A Pharmacist-Managed Oral Chemotherapy Program

An economic and clinical opportunity

by Robert Mancini, PharmD, and Dave Wilson, RPh

In 1953 the first oral chemotherapy agents—mercaptopurine and methotrexate—were approved. Over the next 40 years another dozen oral chemotherapy agents were approved for various cancer indications. However, only in the last decade has oral chemotherapy taken hold as a common and accepted treatment for cancer. Since the 1998 approval of capecitabine, 20 new oral agents have been approved; today up to 35 percent of new oncologic agents in development are oral formulations.[1] As a result, a shifting paradigm in the workflow associated with cancer centers is taking place.[2] Traditionally, patients on intravenous chemotherapy are closely monitored for adherence, side effects, and efficacy in the safety of the cancer clinic. The shift towards oral agents, which are administered in the home, has huge implications for both patients and community cancer centers. In terms of economic impact, when prescriptions are sent to an external pharmacy, no income is provided to the cancer center.[3] This change is potentially problematic because staff time involved in assisting patients with obtaining their anticancer medications is significant and not billable.[4] Here is how St. Luke's Mountain States Tumor Institute (MSTI) has approached the issue, and a look at the clinical and economic benefits that a pharmacist-managed oral chemotherapy program has provided.

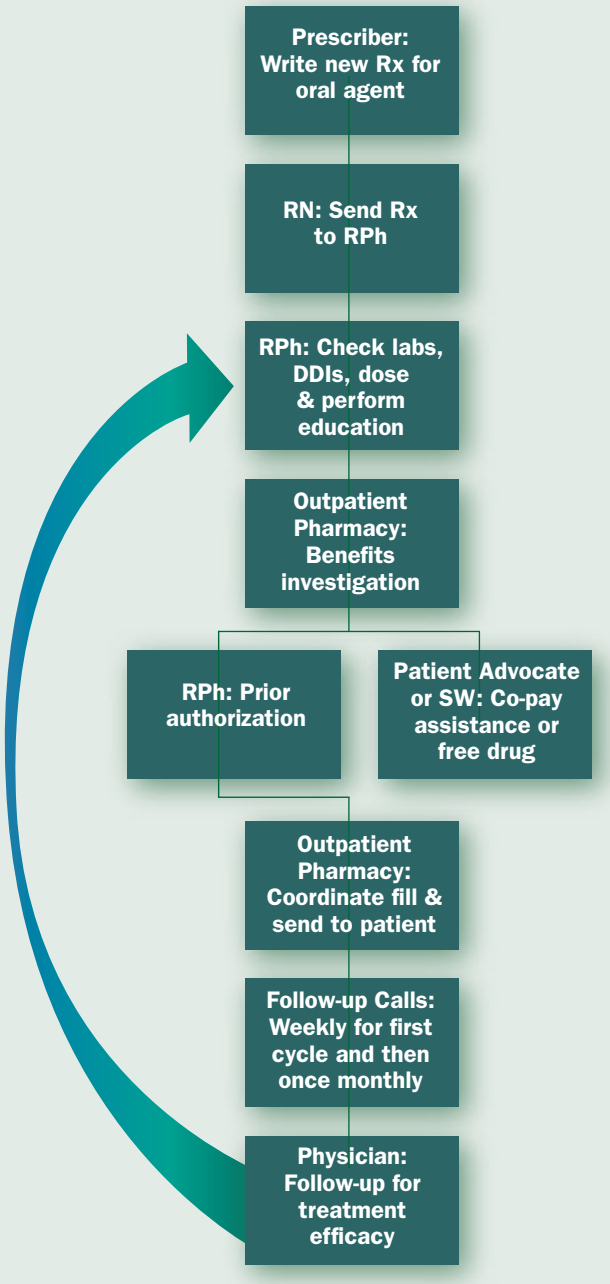
How the Program Works

St. Luke's MSTI Oral Chemotherapy Program is a centralized office that serves five MSTI cancer clinics located throughout southern Idaho. When a prescribing physician decides to start a patient on an oral oncologic agent, the prescriber orders it using a standardized order form. The prescribing physician's primary nurse then takes the order and sends it to the oral chemotherapy office where it is received by the oncology pharmacist. The pharmacist:

- Evaluates the order for appropriateness in terms of dose and indication
- Checks labs
- Evaluates for drug interactions
- Performs patient counseling.

