

COVINGTON

Summary of FDA Advertising and Promotion Enforcement Activities

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Food & Drug

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 recent months, FDA's Office of Prescription Drug Promotion (OPDP) posted the following letters on FDA's website:

- Untitled Letter to ASCEND Therapeutics US, LLC re: NDA #021166 EstroGel 0.06% (estradiol gel) for topical use MA #359 (June 23, 2015) ("ASCEND Untitled Letter")
- Untitled Letter to Oak Pharmaceuticals, Inc. re: ANDA 083246 Nembutal Sodium Solution (pentobarbital sodium injection, USP) CII MA #20 (May 15, 2015) ("Oak Pharmaceuticals Untitled Letter")
- Untitled Letter to Actavis Laboratories UT, Inc. re: NDA 022206 Rapaflo (silodosin) Capsule for oral use MA #242 (May 19, 2015) ("Actavis Untitled Letter")
- Untitled Letter to Otsuka Pharmaceutical Development & Commercialization, Inc. re: NDA 021436 Abilify (aripiprazole) Tablets (April 17, 2015) ("Otsuka Untitled Letter")
- Untitled Letter to Discovery Laboratories, Inc. re: NDA 021746 Surfaxin (lucinactant) Intratracheal Suspension MA #29 (March 3, 2015) ("Discovery Untitled Letter")
- Untitled Letter to Semel Institute for Neuroscience and Human Behavior re: [F-18] FDDNP MA #1 (February 20, 2015) ("Semel Untitled Letter")
- Untitled Letter to Luitpold Pharmaceuticals, Inc. re: NDA #203565 Injectafer (ferric carboxymaltose injection) MA #34 ("Luitpold Untitled Letter")

FDA's Office of Compliance and Biologics Quality (OCBQ) posted the following letter on FDA's website:

- Untitled Letter to Protein Sciences Corporation re: Flublok (Influenza Vaccine) BLA STN # 125285 (March 12, 2015) ("Protein Sciences Untitled Letter")

The Office of Compliance (OC) in FDA's Center for Devices and Radiological Health (CDRH) did not post any enforcement letters relating to advertising and promotion on FDA's website.

This alert merely summarizes the allegations contained in FDA's letters. It does not contain any analysis, 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.

Letters Issued by Office of Prescription Drug Promotion (OPDP)

ASCEND Untitled Letter

OPDP contended that a professional EstroGel Zazzle Card A-IS (Zazzle Card) for EstroGel 0.06% (estradiol gel) for topical use (EstroGel) was false or misleading because it omitted important risk information regarding the product.

Omission of Risk Information: OPDP alleged that the Zazzle card was misleading because it included efficacy claims regarding EstroGel, but it omitted important risk information. In particular, FDA stated that the Zazzle card failed to include information from the boxed warning. FDA also noted that the Zazzle card included the following statement: “Estrogen therapies increase the risk of certain cancers, cardiovascular disorders, and probable dementia.” However, OPDP noted that the card failed to discuss specific risks related to cancer and cardiovascular disorders in the Boxed Warning. Finally, OPDP noted that the card failed to discuss the drug’s contraindications. For these reasons, OPDP concluded that the Zazzle card omitted important risk information, and thus was misleading.

Oak Pharmaceuticals Untitled Letter

Omission of Risk Information: OPDP found that a Booth Graphic 48x60 Vinyl banner (exhibit banner) for Nembutal Sodium Solution (pentobarbital sodium injection, USP) CII (Nembutal) was misleading because it omitted important risk information about the product. OPDP identified statements in the exhibit banner, such as “Control the Uncontrollable” and “the control you need when seizures are their worst,” but noted that the exhibit banner omitted all contraindications, warnings and precautions, and common adverse reactions associated with the product’s use.

