COVINGTON

FDA Advertising and Promotion Enforcement Activities: Update

January 21, 2020

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

- Warning Letter to Alkermes, Inc. re: NDA 021897 VIVITROL® (naltrexone for extended-release injectable suspension), for intramuscular use, MA 864 (Dec. 2, 2019) ("Vivitrol Warning Letter")

The Vivitrol Warning Letter was the tenth enforcement letter OPDP issued in 2019. FDA's Center for Devices and Radiological Health (CDRH) Office of Compliance (OC) did not post any enforcement letters related to advertising and promotion in December 2019. FDA's Advertising and Promotional Labeling Branch (APLB) in the Office of Compliance and Biologics Quality (OCBQ) did not post any enforcement letters in 2019.

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)

Vivitrol Warning Letter (December 2019)

OPDP's warning letter to Alkermes states that the company's print advertisement misbrands Vivitrol (naltrexone for extended-release injectable suspension) under sections 301(a) and 502(n) of the Federal Food, Drug, and Cosmetic Act (FDCA) and 21 CFR 202.1(e)(5). Vivitrol is an intramuscular product indicated for the prevention of relapse to opioid dependence following detoxification. Specifically, OPDP alleges that the print advertisement omits information concerning the "serious and potentially fatal risk" of opioid overdose.

False or Misleading Risk Presentation

OPDP alleges that the print advertisement includes claims and representations about Vivitrol's benefits but "fails to communicate information … concerning vulnerability to opioid overdose, a

potentially fatal risk." Vivitrol is designed to block the effects of opioids for approximately 28 days following each injection. According to the Vivitrol prescribing information, however, as that blockade fades, patients treated with Vivitrol "may respond to lower doses of opioids than previously used, just as they would have shortly after completing detoxification. This could result in potentially life-threatening opioid intoxication … if the patient uses previously tolerated doses of opioids." Overdose can also result from attempts to overcome the blockade effect by taking large doses of opioids. The Vivitrol Warning Letter concludes, therefore, that "[p]atients should be told of the serious consequences of trying to overcome the opioid blockade."

ODPD further states that by omitting this "serious and potentially fatal risk" of opioid overdose, the advertisement fails to provide material information about the consequences that may result from use of Vivitrol. The Vivitrol Warning Letter states that "[t]his is extremely concerning from a public health perspective because of the potential for fatal overdose in this vulnerable patient population."

OPDP alleges that, in addition to omitting the risk of overdose, the print advertisement fails to mention "other important warnings and precautions." Specifically, OPDP states that the advertisement does not mention "the risk of injection site reactions (one of the risks addressed by the Vivitrol Risk Evaluation and Mitigation Strategy (REMS)), and the most common adverse reactions associated with the use of [the] drug." OPDP acknowledges that the advertisement includes the following statement "in small print at the bottom of the print ad" (emphasis in original):

> **For additional Important Safety Information, please see the Brief Summary of Prescribing Information on adjacent pages.**

However, the agency states that "this statement and the inclusion of the brief summary on adjacent pages do not mitigate the misleading omissions of material risk information from the main body of the print ad."

Prior Communications

OPDP states that it provided advisory comments to Alkermes on proposed promotional materials for Vivitrol in 2011. In addition, OPDP notes that the Division of Anesthesia, Analgesia, and Addiction Products (DAAAP) sent an information request to Alkermes in 2018, requesting that the company "describe any efforts you have made to ensure that prescribers and patients are aware of the risk of overdose." According to OPDP, the company's response letter stated that it had "undertaken numerous efforts to ensure that prescribers and patients are aware of the risk of overdose" and that one measure was the "[i]nclusion of the risk of opioid overdose within the text of promotional materials for healthcare professionals, caregivers and consumers." As a result, OPDP states that it "is concerned that Alkermes continues to promote Vivitrol in a manner that fails to adequately present this important risk information in a truthful and non-misleading manner."

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
Beth Braiterman*	+1 202 662 5864	bbraiterman@cov.com

*District of Columbia bar application pending; supervised by principals of the firm.