The pharmacist then sends the prescription to a dedicated pharmacy technician within St. Luke's outpatient retail pharmacy for benefits investigation. If prior authorization is required, the pharmacist assists with completion of the form. If the patient faces a high co-pay or the patient is uninsured, the technician contacts patient financial advocates or social workers to assist the patient in enrolling in a co-pay assistance program or applying to a free drug program. Once any financial issues have been resolved, the prescription is filled and sent to the patient. For the first cycle, the patient is called by the pharmacist on a weekly basis to follow up for adherence and side-effect management. This

Figure 1. Oral Chemotherapy Process



Legend: RN = registered nurse; RPh = registered pharmacist; SW = social worker; DDI = drug–drug interactions

Table 1. Regimen for Metastatic Breast Cancer: Lapatinib/Capecitabine (FDA-Approved Dosing)

Regimen:
- Lapatinib 1,250 mg daily (continuous)
- Capecitabine 1,000 mg/m^2 twice daily (14 days on, 7 days off)

Assuming a patient has a body surface area (BSA) of 2.05m^2, the treatment regimen would be:
- Lapatinib 1,250 mg daily (available as 250 mg tablets = 5 tablets daily)
- Capecitabine 2,000 mg twice daily (available as 500 mg tablets = 4 tablets, twice a day)

Factors contributing to complexity:
- Patient is taking a total of 13 fairly large pills per day, most days
- Patient is taking a week break from capecitabine, but not lapatinib
- Patient must take capecitabine with food twice daily and lapatinib on an empty stomach during a single day of treatment

Source: Geyer CE, Forster J, Lindquist D, et al. Lapatinib plus capecitabine for HER2-positive advanced breast cancer. *N Engl J Med.* 2006;355:2733-2743.

process is integrated with physician visits by having the pharmacists review their dictations to ensure continuity of care throughout the patient's treatment. After the first cycle, the patient is called one week prior to each refill for reassessment (see Figure 1, page 28). This process allows MSTI to adhere to the American Society of Clinical Oncology and Oncology Nursing Society Guidelines for Chemotherapy Administration Safety published in 2009.[5]

Risks of Oral Chemotherapy & Areas for Clinical Opportunity

Many issues surround the transition to oral chemotherapy treatments. Risks amenable to clinical interventions include adherence, accessibility, financial concerns, evaluation for food and drug interactions, side-effect management, and perceived lack of efficacy.[1-4,6-7] Other areas amenable to change include access to medication, cost-related problems, medication belief (such as side-effect severity, perceived lack of benefit, or other issues patients may find on the Internet), and depression.[8] To improve clinical aspects of oral chemotherapy treatment, a program to assist patients with access, cost, and counseling issues is essential.

The issue of adherence is serious for cancer patients. Poor medication adherence can lead to unnecessary disease progression, complication of treatment, reduced functional abilities, lower quality of life, and premature death.[9] Adherence issues can arise due to complex dosing schedules and pill fatigue, where the sheer number of pills can be overwhelming to patients. For an example of a complex regimen, see Table 1, this page. Patients can find it difficult to go from relatively few medications to this type of complex dosing schedule. Providers can assist with adherence by:
- Conducting frequent follow-up
- Giving specific instructions
- Filling only one cycle at a time
- Providing patients with dosing calendars to assist with timing.

In addition, having the pharmacist control refills, instead of refills by patient request, allows for assessment for adherence, as well as prevention of late refills.

Changes in accessibility and financial concerns are also important areas of clinical opportunity as these concerns can lead to a type of non-adherence called 'nonfulfillment,' where patients never fill their medication prescription.[10] The cost of these agents can range from a few dollars (e.g., cyclophosphamide) to several thousand dollars per cycle (e.g., sunitinib or lenalidomide). As noted previously, transitioning to oral therapy moves patients out of infusion centers, decreases reimbursable staff time, creates more complex medication reimbursement strategies due to prescription benefit versus medical benefit coverage, and leads to an inability to fully track doses administered. Our pharmacist-managed oral chemotherapy program helps reduce the nonfulfillment accessibility risk by:
- Having an outpatient pharmacy that routinely stocks these oral agents
- Facilitating early assistance with prior authorization
- Providing direct involvement of support staff to assist with financial issues.

