Off-label Drug Use

What is off-label drug use?

In the United States new drugs are tested in clinical trials (research studies) before they are approved by the US Food and Drug Administration (FDA) for use in the general public. The clinical trials are done to show that the drug:

- Works to treat a certain medical condition
- Works the way it's expected to
- Is safe when used as directed

When the FDA is satisfied that the drug works and is safe, it and the maker of the drug create the *drug label*. This is not an actual label that sticks to a bottle, but a report of very specific information about the drug. The FDA must approve this report, which is made available to all health professionals who prescribe or sell the drug.

The drug label gives information about the drug, including the specific medical condition(s) it's approved for (called the *indication(s)* for use), the doses to be used, and how it's to be given. When a drug is used in a way that is different from that described in the FDA-approved drug label, it's said to be an "off-label" use. This can mean that the drug is:

- Used for a different disease or medical condition
- Given in a different way (such as by a different route)
- Given in a different dose than in the approved label

For example, when a chemotherapy drug is approved for treating one type of cancer but is used to treat a different cancer, it's off-label use. The same is true if a drug is approved to treat a type of cancer at a specific stage (extent of spread), but it is used to treat a cancer at a different stage.

Off-label is also called *non-approved* or *unapproved* use of a drug.

Is off-label drug use legal?

The off-label use of FDA-approved drugs is not regulated, but it is legal in the United States and many other countries. An exception to this is the use of some controlled substances, such as opioids (pain medicines like morphine and fentanyl). These drugs cannot legally be prescribed in the United States except for approved purposes.

While it's legal for doctors to use drugs off label, it's not legal for drug companies to market (advertise or promote) their drugs for off-label uses. Off-label marketing is very different from off-label use.

Why are drugs used off-label?

Older, generic (non-brand name) medicines are the ones most often used off label. New uses for these drugs may have been found and there's often medical evidence from research studies to support the new use. But it's often too costly for the makers of the drugs to put them through the formal, lengthy, and expensive process required by the FDA to officially approve the drug for new uses.

Off-label drug use is common in cancer treatment because:

- Some cancer drugs are found to work against many different kinds of tumors. Chemotherapy treatments often combine drugs. These combinations might include one or more drugs not approved for that disease. Also, drug combinations change

of cancer.
- Oncologists and their patients may be more willing to try off-label drugs than other medical specialties.

What problems can be caused by off-label drug use?

Reimbursement

The biggest problem is getting insurance plans to pay (reimburse) for off-label drug use. Many insurance companies will not pay for an expensive drug that's used in a way that's not listed in the approved drug label. They do this on the grounds that its use is "experimental" or "investigational."

In cancer treatment, these issues have been largely addressed through 1993 federal legislation that requires insurance to cover medically appropriate cancer therapies. This law includes off-label uses if the treatment has been tested in careful research studies and written up in well-respected drug reference books or medical journals. In 2008, Medicare rules were changed to cover more off-label uses of cancer treatment drugs.

Still, the health insurance coverage laws and regulations are complex. If your doctor is thinking about off-label drug use, you and your doctor should carefully check your health plan's coverage. If you are denied coverage, it might help if the doctor sends the insurer copies of peer-reviewed journal articles or other respected sources that support the off-label use.

Legal risk

Another problem is that off-label drug use often does not reflect "standard of care" treatment. This could raise concerns about the legal risk to the health care provider should a patient have an unwanted or bad outcome from the treatment.

Lack of regulation and information

The FDA does not regulate the practice of medicine. In general, once the FDA approves a drug, licensed doctors can use it for any purpose they consider medically appropriate.

One of the biggest problems related to widespread off-label use is the lack of information about how to best use the drug other than for what it was approved. The drug label is one of the most reliable and easy-to-find sources of information available to

health professionals, caregivers, and patients. But the label can only contain the information that's been approved by the FDA, and it does not cover off-label uses.

The medical literature reports clinical trials, including those that are not part of the FDA approval process. This is the main source of off-label use information. Some professional health organizations develop treatment guidelines that may offer options including off-label drug uses. Treatment guidelines are based on information from medical literature, including clinical trials, and recommend standard ways to treat certain diseases.

Lack of information on off-label drug use and outcomes may also put patients at a higher risk for medication errors, side effects, and unwanted drug reactions. It's important that the patient and doctor talk about the possible risks of using the drug and weigh them against the possible benefits.

How common is off-label drug use?

Little information is available on off-label prescribing in oncology in the US. Off-label use can vary greatly from one doctor to another, depending on doctors' preferences, knowledge, and past patient experiences. A 2008 study found that 8 out of 10 cancer doctors surveyed had prescribed drugs off-label. Off-label drug use is also well-documented and very common in certain other settings, such as in pediatrics and HIV/AIDS care.

Studies have reported that about half of the chemotherapy drugs used are given for conditions not listed on the FDA-approved drug label. In fact, the National Cancer

treating certain types of pain.

Another example is lorazepam (Ativan®), an anti-anxiety drug that is often used as an anti-nausea drug in cancer treatment. In oncology, lorazepam is most commonly given under the tongue (the sublingual route), which is also not listed on the drug label. In this case, it's being given for an off-label use and by an off-label route.

What questions should I ask my doctor about off-label drug use?

Here are some questions you might want to ask your doctor. Start by asking if all the drugs recommended for your cancer treatment are approved for the planned use. If any of the drugs are not, you can ask:

- Is there evidence to support the off-label use of this drug to treat my type of cancer?
- Is this off-label drug likely to work better than an approved drug?
- What are the risks and benefits of off-label treatment with this drug?
- Will my health insurance cover off-label treatment with this drug?
- If my treatment involves a combination of drugs and one of the drugs is being used off label, will my health insurance cover it?

Hyperlinks

1. www.cancer.gov
2. www.fda.gov/cder

Additional resources

Thakkar S. Oncologists judge themselves the best judges of cancer treatments. *J Natl Cancer Inst*. 1997;89:1188-1189.

United States General Accounting Office. Off-label drugs, reimbursement policies constrain physicians in their choice of cancer therapies (report GAO/PEMD-91-14). September 1991. Washington DC. Accessed at http://archive.gao.gov/d18t9/144933.pdf on March 17, 2015.

Last Revised: March 17, 2015

Written by

The American Cancer Society medical and editorial content team (https://www.cancer.org/cancer/acs-medical-content-and-news-staff.html)

Our team is made up of doctors and oncology certified nurses with deep knowledge of cancer care as well as journalists, editors, and translators with extensive experience in medical writing.