FDA Regulatory and Compliance Monthly Recap

OCTOBER 2018

KEY FINDINGS

Proposed HHS rule to require drug price disclosure in DTC television ads for certain drugs

The proposed rule aligns with the Department of Health and Human Services' (HHS) blueprint for lowering drug prices and would require that drug prices be disclosed in direct-to-consumer (DTC) television advertisements for drugs covered under Medicare or Medicaid and costing more than $35 each month. HHS Secretary Alex Azar said the rule is meant to allow drugmakers to lower their prices while providing greater transparency in prescription drug prices.

HHS proposed a new rule to mandate that pharmaceutical companies disclose drug prices in DTC advertisements for prescription drugs and biologics covered under Medicare Parts A, B, C and D programs or Medicaid. The proposed rule, filed by the Centers for Medicare & Medicaid Services (CMS), would revise the federal health insurance programs for the aged and disabled by requiring the disclosure of the wholesale acquisition cost (WAC) or list price of drugs costing more than $35 each month.

The CMS said the rule is meant to improve the efficient delivery of Medicare and Medicaid programs by arming consumers with the information they need to make informed decisions and facilitate price shopping. The rule is being proposed under HHS' authority under the Social Security Act and its rulemaking authority under the Medicare program. While it recognizes that it hasn't been granted explicit authorization from Congress to require drug price disclosure, HHS says Congress has directed it to ensure Medicare and Medicaid operate efficiently. As such, promoting price transparency falls within the scope of that mandate, since HHS has determined that the regulation is needed for efficient administration of the programs. The rule also cites Supreme Court precedent recognizing that the government may implement special steps to make sure viewers are given appropriate information (*Red Lion Broad. Co. v. FCC*).

HHS said that while sellers traditionally provide potential purchasers with the prices of their products, that hasn't been the case in the pharmaceutical market, where price information is difficult to find. "Due at least in part to the market-distorting effects of third-party payors, pharmaceutical manufacturers tend not to compete based on list price, and hence there is little to no market pressure to voluntarily disclose a product's list price," the CMS states. As such, the rule is designed to establish incentives for pharmaceutical companies to do so — and lower prices as a result. The proposed rule aligns with the HHS blueprint for lowering drug prices, "American Patients First," which identified high list prices as an issue in the U.S. pharmaceutical market and outlined HHS' mandate to bolster competition and establish incentives for industry to lower costs.

The proposed rule, which applies to broadcast, cable, streaming and satellite communications, would require that advertisements include a statement outlining the price for a typical 30-day regimen of the drug or biologic, as determined on the first day of the quarter in which the advertisement is broadcast. The statement would be as follows: "The list price for a [30-day supply of] [typical course of treatment with] [name of prescription drug or biological product] is [insert list price]. If you have health insurance that covers drugs, your cost may be different." The price needs to be current as of the date of broadcast and, since the typical course of treatment may vary based on the condition, must reflect the general course of treatment associated with the indication discussed in the advertisement. Per the rule, the price needs to be presented in "a legible textual statement at the end of the advertisement, meaning that it is placed appropriately and is presented against a contrasting background for sufficient duration and in a size and style of font that allows the information to be read easily." The rule will allow drugmakers to include an up-to-date competitor product's list price as long as it is provided in a truthful, non-misleading way. An exception would also be granted for products that cost less than $35 per month for a 30-day supply or a typical course of action.

The rule would also require that HHS maintain a publicly available list of drugs and biological products advertised in violation of the rule, which would be available on the CMS website annually. The rule doesn't propose any additional enforcement mechanisms, and HHS notes that it anticipates the primary enforcement vehicle will be "the threat of private actions under the Lanham Act 3(a), 15 U.S.C. 1125(a), for unfair competition in the form of false or misleading advertising." Per HHS, the risk of meritless litigation under Lanham is acceptably low and the rule will pre-empt any state-law-based claim based on the pricing statements required.

First OPDP warning letter of 2018 sent to MannKind over Facebook post promoting inhaled insulin

The Office of Prescription Drug Promotion (OPDP) issued its first warning letter of 2018 to MannKind over a Facebook post for Afrezza, an inhaled insulin indicated for glycemic control in adult patients with diabetes mellitus. The letter raises concerns about the post suggesting there are no safety concerns associated with the treatment, which is the subject of a boxed warning and is associated with several serious risks.

OPDP sent a warning letter to MannKind after the office's Bad Ad Program received a complaint regarding posts on the Facebook page for Afrezza (insulin human) inhalation powder for oral inhalation use. OPDP determined that the posts, made on Feb. 9 and March 9, 2018, made false or misleading claims and/or representations about the risks associated with the drug. The posts included claims suggesting that insulin "is not the bad guy," that Afrezza will help a patient's "body work its best" and that Afrezza offers protection from health complications with "no drama."

