?
   a. Although oral monotherapy may avoid the inconvenience of an office visit, many combination therapies include parenteral therapy, and therefore require an office visit anyway.
   b. Most oral chemotherapy regimens are simple for the patient to manage.
   c. Oral chemotherapy will shift some aspects of managing chemotherapy to the patient; not all patients respond positively to this empowerment.
   d. Only a and c above
   e. a, b, and c above

4. Which of the following is/are common misperceptions about oral chemotherapy?
   a. Oral chemotherapy has fewer side effects than parenteral chemotherapy.
   b. Oral chemotherapy is particularly appropriate for frail elderly patients.
   c. Monitoring the side effects of oral chemotherapy is easier than monitoring the side effects of parenteral therapy.
   d. Only a and b above
   e. a, b, and c above

5. Which of the following is/are TRUE about adherence to oral chemotherapy?
   a. Adherence is an important factor that can NOT be easily assessed with a questionnaire.
   b. Adherence to oral chemotherapy in general is very good, as is illustrated by the excellent long-term adherence to imatinib therapy.
   c. Payor information systems that can capture whether or not the prescription is filled are in place and provide additional evidence of assurance.
   d. All of the above
   e. None of the above

6. Which of the following is/are accepted as reliable techniques for monitoring adherence?
   a. Directly ask the patient
   b. No completely reliable method of monitoring adherence is currently available.
   c. Patient diaries, pill counts
   d. Rates of prescription refills
   e. Only a and c above

7. Which of the following is/are TRUE about the steps that have been taken to ensure the safety of oral chemotherapy?
   a. The same level of checks and balances that are used for parenteral chemotherapy have been developed for oral chemotherapy, thus reducing the risk of medication errors.
   b. Standard order forms have been developed for oral chemotherapy.
   c. Oral chemotherapy prescriptions are routinely reviewed by 3 or 4 licensed health care staff.
   d. All of the above
   e. None of the above

8. What are the key communications issues regarding oral chemotherapy?
   a. Making every effort to obtain an accurate medication history from the patient, electronic medical record, payer information systems, or pharmacy records
   b. Ensuring adequate time to counsel patients
   c. Widespread use of online reporting systems for toxicities
   d. Only a and b above
   e. None of the above

9. Which of the following is/are FALSE about the impact of oral chemotherapy on oncology practice?
   a. The transition to oral chemotherapy will result in an overcapacity of infusion centers.
   b. The oncologist's revenue and office structure is geared around the delivery of parenteral therapy and thus may decline.
   c. Financial incentives favoring parenteral therapy for both patients and physicians may influence treatment decisions.
   d. All of the above are false.
   e. None of the above are false.

10. What are the potential advantages of specialty pharmacies?
    a. The specialty pharmacist interacts directly with the patient, providing additional education and counseling.

b. Specialty pharmacies are more flexible in the number and dosages of pills provided with a single prescription.
c. Dedicated hot lines allow the specialty pharmacists to easily communicate with the prescribing physician.
d. Only a and b above
e. None of the above

11. What are the implications of the "donut hole" in Medicare Part D coverage?
a. The high cost of many oral chemotherapies ensures that many patients will experience a "donut hole" in Medicare coverage.
b. Patient assistant programs adequately address the "donut hole" for many patients.
c. When possible, patients may opt for parenteral therapy to avoid the "donut hole."
d. Only a and c above
e. All of the above

12. Which of the following statement(s) about formulary management strategies for oral chemotherapy is/are TRUE?
a. State mandates have facilitated formularies for oral chemotherapy.
b. Several chemotherapy drug classes have multiple agents, thus limiting formulary management.
c. Head to head trials of oral chemotherapies can serve as the basis of formulary management.
d. Only a and c above
e. None of the above

Post-Test Answer Sheet

Please circle one answer per question. A score of at least 70% on the post-test is required.

1.	a	b	c	d	e		7.	a	b	c	d	e
2.	a	b	c	d	e	f	8.	a	b	c	d	e
3.	a	b	c	d	e		9.	a	b	c	d	e
4.	a	b	c	d	e		10.	a	b	c	d	e
5.	a	b	c	d	e		11.	a	b	c	d	e
6.	a	b	c	d	e		12.	a	b	c	d	e

Please evaluate the achievement of the learning objectives using a scale of 1 to 5.
(1 = Not met; 3 = Partially met; 5 = Completely met)

Outline how oral chemotherapy is financed and how payment issues for oral chemotherapy may differ from those of parenteral chemotherapy
1 2 3 4 5

Recognize the common misperceptions about oral chemotherapy and discuss these with patients
1 2 3 4 5

Utilize patient selection criteria for oral chemotherapy regimens
1 2 3 4 5

Summarize the impact that widespread use of oral chemotherapies may have on oncology practice
1 2 3 4 5

Please indicate the extent to which you agree or disagree with the following statements:
(1 = Strongly disagree; 3 = Not sure; 5 = Strongly agree)

The material was presented in a fair and balanced manner.
1 2 3 4 5

The information presented in this monograph was pertinent to my educational needs.
1 2 3 4 5

The information presented was scientifically rigorous and up-to-date.
1 2 3 4 5

The information presented in this monograph has motivated me to modify my practice.
1 2 3 4 5

I would recommend this monograph to my colleagues.
1 2 3 4 5

NCCN Task Force Report:
Oral Chemotherapy

Release Date: March 31, 2008
Expiration Date: March 31, 2009

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E-mail Address_____

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