Clinical evaluation and counseling help with issues related to drug interactions, food interactions, and side-effect management. For example, a common issue is that specialty mail order pharmacies do not always have the patient's full medication list. Initial evaluation and counseling of the patient by an oncology pharmacist within the patient's healthcare system can help identify drug interactions that are common with oral chemotherapy agents (see Table 2, page 30). This counseling provides the patient with immediate intervention because the oncology pharmacist has direct access to both the prescribing physician and the patient's medical records. In addition, upfront counseling can provide clarification of side effects, along with prophylactic and intervention

Table 2. Common Drug Interactions with Oral Oncologics

Oral Oncologic	Drug Interactions	Food Interactions
Abiraterone	CYP2D6 substrates & CYP3A4 inhibitors and inducers	Must be taken on empty stomach, high-fat meals can increase exposure 10-fold.
Capecitabine	Phenytoin & warfarin	Must be taken with food to reduce side-effect profile.
Dasatinib	Substrate of CYP3A4, caution with use of other agents that inhibit or induce. Requires acidic environment, must evaluate patients on acid suppressors	May be taken with or without food. Interacts with grapefruit juice.
Erlotinib	Warfarin, acid suppressors, CYP3A4 substrates	Must be taken on empty stomach to avoid polyvalent cations from binding medication and reducing absorption.
Imatinib	Potent inhibitor of CYP3A4, CYP2C19, CYP2D6	Must be administered with food to reduce GI irritation.
Lapatinib	Substrate of CYP3A4, caution with use of other agents that inhibit or induce	Must be taken on an empty stomach. Interacts with grapefruit juice.
Nilotinib	Substrate of CYP3A4, caution with use of other agents that inhibit or induce. Requires acidic environment, must evaluate patients on acid suppressors	Must be taken on empty stomach.
Sorafenib	Substrate for CYP3A4, inhibitor of CYP2C9	Must be taken on empty stomach.
Temozolomide	Valproic acid can increase systemic levels of temozolomide	Administer on empty stomach or at bedtime to reduce nausea and vomiting.

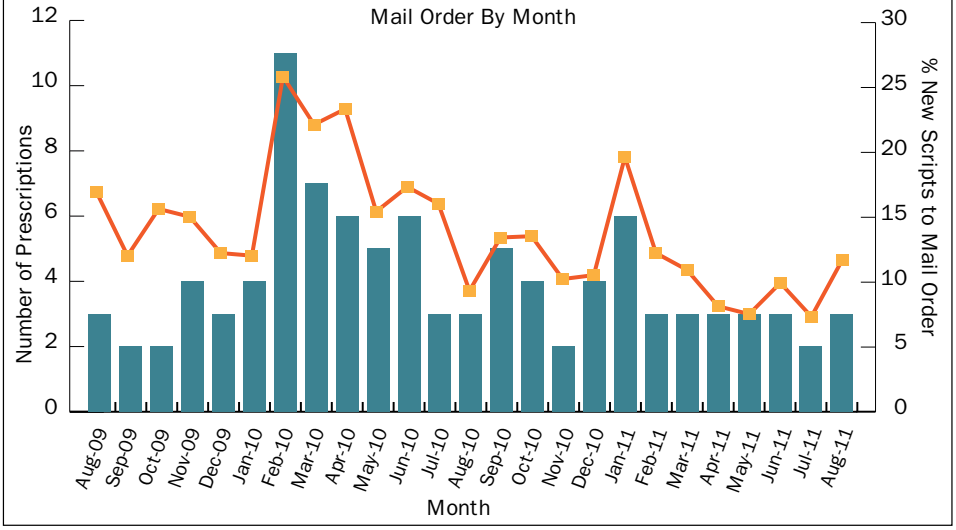
recommendations for side effects, and help patients understand the difference between oral and intravenous agents.

How to Create a Similar Program—Economic Opportunity

The first step in determining whether this type of program is appropriate for your institution is to conduct an analysis of the current state of oral chemotherapy prescribing. It is important to evaluate the:

- Number of patients seen
- Number of oral chemotherapy treatments
- Oral agents most commonly prescribed
- Cost and reimbursement of those oral agents
- Percent of referrals expected.

Figure 2. Prescriptions Required to go through a Mail Order Pharmacy



After this background data is collected, implement a limited pilot program for proof of concept. Some requirements for launching this pilot include: dedicated staff (such as a pharmacy resident), office space, and a retail pharmacy. A trial period of one to two months is needed to gain data to validate and refine your business model. Based on the result of your pilot project, you can develop workload expectations, determine space and equipment needs, and develop staffing requirements to help you create a business plan (see Table 3, page 31).

