Is Off-label **Use Ever Too Risky?**

Learn how and when to prescribe drugs off label, while keeping your patients — and yourself — safe.

Exciting new advances in epidemiological research and disease prevention continue to fuel the age-old practice of using FDA-approved drugs for off-label purposes. Physicians in various medical fields prescribed an estimated 150 million drugs for off-label use in the United States alone in 2001.[1] The FDA allows this practice and will continue to do so as long as the drugs are safe and effective.

The use of drugs to treat conditions other than those for which they are approved has helped physicians in various medical fields develop innovative therapies — and ophthalmology is no different.

New, off-label uses for a wide variety of drugs in retina, glaucoma and cataract care are being tested in clinical trials and discussed on a regular basis. As a new ophthalmologist, you'll need to stay up to date on the latest research available and learn how and when to use drugs off label to care for patients.

This article will discuss the prevalence of off-label drug use, the ethical concerns, how to stay informed and how to protect yourself from potential liability.

A Common Practice

There are many drugs ophthalmologists prescribe and use off label to maximize patient care. Currently, they use intravitreal ganciclovir sodium (Cytovene), a medication originally approved for systemic applications, to treat cytomegalovirus retinitis. Retina specialists use intravitreal triamcinolone acetonide (Kenalog), labeled for intramuscular use, to treat age-related macular degeneration (AMD), diabetic macular edema and retinal vein occlusion and to prevent cystoid macular edema (CME) in patients undergoing retinal surgery.

They use the anti-VEGF agent bevacizumab (Avastin), approved for lung and colorectal cancer, to treat wet AMD and CME. And they use nonsteroidal anti-inflammatory drugs (NSAIDs) after selective laser trabeculoplasty, panretinal laser treatments, vitrectomies and other surgeries to relieve pain and inflammation. General clinicians use corticosteroid drops after LASIK surgery, and NSAIDs, labeled for postoperative inflammation, to relieve pain from viral conjunctivitis. And the list goes on.

Standard of Care

In many instances, these drugs and others, have become the standard of care for treating and managing a variety of eye diseases, preventing surgical complications and alleviating postoperative pain. In fact, in some cases, you have a medical and legal responsibility to use these drugs.

The American Academy of Ophthalmology's (AAO) preferred practice pattern guidelines give doctors recommendations to treat and manage eye diseases with drugs that aren't FDA-approved for those conditions. For instance, fourth generation fluoroquinolones, such as gatifloxacin ophthalmic solution 0.3% (Zymar) and moxifloxacin hydrochloride ophthalmic solution 0.5% (Vigamox), are recommended for the treatment of bacterial keratitis. The drugs are considered so effective against gram-positive bacteria that they're preferred over the other generations of fluoroquinolones. The topical corticosteroid prednisolone acetate (Pred Forte) and the topical NSAID ketorolac tromethamine (Acular) are recommended to treat CME after cataract surgery, although no topical medication has been approved for this condition.

What's more, an intravitreal injection of vancomycin (Vancocin) or ceftazidime (Tazicef) has been named the standard of care for treating endophthalmitis, even though these drugs aren't approved for this surgical complication.

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Ethical Considerations

While using these drugs off-label is a widespread and acceptable practice, it does raise some key concerns about efficacy and patient safety.[2-4] To ensure you make the right decisions when prescribing or using drugs off label, you'll need to ask yourself these questions:

- "Has this drug been tested for efficacy, safety and dosing in a series of clinical trials?"
- "Will this drug pose a significant risk to my patients?"
- "Does the drug have a good track record for efficacy and safety?"
- "And is the drug widely used by other ophthalmologists in the field?"

If you've answered yes to all but the second question, you can begin using the drug with a clear conscience. However, if you're considering using a drug off label that's been established as standard of care, you probably won't need to ask yourself these questions.

The bottom line is that you want to feel confident when making treatment decisions for your patients. And you want to make these decisions based on what's reasonable within the scope of practice.

Protecting Yourself

If a particular drug hasn't been widely used off label or has little or no scientific research supporting its efficacy and safety to date, however, you feel strongly that it's a viable option for your patient, you can possibly protect yourself from liability by having patients sign a consent form. The form should explain that you've explored every treatment option available to cure or manage the disease and that you've decided to use the drug off label for the condition. The form should include the possible risks and complications of the drug. And you should discuss the details point by point with your patient. Tell your patient you're using a drug that has been approved by the FDA for cancer (in the case of Avastin) but not for the eye. Mention that most ophthalmologists don't use the drug routinely for the disease, and why. Then, document on the form that this conversation took place, and ask the patient to sign it. A number of consent forms for off-label drug use are available at omic.com, including forms for bevacizumab and mitomycin C when used in glaucoma and refractive surgery.

Keep in mind, however, that a signed consent form doesn't eliminate all medical and legal risks. But if you use drugs off label that are considered the standard of care for a particular condition, or if they're in widespread use, you shouldn't have a problem.

Staying Informed

The key is to be in a position to make the best treatment decisions. These guidelines can help you use off-label drugs responsibly:

1. Read the literature. Peer-reviewed journals and other professional medical publications publish the results of clinical studies on various drugs being considered for off-label use. They also feature articles in which study authors and leading experts in the field discuss the efficacy, safety and dosing recommendations of the drugs and whether or not they're in widespread use. Visit pubmed.com and the Web sites of the journals and your local ophthalmology organizations to learn about the latest research. Go to aao.org to review the Academy's preferred practice patterns for eye diseases.

2. Attend meetings. At least once a year, try to attend a meeting hosted by the AAO, The Association for Research in Vision and Ophthalmology, the American Society of Cataract and Refractive Surgery and other organizations that may be meeting in your area. You'll hear presentations on the latest cutting-edge treatments and preventive therapies and learn about the latest research in disease management. You'll also meet the leaders in the field, have the opportunity to ask important questions and network with colleagues. This is critical to learning about the drugs the experienced physicians are using off label so you can use them with confidence in your practice.

Lifetime of Knowledge

Acquiring such knowledge is a lifelong — and exciting — endeavor. If you take what you learn from your residency and fellowship training and keep abreast of the latest research, you can become a physician who practices medicine on the cutting edge and provides patients with the highest quality eye care possible. And that's what practicing medicine is all about. nMD

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