Food and drugs: Administer together

September 19 2011

A regulatory bias against taking oral anti-cancer medications with food places many patients at increased risk for an overdose and forces them to "flush costly medicines down the toilet," argues Mark Ratain, MD, an authority on cancer-drug dosing.

In a commentary published early online Sept. 19 in the Journal of Clinical Oncology, Ratain, the Leon O. Jacobson professor of medicine and director of the Center for Personalized Therapeutics at the University of Chicago Medical Center, says it could be safer, more effective and more cost-efficient if the many cancer drugs that are better absorbed with food were studied and, when appropriate, prescribed to be taken with food.

"Instead of taking high doses on a empty stomach—which is how most of these drugs are labeled—patients would be better off taking much lower doses along with a meal," Ratain said. "This could reduce the risks of an overdose, save money and give patients more control over their daily lives."

In the last two decades, drug treatment for cancer has shifted away from drugs given through an intravenous line to drugs taken by mouth. Drug makers have set dose levels for these drugs based on data from patients who take their pills on an empty stomach. But many drugs are absorbed much more effectively with food, especially with a high-fat meal.

"With a monthly outlay measured in thousands of dollars," Ratain said, "we should view drug-drug or drug-food interactions as opportunities to

lower costs."

Abiraterone acetate (ZYTIGA), approved April 28, 2011, for the treatment of metastatic prostate cancer, is a perfect example. It has a "food effect" greater than any other marketed drug. The dose can increase fivefold with a low-fat meal and tenfold with a high-fat meal. Patients are instructed to take it while fasting.

"No food should be consumed for at least two hours before the dose of ZYTIGA is taken and for at least one hour after the dose of ZYTIGA is taken," warns the package insert. "The tablets should be swallowed whole with water."

"Taking this drug according to instructions means the amount of the drug available to fight cancer is decreased by 80 to 90 percent," Ratain points out. "At least three-quarters of it, at a per-patient cost of about $5,000 a month, is literally wasted. It gets excreted and flushed away."

More worrisome is the risk of an overdose if a patient takes the standard dose—1,000 mg daily—after fasting for two hours, then gets hungry and, rather than fast for one more hour, eats a meal. Depending on the caloric intake, he could get up to 10 times the intended dose.

Instead, offers Ratain, patients could take one-fourth of the dose with a healthy, low-fat breakfast. They could get the same anti-cancer benefit, eat when they are hungry and save an estimated $3,750 per month. "This way, the patient gets a simplified schedule, the convenience of eating whenever he wants, and shares the savings with his the insurance company."

Patients should "never launch such experiments on their own," he cautions. Physicians should assess the effects, note person-to-person variations, and learn to predict how individual patients will take up and

metabolize such drugs in the presence of certain foods.

Another drug with a similar food boost is lapatinib (TYKERB), used to treat breast cancer. A meal increases the bioavailability of the drug by 167 percent; a high-fat meal increases uptake by 325 percent.

Although the food effect is smaller than for abiraterone, "we could potentially use 40 percent of the drug and save each patient about $1,740 a month," Ratain said. The major toxicity associated with the drug is diarrhea, which may be caused by unabsorbed drug. So "taking a lower dose with food should increase absorption and potentially reduce this side effect."

A third example is nilotinib (Tasigna) capsules, approved in 2007 for treatment of chronic myeloid leukemia. Patients take nilotinib twice a day on a stomach that has been empty for two hours and must remain empty for another hour. Because elevated nilotinib levels can cause heart-rhythm irregularities and sudden death, the no-food alert appears 11 times in the package insert. Two of those alerts are "black-box" warnings, which is "the industry's way of saying 'if you take this drug with food you might die,' " Ratain said.

For drugs whose absorption is decreased when taken with food, the FDA generally advises taking the pills while fasting. For non-cancer drugs where uptake is enhanced by food, the FDA favors taking them with a meal.

Yet for oral anti-cancer drugs, the FDA appears to have "an apparent bias for fasting," Ratain said. "That is inconsistent with labeling in other therapeutic areas, and with fundamental principles of clinical pharmacology."

Provided by University of Chicago Medical Center