OFF-LABEL USE OF DENTAL PRODUCTS

Terminology

The term "off-label use" refers to any use of approved drugs, licensed biologics, and approved or cleared medical devices in any manner that is inconsistent with the U.S. Food and Drug Administration's (FDA) approved labeling of the medical product. "Clinician-directed application" or "physician-directed application" are also terms that are indicative of off-label use.

Labeling means any written material that may accompany a medical product such as prescribing information, a package insert, and professional product instructions.

Off-label use means the use of a medical product for an unapproved indication, patient population, dosage, route of administration, or use outside of the product labeling.

Background- Regulatory Authority

The FDA evaluates medical products for safety and effectiveness. Additionally, the agency regulates the marketing approval, clearance, and licensing of pharmaceutical, over-the-counter, medical device, and biological products in the United States.

The FDA's regulatory authority extends to the labeling and promotion of medical products. Promotion of the manufacturer's product entails all written, oral, video, or other activities that contribute to the sales growth of the product. Manufacturers determine the appropriate product claims prior to submission of their application to the FDA, based on scientific data.

The FDA does not regulate the practice of dentistry or medicine. Often referred to as the "Practice of Medicine Exception," dentists and physicians may prescribe or administer legally marketed products for an off-label indication.

Generally Accepted Practices/ Standard of Care

The practice of dentistry is regulated by state laws and regulations. Dentists should comply with all relevant federal, state, and local laws and regulations.

While the FDA recognizes the Practice of Medicine Exception, tensions remain in efforts to protect the public's health and safety. Health care practitioners may prescribe any legally marketed product to a patient within a legitimate health care practitioner-patient relationship.[1] Dental professionals may use medical/dental products in the manner they deem appropriate for their patients. Dentists should be aware of product safety concerns and use a sound scientific basis, along with professional judgment, for off-label indications. Adverse patient reactions can be voluntarily reported to the FDA's MedWatch[2] program.

Standard of care is a medical-legal term that changes over time due to experience and the accumulation of data with a medical product. In some instances, the off-label use of a product is considered standard of care.

Legal Developments

Decisions in several recent court cases have changed the landscape for findings in off-label issues. Truthful off-label promotional speech,[3] the FDA's pursuit of misbranding provisions (for statements that were truthful and not misleading),[4] and speech that is solely truthful and not misleading[5] cannot be the basis for a misbranding charge for a manufacturer. Additionally, a problematic decision from the Ninth Circuit[6] appears to confuse the use of adulterated devices caused by unsanitary practices with the use of legally marketed off-label products. Cases may be appealed to the Supreme Court or the FDA may elect to alter their policies.

First Amendment Issues

The FDA recognizes that recent First Amendment jurisprudence creates tension with agency policies intending to protect the public's health. In 2016, the agency convened a Part 15[17] meeting to solicit input from stakeholders. For some patients, approved or cleared products are not available or have failed. The off-label use of medical products by health care professionals provides a necessary treatment for some patients without options.

U.S. health agencies seek to promote robust research and development for medical therapies. Conducting rigorous research studies for some products is difficult, particularly for those therapies intending to treat rare disease indications. The FDA supports medical decision-making for patients in the absence of better options while maintaining a structure meant to incentivize the development of medical products, and encourage the use of labeled indications.

The FDA produced a memorandum[8] in January 2017 summarizing recent court challenges on speech restrictions regarding evidence of intended use, commercial free speech, content and speaker-based restrictions. The document is intended to solicit public feedback on free speech issues while maintaining government interests in protecting the public's health.

Restricted Use of Medical Products

In 2007, a law[9] was passed granting the FDA new authority to require Risk, Evaluation, and Mitigation Strategies (REMS) to ensure that the benefits outweigh the risks for a particular drug or biological product. A REMS designation may require additional safety procedures prior to prescribing, shipping, or dispensing the drug or biologic. Post-approval studies may also be ordered if serious risk is associated with the use of the product.

Elements of a REMS may include a medication guide or patient package insert, a communication plan, elements to assure safe use (ETASU), and an implementation system. The ETASU may require any of the following: prescribers with specific training, experience, or special certifications, pharmacies, practitioners, or health care settings that dispense the drug may need to be specially certified, a drug or biologic may be dispensed only in certain health care settings, a drug or biologic may be dispensed with evidence of laboratory test results, and patients may require monitoring or enrollment in a registry. As such, a drug or biologic with a REMS may be limited to the labeled indications of the product, constraining the practice of medicine or dentistry.

Humanitarian use devices are also restricted for use and are authorized in limited populations, for example, with patients with rare diseases. These types of devices require prior institutional review board (IRB) authorization and must be used according to the FDA approved indication.

FDA Guidance

In 2017, the FDA released two guidance documents[10,11] meant to clarify the agency's current thinking on communications about medical and dental product labeling. The guidance documents are non-binding and do not carry the force of law. Alternative approaches may be used if the requirements satisfy applicable statutes and regulations.

Enforcement Trends

Health care practitioners are not immune from prosecution if they engage in off-label sales and marketing activities on behalf or in conjunction with manufacturers of medical products. It should be noted that off-label promotion is strictly scrutinized by federal authorities.

Traditionally, rather than risk potential criminal or civil enforcement actions as a result of an unfavorable verdict at trial, manufacturers have settled high profile suits alleging off-label promotion. Manufacturers of medical products are reticent to risk exclusion of participation in federal health programs administrated by the Department of Health and Human Services (DHHS). With recent legal verdicts favorable to manufacturers, they may be unwilling to settle future disputes with federal authorities as readily.

Dental Product Example

Silver diamine fluoride is one example of a dental product that is used off-label. While silver diamine fluoride is FDA-cleared as a Class II medical device to reduce sensitivity in teeth, it is often used to delay tooth decay.

Policy Statement

The Academy of General Dentistry believes that dentists may prescribe or administer legally marketed medical and dental products for an off-label use within the Practice of Medicine Exception. Health care practitioners may prescribe legally marketed medical and dental products in an off-label manner if they believe that such an application is in the best interest of their patient. The practice of dentistry is regulated by state laws and regulations. Dentists should comply with all relevant federal, state, and local laws and regulations. Dentists should be aware of product safety concerns and use a sound scientific basis, along with professional judgment, for off-label indications. Adverse patient reactions can be voluntarily reported to the FDA's MedWatch program.

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