

# Need Information on “Off-Label” Uses of Anesthetic Drugs? Just Ask the Pharmaceutical Representative!

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The recent Food and Drug Administration (FDA) action in placing a “Black Box” warning on the use of small-dose droperidol for the prevention of postoperative nausea and vomiting has raised medicolegal concerns among practicing anesthesiologists and nurse anesthetists who choose to continue using this highly cost-effective antiemetic without performing a screening 12-lead electrocardiogram (ECG) and 3 hours of postadministrative monitoring as recommended in the package insert (1). Although there is a wealth of published information in the peer-reviewed medical literature establishing the comparable safety and efficacy of small-dose droperidol (0.625–1.25 mg) to other more costly antiemetic drugs (e.g., ondansetron), this type of information is not always available in the FDA-approved and manufacturer-generated package insert. In some cases, the optimal use of a specific drug may actually contradict what is recommended in the package insert (2). For example, the insert states that ondansetron (Zofran®) should be administered prior to induction of anesthesia when used for antiemetic prophylaxis. However, studies have demonstrated greater efficacy when it is administered near the end of surgery (3,4).

Many practitioners are unaware that the package insert is prepared by the pharmaceutical company based solely on data provided to the FDA by the manufacturer. The prescribing of drugs for unapproved (so-called off-label) uses is entirely proper since the decision regarding how to use a drug is based on what is considered “good medical practice,” regardless of whether or not it conforms to the package insert (5). Drug labeling *per se* is not intended to

set a standard for good medical practice. Ideally, the use of drugs in clinical practice would be based on rational scientific theory, expert medical opinion, and well controlled clinical trials (i.e., evidence-based) rather than the package insert. Thus, while the package insert can be a useful source of information about a drug, it is not meant to determine medical practice and is no substitute for sound medical judgment (5).

In 1997, Congress passed the FDA Modernization Act (FDAMA), which included a provision for relaxing the FDA’s long-standing prohibition on promotion of “off-label” use of previously approved products. Unfortunately, this provision provided inadequate incentives for drug manufacturers to seek agency approval for distributing information regarding off-label uses of their products (6). In 1999, a federal judge ruled that the FDA’s effort to restrict the dissemination of information on off-label uses of drugs, biologics, and medical devices violated the pharmaceutical manufacturer’s rights to free speech under the First Amendment (7). This ruling effectively struck down the FDAMA, which severely limited the industry’s ability to disseminate information on off-label uses (e.g., journal articles, reference texts), as well as their involvement in continuing medical education programs where off-label uses of their products were discussed. The court’s decision on July 30, 1999 in the case of *WA Legal Foundation v. Henney*, stated that the “FDAMA largely perpetuates the policies held unconstitutional by the Court on July 30, 1998 and, therefore, may not be applied or enforced by the FDA” (7). A recent article by Ward (8) addresses the bodies of law related to off-label drug use and discusses the significant changes brought on by the First Amendment challenges which were reflected in a series of federal court cases, most importantly, *WA Legal Foundation v. Henney*. Although these rulings created various “safe harbors,” the Internet was not protected by the safe harbor ruling as a means for information dissemination and is therefore subject to more regulation (8).

Since the FDA does *not* regulate the practice of medicine, it does *not* regulate the prescribing of drugs

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for off-label uses (8). However, the FDA has the authority to regulate the manufacturer's *promotion* of off-label uses of approved drugs. By obtaining peer-reviewed information from high-quality medical journals on the use of anesthetic drugs and devices, anesthesia providers will be able to practice evidence-based medicine rather than "limiting" their practice to the information provided in the manufacturer's package insert. These recent court decisions have made it easier to obtain off-label information by simply asking the pharmaceutical (or device) company representative to provide the relevant published articles!

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