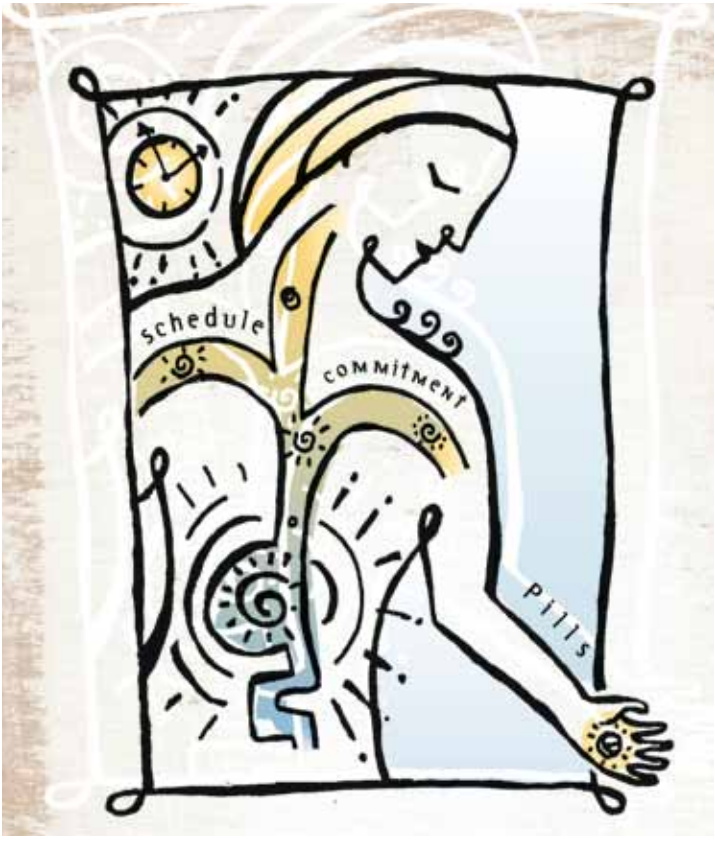
A Patient's Guide to Medication Adherence



Why Taking Your Medicine Is Important ■ Reasons for Non-Adherence ■ **Managing Symptoms** ■ Helpful Tips ■ **Patient-Friendly Advances**

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A Patient's Guide to Medication Adherence

IN THE LATTER HALF OF THE 20TH CENTURY, chemotherapy doled out by a medical team became a mainstay in cancer treatment. Other than the time of arrival at the clinic, patients had little control over their own medication.

MEDICAL RESEARCH has finally begun producing more cancer drugs you can take at home, and not miss a day of work or an afternoon with the grandchildren. Of the more than 40 oral cancer drugs that have been government approved, many of them have appeared only in the past decade, and more are in development. Patients can now be an active and responsible participant in their treatment.

This means adherence is an issue of increasing concern, as one of the biggest advantages of oral treatment is also one of its biggest disadvantages. Pills are easy to take, which means they're also easy not to take. Or to take some days and not others. Or to take just a little, or too much.

Oral drugs may look and feel less impressive, but what is swallowed can be just as important to your health as what comes from an I.V. pump. While relatively few studies have examined the effects of not taking oral cancer drugs properly, data from clinical trials suggest that drugs not taken as prescribed can negatively affect the course of cancer.

Oncologists have now entered a world familiar to their colleagues in most other fields of medicine. It can be called adherence or compliance, but no matter the name, the bottom line is the same: Not all patients are taking their drugs as prescribed. Mostly, adherence has to do with patients not taking enough of their drugs, but doctors also worry that some patients will be so fearful of cancer they will take too much. As with any drug, more does not necessarily mean better.

The good news is that while attention to adherence is relatively new to oncology, this isn't uncharted territory in many other branches of medicine. Findings from other fields can help patients learn ways to improve adherence. An entire body of medical research has been devoted to helping patients take medicine. Some methods work better than others, and some may help one patient and not another.

When there's a reason to stop taking your medicine—the side effects are too severe, the expense is too high, or some other reason—talk to your doctor. There may be alternatives or solutions your medical team can recommend.

The Importance of Adherence

CHEMOTHERAPY ADMINISTERED THROUGH AN I.V. HAS A SPECIAL WAY of announcing itself to the body. The side effects can be notorious, but many patients view the nausea, fatigue, and hair loss as the price of cancer treatment. It also seems logical to think that while the treatment is irritating the healthy cells, it must be giving the cancer a good run, too.

