Prescribing Off-Label, Not Off Base: Incidence, Guidance and Recommendations
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Overview:

The use of drugs to treat medical conditions for which they have not been approved has recently been in the national spotlight through two sources - the motion picture industry and the news media. The Oscar-winning film, The Dallas Buyer’s Club, tells a moving story of a man diagnosed with HIV who sought to use a drug that reportedly showed promise in reducing the symptoms and progression of his disease, but had not been approved by the Food and Drug Administration (FDA). Earlier this year, USA Today published an article about a family’s urgent and repeated requests to a drug company to use an unapproved medication to treat their young son’s life-threatening illness. The article chronicled the outpouring of public support for the family’s plea, as well as the drug company’s apparent public relations dilemma and subsequent refusal to approve the drug for use that does not meet the stated criteria.

Both of these stories make compelling cases for off-label drug use. They also draw our attention to the frustration and desperation of patients who are seeking at best a cure for and, at a minimum, relief from the symptoms of their disease. When traditional therapies fail or produce suboptimal results, the use of drugs for a medical condition other than that for which they were approved, often referred to as off-label drug use, may be a logical next step. This is especially true if there is evidence to support a better patient outcome.

This article will explore the incidence of and reasons for off-label drug use and provide available guidance on the topic. It will also offer recommendations designed to assist healthcare providers who face the challenge of treating patients with the most effective drugs and biologicals while also remaining within what is considered the prudent practice of medicine.

Incidence of Off-Label Use:

To properly frame the issue, some statistics that describe the scope and type of off-label drug use will be helpful. As early as 2007, one study’s findings estimated that off-label drugs accounted for 40 to 60 percent of all prescribed medications. A study of off-label use in pediatric populations was as high as 62 percent. It further appears that certain disciplines are more likely to use medications off-label. By way of example, within a 13-year period, providers moved from prescribing traditional antipsychotic agents in 84 percent of office visits to prescribing non-traditional agents in 93 percent of visits. There is also a greater incidence of off-label prescribing in the treatment of obstetrical patients, reportedly because there are relatively few drugs approved for use within this area of medicine. Off-label use is also prevalent in pain management and in oncology.

Definitions & FDA Guidance:

Off-label drug use involves the use of a drug in an unapproved manner, either by dosage, age, administration or indication. The use of drugs in an unapproved manner is not illegal and although the FDA does not regulate the practice of medicine, it cautions:

“If physicians use a product for an indication not in the approved labeling, they have the responsibility to be well informed about the product, to base its use on firm scientific rationale and on sound medical evidence, and to maintain records of the products use and effects.”
The FDA also distinguishes unapproved versus investigational use of drugs and biologicals by stating, “Investigational use suggests the use of an approved product in the context of a clinical study protocol.” [see 21 CFR 312.3 (b)]. It further describes the “principal intent” of investigational use is “to develop information about the product’s safety or efficacy” and outlines the process to follow.

These definitions demonstrate the fine line providers face in prescribing drugs and biologicals off-label. Even when there are obvious benefits, there are also concerns. Chief among them is the potential liability. Providers are challenged to find an acceptable balance between the risks and rewards.

**Risk Management Recommendations:**

With the foregoing as a foundation, we will turn to recommendations to both guide you and reduce your potential liability in prescribing drugs and biologicals off-label. They include the following:

1. Determine whether the principal purpose of the off-label drug use would more likely be considered investigational rather than a preferred alternative over more traditional therapies. If it is the former, you are obliged to follow the FDA guidance on conducting a clinical trial.

2. Educate yourself on the off-label use of the medication. Ideally, your prescribing should be supported by peer-reviewed articles from scholarly journals.

3. Obtain the consensus of your peers, when able. Consider submitting your research to your hospital’s institutional review board if your use borders on investigational use.

4. Educate your patient and, if he or she permits, a family member or friend on the risks, benefits and alternatives to the off-label drugs and biologicals you are recommending. This is especially true if they are not well-recognized for your intended unapproved use. Document the conversation.

5. Using an informed consent form when you have concerns over medications that may not have strong evidence for your intended use and/or you have particular concerns about the patient.

6. Contact, or have the patient contact, the patient’s insurance company to determine if the unapproved drug is covered under the plan. Cost may be a significant factor in the patient’s willingness to take the drug.

7. Document the patient’s response and outcomes and reasons for continued use, particularly when the results are suboptimal.

8. Query your state’s medical society regarding whether the state has any requirements to obtain patient consent for off-label prescribing. While many states have a “reasonable physician” standard, some may have adopted other standards that impose additional requirements.

9. Ask your malpractice carrier whether off-label prescribing is covered under your policy and if there are any specific requirements to demonstrate support for this practice.

10. Check the hospital formulary or with the pharmacist to determine prescribing requirements if you are planning a hospital admission for a patient for whom you have prescribed off-label medications that may not be well-recognized.

11. Update, organize and retain your research and evidence on off-label medications you prescribe. Published support for off-label use can change from year to year. You may need to justify your reasoning for prescribing several years into treatment and it may be difficult to rely solely on your memory. If you are prescribing an unapproved drug for multiple patients, you may find it helpful to keep a log to aggregate data and outcomes that may be evaluated to help decide continued use of the drug in that manner.

**Summary:**

When anticipated patient outcomes have not been achieved and patient care has not been optimized through the use of approved drugs and biologicals, off-label drug use may be the only available option for your patient. The information on incidence and available guidance coupled with the practical recommendations in this article are designed to assist you in off-label prescribing and reducing the potential liability associated with this practice.
References:

8. Ibid.
9. Ibid.
13. Ibid.

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