



Senate Bill 18-023: The Free Speech in Medicine Act—Concerning the Promotion of Off-Label Use of Pharmaceutical Products

By Linda Gorman

What the Bill Does

Would prevent any action against a manufacturer or its representative for the “truthful promotion” of information about off-label uses of FDA approved prescription drugs. The information provided cannot be misleading or contrary to the facts. It must be consistent with generally accepted scientific principles.

Bill Context

U.S. physicians may prescribe FDA approved drugs and devices as they see fit unless those drugs or devices are controlled substances like opioids. When the FDA approves a drug, it also approves a label. The label is an FDA statement intended to provide healthcare professionals with information about the specific medical conditions a drug is approved for, the doses to be used, and how it is to be given.

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Label information is usually based on FDA regulatory information derived from the new drug application process. A drug may initially be approved for only one condition or patient population. Due to the lengthy and expensive regulatory process required to change them, drug labels are seldom updated to reflect new knowledge. Physicians at the forefront of medical progress rely on expert discussion, professional literature,

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Avastin was originally approved to treat colon cancer. It was later found to be effective in treating age-related macular degeneration and rapidly became the worldwide standard of care. Seven years later, the National Institutes of Health sponsored a randomized trial that found it equivalent to the FDA approved macular degeneration treatment.

A 2004 JAMA study of off-label drug treatment of children hospitalized in 31 US children’s hospitals by Shahn *et al.* found that 79 percent of children received at least one off-label drug including morphine, methadone, azithromycin, and albuterol. A 2010 study by Conti *et al.* estimated that 30 percent of intravenously administered US chemotherapy treatments were off-label.

Medicare covers off-label drug use. Some states have laws requiring insurers to cover off-label drugs when they are the standard of clinical practice. In Colorado, no health benefit plan can refuse to cover off-label uses of a cancer drug provided the drug is recognized for the treatment of cancer and the treatment is for a covered condition. [CRS 10-16-1046].

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The FDA has historically barred manufacturers from providing information about off-label uses of their products. It has prosecuted pharmaceutical companies and their representatives for discussing off-label uses with physicians. It has even prosecuted pharmaceutical representatives for distributing articles from medical journals describing off-label use. In effect, the FDA has asserted that any claims about prescription drugs are to be considered untruthful until it has examined them. Its stance on off-label use has triggered False Claims Act, consumer fraud, and tort litigation that increases health care costs by billions of dollars.

Analysis

The question is whether prohibiting the dissemination of truthful medical information about off-label use of prescription drugs does more good than harm.

Those who support the dissemination of truthful information about off-label drug use make two

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main points. The first is that allowing manufacturers to provide truthful information about off-label drug use improves patient care by more rapidly diffusing information about new drug uses. The second is that giving the FDA a monopoly on speech about scientific results gives government power that it should not have under the U.S. Constitution.

People who believe that the FDA should control information about drug use think that pharmaceutical manufacturers provide biased and unreliable information. They believe the FDA is a neutral arbiter, and that it should be the judge of information on drug safety and effectiveness.

The FDA is not the only provider of evidence on safe drug use. Other sources of evidence include drug regulators in other countries, academics,

large randomized controlled studies, medical groups, joint ventures among hospital groups, research non-profits, expert reviews like those in the *US Pharmacopoeia*, and other government organizations. The FDA has been notoriously slow in its evaluations. Patients suffer and die when their physicians do not know about off-label cures just as they suffer and die from unknown side effects from approved medications or while waiting for FDA approval of off-label use that is approved in other countries.

Though the benefits of off-label prescribing are clear, there have been cases in which off-label use has harmed patients, notably the “fen-phen” weight loss drug combination associated with heart valve problems in the 1990s. Critics often forget that fenfluramine and phentermine were approved separately in 1959 and 1973.

In July 1997, physicians at the Mayo Clinic alerted the medical profession about heart valve defects in 24 women taking the “fen-phen” drug combination. Further scrutiny of existing data linked fenfluramine to valve abnormalities. It was withdrawn from the market.

As the off-label use of fenfluramine exposed unknown side effects in an already approved drug, it is not a good example of harm caused by dissemination of information about off-label use by manufacturers. It

is a good example of how private monitoring of off-label outcomes complements FDA regulation and how rapid dissemination of findings benefits patients. Results from a systematic literature review in *BMC Health Services Research* by Lubloy in 2014 suggest that early adopters of new medicines, and, presumably, new off-label treatments, are more likely to participate in clinical trials and treat many patients in their specialty.

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