Oral cancer drugs can seem much gentler. It doesn't look any more imposing than aspirin. Treatment is over so quickly. You don't even have to get out of your pajamas. Usually, it doesn't make you feel entirely different right away. But the importance of adherence can't be emphasized enough. The first indication of the significance of treatment comes from clinical trials, studies in which a new drug is compared with another treatment, another dose, or a placebo. These studies are necessary to prove safety and effectiveness for a new drug to be approved.

One of the longest used and most familiar oral drugs is tamoxifen, a hormonal therapy used for both treatment and prevention of breast cancer. Among women diagnosed with early-stage breast cancer with estrogen-positive tumors, clinical trials have indicated that five years of tamoxifen use may reduce the risk of cancer recurrence by one half. In other words, women participating in the research who took the pills were more likely to be alive and cancer-free five years later.

What would those numbers look like if women didn't take the medicine as prescribed? The answer is less clear than you might think, and little research has addressed the question directly. While adherence in other medical fields has a long history of investigation, the problem is a relatively new issue in oncology. Much of the knowledge is based on anecdotal exchanges among doctors, who increasingly find themselves comparing notes about a patient whose chemotherapy didn't seem to be working—only to find out the person wasn't taking the drug. That said, some true scientific data are also emerging.

Just recently, researchers announced the findings of one of the first and largest studies to examine the impact of medication adherence on real-world survival rates among women prescribed tamoxifen. The results, described at the American Society of Clinical Oncology Breast Cancer Symposium in September 2007, found that women who took less than 70 percent of their prescribed dose of tamoxifen had a 16 percent increase in the risk of death compared with the women who took the recommended amount. The study was based on 1,633 women prescribed the drug for about two and a half years.

The development of aromatase inhibitors, drugs that interfere with the body's production of estrogen in postmenopausal women, led to a new generation of oral drugs for breast cancer. Like their tamoxifen cousin, these drugs also need to be taken as prescribed to be fully effective, and some studies have suggested an even longer survival time compared with tamoxifen. Nonetheless, the possibility of a greater benefit has not seemed to improve adherence. A 2006 study in the journal *Oncology* from researchers at Harbor-UCLA Medical Center in California suggested

adherence to aromatase inhibitors was no different from tamoxifen.

Or consider another oral medicine, Gleevec (imatinib), which can keep chronic myeloid leukemia in check. Clinical trials have measured whether Gleevec affects the progression of the disease, and for many patients the results are reassuring. A 2006 study in *The New England Journal of Medicine* reported that after five years of taking Gleevec, 89 percent of CML patients were still alive, a remarkable success given the natural history of the disease.

Few researchers have examined whether that number could hold when patients have breaks in their treatment schedule. However, studies are starting to probe into the issue, even just to get a sense of the scope of the problem. A phase III study published in the *Journal of Clinical Oncology* in 2007 found that interruption of Gleevec treatment in patients with advanced gastrointestinal stromal tumors resulted in rapid progression in most patients—26 of 32 patients in the interrupted group had their disease progress compared with eight of 26 in the continuous therapy group.

Oral drugs are also available that go beyond prevention of recurrence or suppression of cancer, and target tumors themselves. The oral chemotherapy drug Xeloda (capecitabine) is designed to treat metastatic breast and colorectal cancers. Patients need to take it twice a day in 21-day cycles. In clinical trials, patients who took Xeloda experienced a somewhat longer survival rate than patients on the standard chemotherapy.

The experience in other fields indicates that adherence is paramount to getting the full benefit of a drug. For example, a 2005 study of four major conditions—high blood pressure, diabetes, high cholesterol, and heart failure—found that patients who took their medicine as prescribed had significantly lower chances of entering the hospital than patients who didn't stick to the treatment.

While the consequences of stopping Xeloda and other cancer drugs may still be unpredictable, doctors aren't eager for their patients to launch their own personal clinical trial. Yet as oral cancer drugs become a larger part of cancer treatment, the consequences of stopping treatment will be an increasing area of medical study.

Reasons for Non-Adherence

FEW PEOPLE FILL A PRESCRIPTION without intending to take the medicine. When the diagnosis is new, the determination is strong. But things change.

Each patient who stops taking a medicine, or doesn't take it as prescribed, does so for a specific reason. Before doctors can improve adherence, they—and the patients themselves—have to understand why and how non-adherence occurs.

A quarter of all cancer patients currently use oral medications to manage their cancer or side effects from the disease and its treatment, according to a recent national study by Harris Interactive. Of those, a third admitted they didn't always follow their doctors' directions and more than half said they forgot to take their medicine.