Omission of Material Facts: OPDP also contended that the exhibit banner was misleading because it omitted material facts regarding Nembutal’s FDA-approved indication. OPDP noted that the exhibit banner made claims regarding Nembutal’s use for the treatment of seizures. However, OPDP found that the exhibit banner omitted the following from the Indications and Usage section: “Anticonvulsant, in anesthetic doses, in the emergency control of certain acute, convulsive episodes, e.g., those associated with status epilepticus, cholera, eclampsia, meningitis, tetanus, and toxic reactions to strychnine or local anesthetics.” Because the exhibit banner omitted such information about the approved indication, OPDP found that the banner was misleading.

Actavis Untitled Letter

Unsubstantiated Claims: OPDP determined that the homepage of the website for RAPAFLO (silodosin) Capsule for oral use (Rapaflo) was misleading because it included unsubstantiated claims. OPDP found that a claim and a presentation on the website were not supported by adequate and well-controlled clinical studies. Specifically, OPDP identified the following statement, “BPH symptom relief that works nights so he can work days” and a picture of a man who was walking to the bathroom from bed at night. OPDP found that those representations were misleading because they implied that Rapaflo had been demonstrated to improve sleep disturbance and work productivity. However, OPDP noted that the website cites to no references for support of such claims. OPDP also noted that the pivotal studies of the drug did not measure individual symptoms, and they did not study the effect of Rapaflo on sleep quality or work productivity. Thus, OPDP found that such claims were not supported by substantial evidence.

Otsuka Untitled Letter

OPDP alleged that a pharmacology aid for ABILIFY (aripiprazole) tablets (Abilify) was false and misleading because it included “misleading claims and presentations about the drug.”

Misleading Claims and Presentations: OPDP contended that the pharmacology aid’s claims about the mechanism of action of Abilify were false and misleading. OPDP first alleged that the totality of the claims “misleadingly implies a greater degree of certainty about the mechanism of action of Abilify in humans” than currently exists. OPDP noted that the references cited in the pharmacology aid failed to support the claims in the aid. OPDP also found that in their entirety, the claims were misleading because the claims implied that Abilify possessed advantages over other approved treatments for bipolar disorder and major depressive disorder.

Discovery Laboratories Untitled Letter

OPDP alleged that a webpage for SURFAXIN (lucinactant) Intratracheal Suspension (Surfaxin) was false and misleading because the webpage included unsubstantiated superiority claims and lacked adequate directions for use.

Unsubstantiated Superiority Claims: OPDP alleged that the website’s claims were misleading because they included comparisons to other drugs that were not supported by substantial evidence. The claims on the website included “Surfaxin, the only available synthetic alternative to animal-derived surfactants approved by the FDA” and “Direct clinical comparisons to Exosurf, Survanta, and Curosurf.” OPDP contended that the comparisons were misleading because they implied that Surfaxin was superior “because it has ‘evolved’ from more primitive, animal-derived surfactants.” OPDP also contended that there is no substantial evidence to support claims that Surfaxin is superior to other approved drugs. Finally, OPDP contended that the claims were misleading because they implied that there had been a “therapeutic evolution” in the class of drugs.

OPDP also contended that the webpage was misleading because it included claims that “Sinapultide (KL₄ peptide) mimics critical surfactant protein B function.” OPDP stated that FDA was unaware of substantial evidence to support claims that KL₄ “mimics endogenous human SP-B.” Finally, OPDP contended that the claim “Neonatologists and parents share concerns regarding animal-derived medications” was misleading because it implies that Surfaxin is superior to other surfactants because of its synthetic formulation.

Lack of Adequate Directions for Use: OPDP contended that the website’s claims were misleading because they provided evidence that Surfaxin was intended for a use for which it had not received approval. In particular, OPDP identified that statements such as “Surfaxin, the only available synthetic alternative to animal-derived surfactants approved by the FDA” and “First U.S. FDA approved alternative to surfactants made with animal extract in more than 20 years.” OPDP alleged that these claims implied that Surfaxin was an alternative to other surfactants for all uses. OPDP contended that Surfaxin’s label lacks adequate directions for use for those purposes.

Semel Untitled Letter

OPDP contended that a website for the investigational new drug [F-18] FDDNP (FDDNP) constituted pre-approval drug promotion.

