

Increase in Oral Cancer Drugs Raises Thorny Issues for Oncology Practices

By Karyn Hede

The recent announcement of the prestigious 2009 Lasker clinical research award to the developers of imatinib (Gleevec) recognizes the advent of a new generation of targeted therapies, many of them taken as pills, that have transformed cancer treatment for many patients. In the last 5–10 years, oral agents such as gefitinib, erlotinib, lapatinib, and capecitabine have followed imatinib. And more are on the way. According to a 2008 National Comprehensive Cancer Network task force report, at least one-fourth of all chemotherapy agents now in development are expected to be delivered orally.

“Even if there is parity [in coverage] between an oral and an i.v. agent, you still have the problem of accessibility, affordability, and management.”

For some patients, oral agents have replaced the long sessions in doctors' offices where intravenous (i.v.) chemotherapy drugs are administered in specially equipped and staffed infusion rooms. And for oncology practices, the agents have raised a series of management issues, including strained finances and new demands on staff time. Systems to ensure patient safety and adherence to oral chemotherapy have yet to be implemented in many practices. And the complexity of reimbursement from both Medicare and private insurers has stretched many oncology clinics, particularly smaller private practices, nearly to the breaking point.

Now several professional groups are giving recommendations and suggesting tools to help practices adapt to the changes that oral chemotherapy has brought.

One major issue for many providers is financial. Historically, a substantial portion of their income has come from reimbursement for i.v. agents delivered in clinic, and oral chemotherapy has upset this income stream.



Mary Kruczynski

“It's becoming more and more common that we put people on orals as opposed to i.v. treatment,” said Justin Favaro, M.D., Ph.D., of Oncology—Charlotte, a four-physician oncology practice based in Charlotte, N.C. “We struggle with [the question of] how do we keep our chemo infusion suite.”

In fact, the cancer care delivery system is entering crisis mode because of the substantial cut in payments for oral cancer drugs, according to Patrick Cobb, M.D., president of the Community Oncology Alliance (COA), a lobbying organization composed of small community oncology practices. According to COA member surveys, community cancer clinics have had to close satellite facilities and cut staff, and smaller clinics are struggling to operate.

Adding to the financial strain, oral chemotherapy requires substantial unreimbursed staff time to educate and monitor patients who now must administer potentially toxic drugs themselves, say some oncologists. "Some of these drugs, even though they are given by pill . . . have a lot of side effects that can be severe, sometimes life-threatening, so we put extra time in teaching about the drug," Favaro said. In the Charlotte practice, each patient receives a 45-minute teaching session with a nurse practitioner. The practice also employs a liaison who works to secure copay assistance for patients. None of these activities is reimbursed, said Favaro.

For patients, the help with financial issues can be critical. Since 2006, when Medicare converted payment for specialty medications, including oral cancer drugs, from Part B to Part D, the outpatient drug benefit, many patients have found themselves unable to afford their oral chemotherapy drugs, which are notoriously expensive. The Part D prescription drug plan requires patients to pay 25% of drug costs from \$265 to \$2,510, and then to pay all drug costs between \$2,510 and \$5,726, the so-called donut hole, before catastrophic coverage kicks in. Many private insurance plans also cover oral chemotherapy agents as a prescription drug benefit with low coverage limits that require substantial out-of-pocket payments.

The uneven coverage has resulted in new laws in Oregon and most recently, Indiana, to require insurance companies to cover oral and i.v. agents equally. Similar legislation is pending in other states. But these legislative efforts are just putting a bandage on the larger problem, according to Mary Kruczynski, COA's director of policy.

"Even if there is parity between an oral and an i.v. agent, you still have the problem

of accessibility, affordability, and management," said Kruczynski, who led a COA committee that issued a report with recommended policy changes in October. The report recommends that practices provide a full-time liaison to work with health plan medical directors on reimbursement issues and that they move to electronic medical records if they have not already done so.

Patient Adherence

Financial issues surrounding oral agents are not the only problems confronting oncologists. Concerns about how well patients are willing and able to manage self-administration of oral chemotherapy arose almost as soon as the new oral drugs became widely available. In 2002, Ann Partridge, Ph.D., Eric Winer, M.D., and colleagues at the Dana-Farber Cancer Institute, Boston, reviewed available studies on patient compliance with oral chemotherapy. They pointed out that few studies measuring patient adherence had been done outside the clinical trial arena, a finding that still holds true today. One exception, an analysis of pharmacy claim data presented at the American Society of Clinical Oncology (ASCO) annual meeting in 2006 by Jean-Patrick Tsang, Ph.D., a pharmaceutical consultant, found that only half of 4,043 patients receiving imatinib over 24 months took their medication exactly as prescribed.