Another important consideration is your program's ability to fill the medication prescription based on the patient's insurance requirements. In many cases, a patient's insurance will dictate use of a specific specialty mail order pharmacy. By working with the insurance companies, this hurdle can be overcome, most often by becoming a contract pharmacy with that third-party payer. In some cases, this step can be as easy as filling out a form. Assessing the percentage of patients who will need to have prescriptions filled by mail order can help. Based on MSTI's data over the last two years, roughly 10 percent of our patients are still required to go through mail order pharmacies (see Figure 2, this page).

Another consideration is that with each new drug that comes out the potential increase in workload is quite significant; therefore, the increasing growth potential of the pharmacist-managed oral chemotherapy program must also

Table 3. Business Plan: Break Point Analysis*

Costs	Dollar Amount
Salaries	$170,000
Non-salary Overhead	$5,000
Prescription Parameter	**Value**
Number of Rx's	422
Average Rx Price	$3,127
Average Rx Markup	$1,883
Bad Debt Percentage	3.00%
Projected from Pilot	
Gross Revenue	$1,357,574
Cost of Goods Sold	$562,948
Fixed Costs	$175,000
Bad Debt	$40,727
Net Revenue	**$619,626**
Assumptions	
Patients on active treatment	844
% patients on oral chemotherapy	25%
% referrals to oral chemotherapy	50%
Rx's and referrals/patient/year	4
Yearly Rx & referrals for BEP	82

*Numbers here are estimates only and do not represent our actual experience. For actual numbers, see Table 4.

Table 4. Example of New Drug Impact on Oral Chemotherapy Program*

Abiraterone acetate (Zytiga®) was approved for metastatic castrate-resistant prostate cancer (mCRPC) on April 28, 2011. The medication became available through our outpatient pharmacy the following week. Below describes the increase in workload over the subsequent three months with extrapolation to a yearly impact.

Zytiga Statistics*	
Average Rx/week (new and refill)	3.5
Assumed Rx/year	182
Average wholesale price (AWP)	$6,252
Wholesale acquisition cost (WAC)	$4,804
Average reimbursement rate	$5,150
AWP cost impact/year	$1,137,864
WAC cost impact/year	$874,328
Potential revenue/year	$937,300
Current Statistics (All Meds)*	**Impact**
Average Rx/week	↑ 15%
Prescriptions/year	↑ 15%
AWP cost/year	↑ 19.2%
WAC cost/year	↑ 18.3%
Revenue/year	↑ 18.9%

*Statistics calculated based on 3 months of reimbursement data, cost, and fills as of 8/21/11 and revenue extrapolated to average reimbursement regardless of medications to WAC+4%. Data does not reflect actual dollars in the system, but rather approximations that can be applied to individual institutions.

be re-evaluated annually (see Table 4, this page). Our data show that as little as five new oral medications can double the workload of our program based on current numbers, especially if they are highly anticipated treatment options.

Lastly, you will need to provide continued justification of the resources used by your pharmacist-managed oral chemotherapy program. Potential areas of evaluation include patient and staff satisfaction, improvement of patient safety, and financial impact. Within MSTI, our pharmacist-managed oral chemotherapy program has helped reduce write-offs due to lack of reimbursement to less than one percent. In addition, assistance from financial advocates has helped patients procure over $1 million dollars in free drug from manufacturers and over $200,000 in patient assistance funds. The program as a whole has shown profit margins to more than justify a full-time pharmacist, a full-time technician, and a full-time pharmacy billing specialist.

The Bottom Line

Programs like the pharmacist-managed oral chemotherapy program at MSTI can help improve clinical and economic outcomes for patients with cancer and community cancer centers and health systems across the continuum of care. Community cancer centers have staff dedicated to intravenous chemotherapy treatment and should implement the same standard for oral chemotherapy treatments.

Our experience with a pharmacist-managed oral chemotherapy program provides data and a framework for implementing similar programs in other cancer centers. The many benefits of having an oncology-trained pharmacist involved in this process include closer evaluation of drug and food interactions, side-effect profiles, and adherence counseling and assessment. The future of cancer care is clearly shifting toward more oral agents, and it is important for our health systems to adjust to the increasing use of oral therapies to provide better care for our patients.

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