

What does “off-label use” mean?

The FDA-approved use or uses for a medication are narrowly defined in the professional product label. These include the disease being treated, the dose, the duration of treatment, and the age group of patients for which the medication is intended. The professional product label, or package insert, is the tightly folded paper written in small type and filled with dense technical jargon that must accompany every medication delivered to the pharmacy. Package inserts are not routinely distributed to consumers at the time a prescription is dispensed, but they can be requested from the pharmacist.

What constitutes off-label use of an approved drug?

When a medication is prescribed for a use or in a way that has not been approved by the FDA, this activity is commonly referred to as an “off-label use.” A more accurate term would be off-label prescribing because patients, for the most part, do not know when they are receiving a medication for an off-label use.

Are physicians allowed to prescribe any marketed drug for any use?

Yes. In general, there are no laws or regulations preventing physicians from prescribing medications for uses that have not been approved by the FDA. However, some insurance companies, managed care organizations and governmental programs may not cover the cost of medications prescribed for off-label uses, noting that these uses are experimental and that the medication has not been shown to be safe and effective for the prescribed purpose.

Likewise, there are no laws or regulations requiring physicians or pharmacists to disclose to patients when a drug has been prescribed for an unapproved use.

Why is promotion of off-label use not allowed?

The major reason for such an advertising prohibition is public safety. The promotion of prescription medications for off-label uses is considered to be false and misleading based on current laws and regulations. It is illegal to make claims about the effectiveness of a medication when there is no FDA-validated scientific evidence that the medication actually works, or claiming that a medication is safe when, in fact, the safety of the medication has not been



studied for the use that is claimed.

Unfortunately, there have been far too many tragic situations leading to serious injuries as a result of prescribing medications when there was no evidence that giving the medication would result in a therapeutic benefit to the patient.

Is it possible that benefits and harms differ when drugs are used according to the approved label versus off-label?

This is certainly possible because a drug that is being prescribed for an off-label indication has not been documented by an FDA review of scientific studies to be safe or effective in the condition for which it was prescribed off-label. For certain off-label indications, efficacy and safety information is available and has been judged to be unfavorable. For other such indications, there is insufficient data available.

When interviewed in 2002 for a Knight-Ridder newspaper series on off-label use, Arnold Relman, a former editor of the prestigious *New England Journal of Medicine*, said, “Sometimes it may help, sometimes it may do more harm than good, and sometimes it may kill people.” No one knows for sure the results when prescribing off-label.

Why is off-label use so common?

A recent survey of 160 commonly prescribed medications revealed that 21 percent of prescriptions were for off-label uses. One reason is cavalier physicians, who view off-label use as “cutting-edge” medicine when there is little or no acceptable evidence supporting their practice.

Another reason is that the economic rewards to manufacturers of off-label use sales can be enormous. There also may be significant economic benefits to prescribers who accept cash and other gifts to prescribe medications off-label.

Aggressive, and sometimes illegal, pharmaceutical industry marketing has been cited as a contributory cause of off-label use. A recent, famous whistle-blower lawsuit involved the drug gabapentin (Neurontin). This medication was originally approved by the FDA for a certain type of seizure in children. This is not a large, lucrative market and the management of the company made the calculated decision to bypass the FDA’s drug approval process. It marketed Neurontin through medical education programs to physicians, questionable research reports, and medical journal publication, indicating 11 other uses for which gabapentin had not been shown to be safe or effective.

Gabapentin reached the Wall Street definition of a “blockbuster medication” with billions of dollars in sales. An unknown number of patients were prescribed gabapentin without acceptable evidence of safety or

effectiveness for the conditions being treated. The lawsuit was settled for \$468 million, which was just a small fraction of the profits made by the company through the illegal off-label promotion of gabapentin.

Off-label medication promotion also may spawn new medical specialties or industries. A former physician executive of a major pharmaceutical company alleged that his employer illegally promoted human growth hormone as a treatment to delay the normal aging process. The company supported financially the establishment of anti-aging clinics. At this time, however, there is no good scientific evidence to support the use of growth hormones as an anti-aging treatment, and there are suggestions that it may be harmful when prescribed off-label for this indication.

The FDA has a role in ensuring that medications are not promoted for off-label uses. However, the FDA has been chronically underfunded by Congress, leaving the public in a marketplace for medications with less-than-adequate protections.

Key messages

- ✓ Off-label use means that an approved drug is used for a condition that is not approved by the FDA.
- ✓ Physicians can prescribe any available marketed drug for any indication, since medical practice is not regulated by the FDA.
- ✓ It is illegal for drug companies to promote drugs for off-label use.
- ✓ Benefits and harms can be different when drugs are used off-label.
- ✓ As off-label use is common, ask your physician whether you are taking any drugs off-label.