Promotion of an Investigative Drug: OPDP contended that the website detailed the use of FFDNP in brain PET scans for the diagnosis of traumatic brain injuries, Alzheimer’s disease, and certain neurological conditions. OPDP noted that those particular uses of the drug would require a prescription from a physician. OPDP listed various claims on the website that OPDP contends promoted the drug for the purpose for which it was investigated. These included statements such as “Protecting our athletes who want to know about the consequences of concussive brain injuries;” “Get started, get safe;” and “The FDDNP PET scan... is the only currently available method to measure brain tau proteins in living people.” OPDP also stated that the website implied the safety and efficacy of the product, but FDA has not approved the product for any use.

Luitpold Untitled Letter

OPDP alleged that a video segment about Injectafer (ferric carboxymaltose injection) (Injectafer) provided evidence that the product was intended for an unapproved new use and that its labeling lacked adequate directions for use.

Lack of Adequate Directions for Use: OPDP contended that the video segment was misleading because its claims implied that Injectafer can be used to treat all patients with iron deficiency anemia (IDA) “regardless of concomitant disease or prior treatment, in addition to the two limited subsets of patients specified later in the claim.” In contrast, FDA only approved Injectafer for use as a “second line treatment in adult IDA patients who have an intolerance or unsatisfactory response to oral iron, or to patients who have non-dialysis dependent chronic kidney disease.” OPDP stated that Injectafer’s approved labeling omits instructions for use in all patients who have IDA.

Minimization of Risk: OPDP also contended that the video segment was misleading because it failed to “convey significant risk information associated with Injectafer.” In particular, the video segment included interviews discussing Injectafer’s benefits, but it omitted discussions of any risks associated with the product. The only statement regarding risk in the video segment was a display of the risk information on screen for 30 seconds without any audio. OPDP found that this presentation was “misleading” because the video failed “to provide sufficient emphasis for Injectafer’s important risk information in the main part of the video.”

OPDP also contended that the video segment minimized risk information because it included a dialogue discussing risks associated with other IDA treatments, but it omitted statements that Injectafer is associated with many similar risks. OPDP found that this unbalanced discussion of risk further worsened the misleading nature of the video segment.

Omission of Material Fact: OPDP found that the video segment was misleading because it did not provide information about the approved dosing regimen for Injectafer. Specifically, the video segment included a statement that Injectafer is “the first FDA-approved iron approved as a high single dose IV iron and a total dose of IV iron.” OPDP determined that this claim was misleading because it suggests that Injectafer can be administered as a “single, high dose of iron,” which is not the dosing regimen for which FDA approved the product.

Misleading Claims: OPDP determined that the video segment included claims suggesting that Injectafer could “drastically improve” the quality of life of an IDA patient. In particular, OPDP found that statements such as Injectafer “really changed her life” and the patient “blossomed like a rose” were misleading because they indicated that the product had a broad positive

impact on a patient's life. OPDP also found that statements that implied that Injectafer possesses advantages over existing approved treatments were misleading.

Letters Issued by the Center for Biologics Evaluation and Research (CBER)

Protein Sciences Untitled Letter

CBER contended that a video interview with Protein Science's CEO that was entitled "Watch us on Lifetime—The Balancing Act" and concerned Flublok (Influenza vaccine) was misleading.

Misleading Efficacy Claim: CBER alleged that the video interview was misleading because it portrayed Flublok as more effective than has been demonstrated by substantial evidence. Specifically, CBER alleged that the video's statement that Protein Sciences "is able to put three times more protein in there, so it is also a high dose vaccine. More protein means your body will form more antibodies that will help you fight the flu" was a misleading efficacy claim. CBER found that this statement was misleading because it implied that Flublok's higher antigen content resulted in greater protection. CBER noted that this was not established by well-controlled clinical trials.

Omission of Risk Information: CBER also contended that the video interview omitted risk information because it included multiple efficacy claims regarding Flublok. In the letter, CBER identified the efficacy statements such as "helps you fight the flu." However, CBER noted that the video failed to provide any important safety information from the product's prescribing information.

If you have any questions concerning the material discussed in this client alert, please contact the following members of our Food & Drug Practice Group:

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