For cancer patients, the most common challenge to adherence is side effects. All cancer drugs can have side effects, and many of these side effects go beyond simple aches and pains. When they occur, a person has to decide whether the immediate threat of side effects today is greater than the potential long-term benefit of the drug tomorrow.

Unfortunately, many patients report they have trouble making doctors understand this dilemma, leaving a patient to weigh the decision alone, without professional guidance. Nonetheless, experts stress the importance of talking to your doctor about managing side effects to avoid any disruption in therapy.

Sometimes people want to take the medicine, but cost becomes a barrier. Many oral cancer drugs are new and do not have generic alternatives, and insurance coverage can be unpredictable. Sometimes the drugs are considered investigational (still in clinical trials) and aren't covered when prescribed off-label. And approved drugs that are covered may carry eye-popping co-payments or deductibles. Faced with choosing among medicines, patients may choose the drug that makes them feel better immediately, not necessarily a drug prescribed in hopes of preventing cancer from recurring.

Then there are reasons that have more to do with denial than actual logistical and physical problems. That pill, every time it comes out of the bottle, is a reminder that a person now has cancer, or had cancer, or lives under the specter of cancer. After going through surgery, radiation, or intravenous chemotherapy at a clinic, people can get tired of being reminded about their illness.

Patients also get discouraged from taking their medication because of the complexity of the treatment regimen. If a person is taking other drugs, scheduling pills can be like air traffic control. Sometimes this pill can't be taken too close to another one, but it has to be scheduled for a certain time of day. Some have to be taken with food, but not with certain foods. Some have to be taken on an empty stomach. And what if you miss a dose?

All of these challenges can be managed, but you may need help. Medical research has provided insights to help patients stick to their treatment schedule. The advice varies, depending on the reason for not complying. Consult with your health care team to figure out which approach is best for you.

Tips for Taking Your Pills

DOCTORS, NURSES, AND MEDICAL RESEARCHERS want patients to realize the full benefit of oncology medication, but they also recognize that taking pills regularly isn't as straightforward as it sounds.

Researchers have studied ways to help patients remember to take their pills and to ease side effects. In addition, organizations and manufacturers are working to help make medications more affordable. However, none of these solutions has demonstrated dramatic effects overall. What matters most is the solution that works for you.

Health Belief Model

Public health experts in the 1950s developed a way to predict behavior through a system called the Health Belief Model. Though developed as a way to understand the response to tuberculosis screening, the concepts apply to modern drug treatment.

Simply speaking, the Health Belief Model operates on the general principle that patients work out a mental balance sheet when making health decisions. They have to believe not only that the illness is serious, but that they are vulnerable to it, that the prescribed treatment will help, that they can stick with the regimen, and other constructs. The general concept applies to many types of decisions related to improving health—even seeking routine mammograms.

Using the concepts of the Health Belief Model and other guides, patient educators can discuss other mental barriers to adherence, and tailor help just for you. Experts say these and other steps show that help with compliance doesn't have to be complicated or highly technical. A solution might be as simple as using a pill box: a full compartment can be a reminder to take the drug, and an empty one can be reassurance you haven't forgotten. Another approach might be to create a mental contract with yourself: After filling the first prescription, come up with a plan to take the pill, such as "when I watch the news every evening," and then set the pill bottle on the television.

Clear Communication

At the core of many problems is communication, which starts during the first office visit when your doctor gives you the white slip of paper. Look at the prescription to make sure you can read it and you understand it. Patients need a full description of possible side effects, including severity, frequency, and options for management. Throughout the process, patients need open and accessible relationships with their doctors and other health care providers to discuss their doubts or frustrations.

Oncologists traditionally aren't accustomed to thinking about therapy carried out at home, so they might not ask how things are going, and you might not even have an appointment to see them for months. (This mindset is changing, though, as more oral drugs come on the market, and oral cancer therapy becomes a mainstay of treatment.)

Patients themselves have a responsibility to speak up when they're having problems, or when they have questions about how to take a pill or about the pill's significance to their health. Patients need to make it clear how the concern about side effects impacts their lives. A rash may not be a significant problem

for one person, but for a sales representative who must look his or her best to customers, a rash can threaten a job.

A doctor who doesn't grasp that a patient is having problems—or doesn't know the extent to which those problems are interfering with daily life—won't be able to suggest alternatives, to offer tips to make taking the medicine easier, or even find financial assistance programs. A doctor's office might even have a system—or point you to one—that would offer tools that fit with your needs and lifestyle.

