

FDA Advertising and Promotion Enforcement Activities: Update

December 12, 2017

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.

In November, the Office of Prescription Drug Promotion (OPDP) posted the following letter on FDA's website:

- Warning Letter to Amherst Pharmaceuticals, LLC, and Magna Pharmaceuticals, Inc. re: NDA 022196 Zolpimist (zolpidem tartrate) Oral Spray (C-IV) (Nov. 14, 2017) (["Zolpimist Warning Letter"](#))

This is the third enforcement letter OPDP has posted in 2017. The FDA's Center for Drug Evaluation and Research (CDER) Office of Compliance, Center for Devices and Radiological Health (CDRH) Office of Compliance, and FDA's Office of Compliance and Biologics Quality (OCBQ) did not post any enforcement letters relating to advertising and promotion on FDA's website in November.

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)

Zolpimist Warning Letter (November 2017)

OPDP states that Amherst Pharmaceuticals' webpage and Magna Pharmaceuticals' booth and exhibit panels, which were displayed at the SLEEP 2017 Annual Meeting of the Associated Professional Sleep Societies, LLC (APSS), make false or misleading claims and/or representations about the safety and efficacy of Zolpimist. OPDP also states that these promotional materials were not submitted at the time of initial dissemination or publication as required by 21 CFR 314.81(b)(3)(i).

False or Misleading Risk Presentation:

OPDP's letter highlights the risks associated with Zolpimist, as indicated in the FDA-approved product labeling (PI). Specifically, OPDP states that Zolpimist's PI contains warnings and precautions regarding central nervous system (CNS) depressant effects and next-day

impairment, severe anaphylactic and anaphylactoid reactions, abnormal thinking and behavioral changes, and withdrawal effects, among others. OPDP also points out that Zolpimist is contraindicated in patients with a known hypersensitivity to zolpidem, and that common adverse reactions to Zolpimist include drowsiness, dizziness, diarrhea, and “drugged feelings.”

OPDP states that although the webpage and exhibit panels include claims and/or representations about the efficacy of Zolpimist, both fail to communicate any risk information. OPDP alleges that this failure to communicate risk information “create[s] a misleading impression about the drug’s safety,” which is “especially problematic from a public health perspective given the serious and potentially life-threatening risks associated with the drug.”

False or Misleading Claims about Efficacy:

OPDP states that the webpage and exhibit panels misleadingly suggest that: Zolpimist is superior in efficacy to other oral zolpidem products; patients treated with Zolpimist require less frequent treatment compared to those on the tablet formulation; Zolpimist has an established therapeutic onset of action of 10 minutes; and Zolpimist has no food effect that mitigates the efficacy of other zolpidem products. OPDP identifies the following examples of misleading claims on the webpage and exhibit panel claims:

- “Zolpimist® is engineered to outperform the oral tablets”
- “Using a proprietary and patented technology we deliver the drug as a fine mist into the mucosal membranes lining the cheeks in the mouth (buccal delivery). This mode of delivery offers some very clear advantages as compared to other delivery methods:
 - Fast onset of action; Zolpimist® induces sleep three times faster than oral tablets – 10 minutes as compared to 30 – 40 minutes for oral tablets.
 - No food effect that mitigates the efficacy of other zolpidem products”
- “Zolpimist Oral Spray works so fast, patients only take when needed and may avoid nightly tablet-formulation dependency!”

OPDP states that FDA is not aware of data to support the claims that Zolpimist is clinically superior to other oral zolpidem products, that patients with Zolpimist require less frequent treatment, or that Zolpimist has a therapeutic onset of action of 10 minutes. Furthermore, FDA points out that Zolpimist, approved as a 505(b)(2) application, is bioequivalent to a zolpidem oral tablet (Ambien), and that Zolpimist’s PI indicates that “[t]he effect of Zolpimist . . . may be slowed by ingestion with or immediately after a meal.”

OPDP also states that the webpage and exhibit panels are misleading because they fail to include material information regarding the FDA-approved indication for Zolpimist. Specifically, the webpage and exhibit panels represent that: Zolpimist is an “FDA approved bioequivalent version of the market leading *sleep aid*, Ambien®”; “Zolpidem is the most commonly prescribed agent for the *treatment of insomnia*”; and “Zolpimist is well absorbed and *may facilitate all-night sleep*” (emphasis added by OPDP). The full, FDA-approved indication for Zolpimist states, however, that Zolpimist is indicated for “the *short-term treatment of insomnia characterized by difficulties with sleep initiation*. Zolpidem tartrate has been shown to decrease *sleep latency* for up to 35 days in controlled clinical studies The clinical trials performed in support of efficacy were 4-5 weeks in duration with the final formal assessments of *sleep latency* performed at the end of treatment” (emphasis added by OPDP).

Failure to Submit Under Form FDA-2253

Finally, the Zolpimist Warning Letter also alleges that publication of the webpage and dissemination of the exhibit panels for Zolpimist violated 21 CFR 314.81(b)(3)(i) because Amherst Pharmaceuticals and Magna Pharmaceuticals did not submit the materials to FDA under cover of Form FDA-2253 at the time of initial dissemination.

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:

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