"There's this diffusion of responsibility that goes on in an oral [chemotherapy] prescription," said Ronald Walters, M.D., professor of breast medical oncology at the University of Texas M. D. Anderson Cancer Center in Houston and coauthor of the 2008 National Comprehensive Cancer Network report. The doctor may make some general statements, but the amount of patient education can range from a detailed session with a nurse practitioner to simply handing the patient a pamphlet, he said.

"There's really no SOP [standard operating procedure] in any office, hospital based or community based, that I'm aware of to effectively prescribe . . . and manage these oral oncolytics," said Kruczynski.

A 2006 survey of 48 U.S. cancer centers published in the *British Medical Journal* highlighted the problem. The survey found half

the centers had no safeguards for prescription writing and 10 had no formal process for monitoring patient adherence or side effects.

Last December, ASCO and the Oncology Nursing Society held a workshop to develop consensus standards for safe administration of all chemotherapy and specifically to address the complexities of oral chemotherapy prescribing in the outpatient setting. The new standards, published in the *Journal of Clinical Oncology* in September, spell out minimum safeguards that should be in place, including provision of written or electronic patient education materials about oral chemotherapy before or at the time of prescription. Providers should ensure that patients are educated about administration and disposal of oral chemotherapy pills, according to the standards, and the education plan should include family, caregivers, or others to assist patients with managing their oral chemotherapy regimen.

"We recognized that the growing use of oral chemotherapy was a particular vulnerability for us as oncologists and for our patients," said Joseph O. Jacobson, M.D., of North Shore Medical Center in Salem, Mass., and lead author of the standards. "We felt that there should be no distinction made between oral and parenteral routes of chemotherapy in terms of expectations of care, ranging from documentation and communication to education and monitoring." To help practices implement the practice standards, ASCO and the Oncology Nursing Society will provide online tools and resources at <http://www.asco.org/safety> and <http://www.ons.org/clinical>.

The guidelines also recommend use of an electronic medical record system, which may help remove some of the risk for prescribing errors.

Sylvia Bartel, director of pharmacy and clinical support services at the Dana-Farber Cancer Institute, said that since the 2006 survey, she has worked to put critical information in her institution's electronic medical record system to ensure that safeguards such as the ability to calculate dose per body weight, indicate a dose reduction, and record other medications the patient is also taking. The pharmacy also provides educational

tools to patients, such as a dosing calendar, when they pick up their medication.

In major medical centers with outpatient clinics, some practices are moving to assist pharmacists on site with prescribing and monitoring patients. “What I found with the growing complexity in chemotherapy, and with supportive-care issues, is that we needed to have more clinical pharmacists in the clinic like we have pharmacists in the hospital that go on rounds and work with the medical staff,” said Niesha Griffith, director of pharmacy at James Cancer Center, Ohio State University, Columbus.

But evidence that patient education makes a difference in patient adherence to oral chemotherapy is still lacking. To address that gap, Susan Schneider, R.N., Ph.D., and her colleagues at Duke University Medical Center in Durham, N.C., are conducting a National Cancer Institute-

sponsored randomized clinical trial to test whether tailored educational intervention can increase adherence to oral chemotherapy. The trial will measure adherence rates in 150 newly diagnosed breast or colorectal cancer patients started on an oral chemotherapeutic agent at Duke. A control group will receive standard chemotherapy education, whereas participants in the experimental group work with an advanced-practice nurse who will assess their individual needs and follow up with telephone reminders and coaching. Schneider said that this is the first study to use a tailored approach to promote chemotherapy adherence in oncology patients. She said she’d like to see nurse coaching built into the standard of care for patients receiving oral chemotherapy, much as it is for i.v. chemotherapy now.

In a first step toward that end, the Multinational Association of Supportive Care

in Cancer has recently developed an oral agent teaching tool that is available for download in 10 languages. Executive director Cindy Rittenberg said that the tool is based on an evidence-based literature review on best current practices with input from a panel of nurses and other health care professionals.

“People think it’s a pill, so its perfectly fine: ‘If one is good, two is better. I’m going to cure my own cancer.’ [Regulators] don’t realize that patients think like that,” said Griffith. “With 25% of new [cancer] drugs in development being oral chemotherapy, if we don’t build a structure to support safe use of these drugs out of the gate, we are going to start seeing bad things happen. I’d hate to see us be in a reactionary mode in the oncology world. I’d rather be in a proactive stance.”

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