COVINGTON

FDA Advertising and Promotion Enforcement Activities: Update

March 9, 2018

Food, Drugs, and Devices

This e-alert is part of a series of e-alerts summarizing publicly available FDA enforcement letters (i.e., warning letters and untitled letters) relating to the advertising and promotion of prescription drugs, medical devices, and biologics.

OPDP issued the following letter on FDA's website in February 2018:

- Untitled Letter to Collegium Pharmaceuticals, Inc. re: NDA 208090 XTAMPZA ER™ (oxycodone) extended-release capsules, for oral use, CII MA 114 (Feb. 9, 2018) ("XTAMPZA ER Untitled Letter")

FDA's Advertising and Promotional Labeling Branch (APLB) in the Office of Compliance and Biologics Quality (OCBQ) issued the following letter on FDA's website in February 2018:

- Untitled Letter to CSL Behring LLC re: BLA STN# 125582 IDELVION (Coagulation Factor IX (Recombinant), Albumin Fusion Protein (Feb. 27, 2018) ("IDELVION Untitled Letter")

This is the first enforcement letter OPDP has issued in 2018, and the first enforcement letter APLB has issued since 2015. FDA's Center for Devices and Radiological Health (CDRH) Office of Compliance (OC) did not post any enforcement letters relating to advertising and promotion on FDA's website in February.

This alert merely summarizes the allegations contained in FDA's letters. It does not contain any analyses, opinions, characterizations, or conclusions by or of Covington & Burling LLP. As a result, the information presented herein does not necessarily reflect the views of Covington & Burling LLP or any of its clients.

Office of Prescription Drug Promotion (OPDP)

XTAMPZA ER Untitled Letter (February 2018)

OPDP states that Collegium's exhibit booth, which was displayed at the American Society Health-System Pharmacists (ASHP) Summer Meetings & Exhibition in Minneapolis, Minnesota, on June 3-7, 2017, misbranded Xtampza ER because it failed to adequately communicate risk information about Xtampza ER use.

False or Misleading Risk and Benefit Presentations

OPDP alleges that the exhibit booth misbranded Xtampza ER by creating a misleading impression about the drug's safety. Specifically, the booth made representations and/or suggestions about Xtampza ER and failed to adequately provide material information about the drug's limitations of use and other risk information. OPDP states that the exhibit booth prominently displayed abuse-deterrent benefit claims about Xtampza ER, but displayed risk information less prominently. Specifically, the principal display panel included the following benefit claims about the abuse-deterrent properties of Xtampza ER:

> With DETERx technology, Xtampza ER maintains its extended-release profile even under rigorous manipulation
>
> - Cutting
> - Crushing
> - Grinding
> - Chewing
> - Dissolving in ingestible solvents
>
> … and offers the flexibility of multiple administrative options

The principal display panel failed, however, to include any information about the drug's limitations of use. These state that due to the risks of addiction, abuse, misuse, overdose and death, Xtampza ER should be reserved for use in patients for whom alternative treatment options are ineffective, not tolerated, or would be otherwise inadequate to manage pain. The principal display panel also failed to include any information about the drug's serious or life-threatening risks.

Rather, this information was included on a side panel that OPDP alleges was insufficient because the information was not displayed as prominently as the benefit information. Specifically, the principal display panel utilized a blue background and large font size, and the abuse-deterrent benefit claims were presented at eye-level and easy to read. In contrast, the side panel was located several feet away from the principal display panel without any visual elements linking it to the principal display panel, utilized a much smaller font size and plain white background, and was presented at the bottom of the panel near the floor. Furthermore, the OPDP representative viewing the exhibit booth observed that a statement about the limitations of abuse deterrent properties ("However, abuse of Xtampza ER by injection and by nasal and oral routes of administration is still possible.") was obscured by a table and chair so that it was not visible to viewers as a practical matter.

OPDP states that "[p]resenting material information in this manner is not sufficient to ensure that the claims about abuse deterrent properties are truthful and non-misleading." Rather, "[p]romotional materials describing abuse-deterrent properties . . . should adequately present, with sufficient prominence, additional information to explain that . . . these properties only make abuse by such routes more difficult, not impossible," and that "opioid drugs with abuse-deterrent properties still expose users to the risks of addiction, abuse, and misuse."

OPDP also notes that it had previously advised Collegium on proposed presentations with certain similarities to the exhibit booth in advisory comments dated September 9, 2016. At that time, "OPDP recommended that Collegium revise proposed presentations so that they did not misrepresent the approved indication or omit important context; misrepresent or omit important risk information; or omit other material information." OPDP states that it "cautioned Collegium

about failing to present risk information for Xtampza ER with a prominence and readability reasonably comparable to the presentation of benefits."

Advertising and Promotional Labeling Branch (APLB)

IDELVION Untitled Letter (February 2018)

APLB states that CSL Behring's company website (www.idelvion.com), patient brochure, exhibit panel, and sales aid make misleading claims about the effectiveness of IDELVION. APLB cites 21 CFR 202.1(e)(5), which states that an advertisement does not include a "true statement" of information relating to side effects, contraindications, and effectiveness if, among other things, "[i]t fails to reveal facts material in the light of its representations or material with respect to consequences that may result from the use of the drug as recommended or suggested in the advertisement."

Misleading Efficacy Presentation

APLB states that the following claims, appearing each on the website, patient brochure, exhibit panel, and sales aid, "misleadingly overpromise the effect that [IDELVION] will have on a hemophilic patient's activities and overall quality-of-life":

- "He's free to infuse only once every 14 days. Are you?" (Along with an image of a man about to engage in heading or kicking a soccer ball while jumping high in the air.)
- "…[D]elivers high steady-state factor levels with up to 14 day dosing" (Along with the same image.)

APLB highlights that playing soccer is considered a "moderate to dangerous high-risk activity" for hemophilic patients because of the bleeding risks associated with injuries incurred in the sport. Specifically, APLB states that "[t]he initial impact of heading a ball could result in various injuries, including, but not limited to, intracranial bleeding from injury or trauma, a contusion, injury to the face, or concussion," later noting that intracranial bleeding is "one of the most serious types of bleeding that can occur within the body . . ., possibly leading to strokes, which can threaten life, limb, and overall function." APLB also states that "the secondary impact from landing after jumping high in the air could cause injury to the joints or bones," and later notes that "[p]ersistent joint or muscle bleeding can lead to decreased mobility and function, or even permanent disability for these patients."

APLB states that even a patient whose hemophilia is well-managed with IDELVION "will nevertheless still have a serious risk for bleeding while engaging in such activities." APLB concludes that these "claims and presentations misleadingly imply that hemophiliacs taking [IDELVION] can engage in moderate to dangerous high-risk activity without consequences and that such activities are appropriate for typical patients with hemophilia using this product."

If you have any questions concerning the material discussed in this client alert, please contact the following members of our Food, Drugs, and Devices practice:

Scott Cunningham	+1 415 591 7089	scunningham@cov.com
Stefanie Doebler	+1 202 662 5271	sdoebler@cov.com
Michael Labson	+1 202 662 5220	mlabson@cov.com
Amy Leiser	+1 202 662 5916	aleiser@cov.com