OPDP said suggestions that there are no risks associated with the treatment create a misleading impression of its safety. The Facebook posts included a statement directing viewers to the full prescribing information, but the office said that doesn't allay the misleading impression created by the promotional

material. The office said information about the risk of acute bronchospasm in patients with chronic lung disease does appear in text format in a separate pop-up box that appears when the cursor hovers over the Afrezza logo. However, OPDP said presenting the information in such a way doesn't lessen the misleading nature of the post.

The office said the violations are especially concerning when considering that Afrezza carries a boxed warning for the risk of acute bronchospasm. OPDP called on MannKind to cease misbranding Afrezza, as the post misbrands the treatment within the meaning of the Food, Drug, and Cosmetic Act and makes its distribution violative.

FDA draft guidance offers recommendations to make risk and efficacy data more consumer-friendly in DTC advertisements

The draft guidance offers recommendations on how drugmakers should present quantitative efficacy and risk information in DTC promotional labeling and advertisements. This includes recommendations on how to make the language more consumer-friendly. The guidance recommends using a numeric format to display the quantitative efficacy or risk information, using absolute percentages and whole numbers, and considering visual aids for illustrating the quantitative information.

The draft guidance, "Presenting Quantitative Efficacy and Risk Information in Direct-to-Consumer Promotional Labeling and Advertisements Guidance for Industry," details recommendations on how quantitative efficacy and risk information for prescription human drugs and biological products and prescription animal drugs should be presented in DTC promotional labeling and advertisements, including ways of making their language more consumer-friendly. The recommendations apply to DTC promotional materials, regardless of their medium (e.g., print, electronic, audiovisual, broadcast). The guidance covers the following topics as they relates to presenting quantitative efficacy and risk information in DTC advertisements:

- Using numeric formats, such as absolute frequencies, percentages and relative frequencies, to present probability information.
- Formatting quantitative efficacy or risk information to reduce the amount of mental calculation needed to extract meaning from the data.
- Illustrating quantitative efficacy or risk information with visual aids to improve consumer understanding of the numeric values by highlighting patterns.
- Providing the treatment group and the control group with quantitative efficacy or risk data.

The guidance offers examples on absolute frequencies and percentages, relative frequencies, formatting quantitative efficacy or risk information, visual aids, and quantitative efficacy or risk information from the control group. Instead of establishing legally enforceable responsibilities, the guidance describes the agency's current thinking on the topic.

FDA issues guidance on benefit-risk factors for medical devices submitted under 510(k), launches pilot program to expand Special 510(k) program

The FDA finalized guidance to improve the predictability, consistency and transparency of the 510(k) premarket review process. The guidance details the benefit-risk factors the agency will consider in its assessments of medical devices submitted under the 510(k) pathway. The FDA also launched a pilot program as part of a proposed expansion of the eligibility for the Special 510(k) program, and it issued draft guidance that suggests expanding the device changes eligible for the program.

The FDA published final guidance describing the benefit-risk factors that will be considered when the agency assesses medical devices submitted under

the 510(k) pathway that have different technological characteristics than a predicate device but may be "substantially equivalent" to that device. While the document doesn't enact new regulatory requirements for devices or alter the standard for determining substantial equivalence under the 510(k) pathway, it explains that benefit-risk assessments should be conducted to compare the benefits and risks of a new device and predicate in instances in which the benefit-risk profile differs between the two. The guidance also indicates that performance data may be necessary if technological characteristics differ between the devices to determine whether the new device is "as safe and effective" as the predicate, though the type and quantity of performance data may vary based on the device.

The FDA will evaluate the magnitude of benefits, the probability of a patient experiencing such benefits and the duration of the effects. The agency will balance these benefits against risk considerations such as the severity, number, type, and rates of harmful events, as well as the probability and duration of those events. For diagnostics, it will also consider the risk presented by a false positive or a false negative result.

Separately, the FDA launched a pilot program to operationalize a proposed expansion of the Special 510(k) program's eligibility, aimed at offering a least burdensome approach for reviews and clearances when manufacturers have modified their own approved devices. The agency wants to increase the number of 510(k) submissions that can be submitted under the pilot program and has identified three factors to help manufacturers determine whether a device is appropriate for participation:

1. A proposed change was made by the manufacturer authorized to market a device that already has 510(k) clearance.

2. Performance data are not needed, or well-established methods are available to evaluate the changes.

3. Performance data can be reviewed in a summary or risk analysis format.

The pilot will also look at whether the eligibility factors in the Special 510(k) program improve the FDA's efficiency in reviewing the program's submissions.

The pilot program follows the draft guidance on the Special 510(k) program that suggests expanding the device changes eligible for the program. The document is part of the agency's goal of increasing the number of 510(k) submissions that could be submitted under the program, and it suggests including certain device modifications and labeling changes to the program's initial 1998 design. The draft guidance aims to clarify the types of technological changes eligible to be reviewed as Special 510(k)s. The agency believes expanding the Special 510(k) program will help it meet its 510(k) total time to decision (TTD) objectives of decreasing the average TTD for 510(k) submissions to 108 calendar days by FY 2022.