Research What Works for You

For patients who prefer something high-tech, gizmos are available with alarms, pre-sorted pill sets, and automatic dispensers. In June 2007, the Food and Drug Administration approved the Electronic Medication Management Assistant (EMMA), which stores and dispenses medication and lets your doctor monitor your day-to-day well-being, including allowing him or her to adjust doses and medication times.

Some hospitals may schedule a nurse or other provider to regularly call, check on side effects, and give personal reminders. Health care institutions and communities may also have patient navigators, designated individuals or teams who help patients and caregivers locate information and advice on coping with their treatment, finding financial assistance, getting answers to questions about insurance, making lifestyle changes, and helping you better learn to help yourself. These are volunteers or professionals who know the landscape.

And sometimes the best advice can come from those who have been there—support groups. Hearing how someone else remembers to take their pills, or manages the side effects, might provide the most straightforward and practical information. Support groups might also have connections to little-publicized programs from corporations or charities in your area to help with treatment costs.

Sometimes other medical disciplines can offer clues that may help people with cancer. The field of psychiatry has evidence that an approach called compliance therapy helps some patients stick to their antipsychotic drugs. Much of the technique is aimed at self-reflection. Patients are asked open-ended questions that prompt them to say for themselves, and better articulate, the need to stick with treatment. It often emphasizes introspection, freedom, and responsibility. The hope is that critical thinking in a person's own mind can improve motivation.

Motivation can also be found at home. Patients usually don't go through cancer alone, and the same family members who help a person through surgery, radiation, and long hospitalizations might also help with medication adherence. Thinking of dropping the medicine because it is too burdensome? Discuss it with a family member. Having trouble remembering it? Have a friend call and remind you.

Plan on taking your pill bottle and prescription with you on vacation. If you do leave it at home, call your doctor's office right away; the staff may be able to ensure you get the medicine through a nearby pharmacy. Even though you're taking a holiday, the cancer cells do not. Just as cancer becomes a part of daily life, so must the medication.

Making It Simple

ORAL CHEMOTHERAPY IS QUICKER AND MORE CONVENIENT than hours at a clinic. Studies indicate that patients overwhelmingly prefer pills over getting hooked to an I.V. But that doesn't mean it's easy for everyone. Some cancers or their treatments leave a person with difficulty swallowing because of dehydration, inflammation, metastatic tumors, mouth ulcers, and other reasons. Also, because cancer is generally a disease of older people who might have other chronic conditions, such as neurological disorders, the seemingly effortless act of taking a pill can be complicated.

When faced with problems swallowing, people prescribed oral therapies can be left to crush up their pills—which could release the dose too quickly into the body, thus causing more severe side effects—or perhaps just give them up in frustration.

Knowing this, pharmaceutical companies are constantly modifying their products to make them more patient-friendly. Drugs to treat osteoporosis, for example, once had to be taken every day with strict dictates on how and when to take the pills. Yet drugs are available now that can be taken once a month, and a recently approved injection can last a year. Or consider the simple flu shot, which isn't necessarily a shot anymore. It can now be administered as a nasal spray.

Oral cancer drugs are also undergoing innovation. Soltamox, a liquid form of tamoxifen, was approved for use in 2005. An oral spray, Zensana (ondansetron), is being developed to ease the nausea and vomiting brought on by chemotherapy—a particular improvement given that a person who needs the drug would, by definition, have trouble keeping down pills.

Researchers predict other patient-friendly advancements will come to oncology the way they have come to other fields—developments that reduce the number of pills, simplify the way they're administered, and even improve how they taste, a particular issue in pediatric treatments.

But reformulating a drug can be a cumbersome process. A lot of obstacles lie in how patients' bodies metabolize drugs differently, all while making sure the drug reaches the cancer at the right (and safe) dose.

Other fields have overcome many of these hurdles, and doctors predict oral cancer drugs will probably also get simpler as they become more widespread. As such medicines grow in number, the hope is that the obstacles will diminish.

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COVER ILLUSTRATION BY JAN PULTS

Keeping Track of Your Pills

CLIP OUT THIS CHART and use it to help you keep track of your medicines. Take it with you to all doctor appointments, even those not with your oncologist.

Name: **Date:**

Name of medicine and dose	What do I take it for?	How often do I take it?	What time do I take it?	Am I having any side effects?	What do I do if I miss a dose?	Special Instructions?	When do I need a refill?

Known allergies to medicine: