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Client Alert

FDA and Life Sciences

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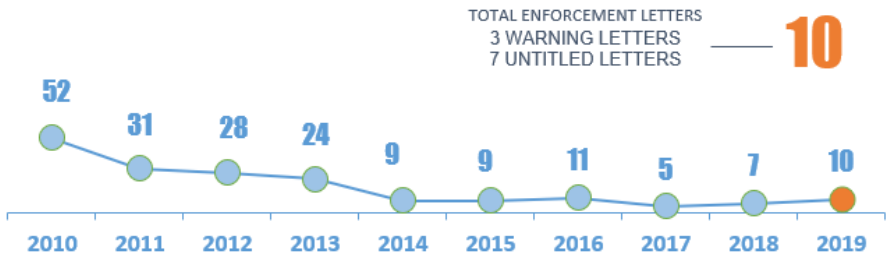
2019 Year in Review: FDA Office of Prescription Drug Promotion

In 2019, the U.S. Food and Drug Administration's (FDA) Office of Prescription Drug Promotion (OPDP) issued a total of ten enforcement letters targeting advertising and promotion violations for prescription drugs. Of the ten letters, three were Warning Letters and seven were Untitled Letters. The total number of letters in 2019 maintains the relatively low average of letters issued in recent years.

OPDP Enforcement Letters 2010-2019



NOTABLE TRENDS IN 2019

This client alert highlights notable trends from OPDP's 2019 enforcement letters. For a summary of each letter cited in this client alert, please refer to the "2019 OPDP Enforcement Year in Review Chart," available here.

The 2019 Warning and Untitled Letters targeted a variety of forms of promotional materials. For promotional materials for approved drugs (not including investigational drugs), nearly all letters targeted consumer-directed promotion and advertising (*e.g.,* consumer website, DTC video interview, DTC patient testimonial video montage, DTC TV ad, and consumer print ad). Only one letter cited materials that targeted healthcare

professionals, which was an HCP email for an insomnia drug, Doral. Another letter targeted criminal justice professionals, which was a print ad for Vivitrol.

- **Most Commonly Cited Violations:** Consistent with past years, OPDP's focus in 2019 centered on presentation of risk information. All eight of the enforcement letters issued for approved drugs included a citation for false or misleading presentation of risk information. OPDP also issued citations for false or misleading efficacy claims, omissions of material fact, misbranding of an investigational drug, and lack of adequate directions for use.

Cited Violation	Number of Letters Containing Violation
False/Misleading Risk Information	8
False/Misleading Efficacy Claim	4
Omission of Material Fact	2
Misbranding of Investigational Drug	2
Lack of Adequate Directions for Use	1

  - **False or Misleading Risk Presentations** - Within this category of violations, OPDP's objections can be summarized to include:
    - **Complete omission of risk information –** *See e.g.*, Triferic Untitled Letter and Stendra Warning Letter.
    - **Omission and minimization of risks** – *See e.g.*, Doral Warning Letter, in which OPDP found that a professional email for Doral, a controlled substance and boxed warning drug, included some risk information but omitted other material warnings and precautions. OPDP also objected to claims and presentations that "Doral's relative likelihood of abuse is considerably lower than some of the widely used sleep aids." OPDP stated that such claims misleadingly minimized the risks of abuse and dependence associated with Doral and incorrectly suggested, without adequate supporting references, that Doral is a safer option than other products.
    - **Presenting facts about the drug in a manner that is misleading about risks** – *See, e.g.,* ParaGard Untitled Letter, issued for a DTC television ad for the intrauterine copper contraceptive. OPDP stated that the net impression of certain claims and presentations in the TV ad, such as "100% HORMONE FREE" and "No hormones not an ounce! With an ingredient I can pronounce" minimized the risks associated with ParaGard. OPDP stated that these claims misleadingly implied that because Paragard is hormone-free, it is a safer choice than other long-acting reversible contraceptives (LARC) that are hormone-based. OPDP emphasized that Paragard is associated with many of the same serious risks as other LARCs and carries its own unique risks as a copper IUD.
    - **Lack of fair balance** – *See e.g.,* Stendra Warning Letter, issued for DTC print ads and banner ads for an erectile dysfunction drug. OPDP found the ads misleading because the risk information did not have comparable prominence and readability as information about the effectiveness of the drug. The print ad prominently presented efficacy claims in large, bolded font size and colorful text and graphics surrounded by a significant amount of white space, while the limited risk information was presented in much smaller font size, surrounded by little white space, and in single-spaced format at the bottom of the ad.
    - **Presenting risk information in a manner that is distracting or confusing to the audience, resulting in minimization of the overall risk message** – *See e.g.,* Livalo Untitled Letter, issued for a DTC patient testimonial video montage for a cholesterol drug. The benefit claims in the video were prominently presented

through patient testimonials, while risk information was presented simultaneously as scrolling text at the bottom of the video during the patient testimonials. OPDP found that the patient testimonials competed for consumers' attention, making it difficult for them to adequately process and comprehend the risk information. This method of presentation of risk information undermined the communication of risk information and minimized the risks associated with the use of Livalo.

- **Renewed Focus on False or Misleading Claims about Efficacy** – The 2019 OPDP enforcement letters also suggest a renewed focus on false or misleading efficacy claims, with four letters citing this violation. Within this category of violations, OPDP's objections can be summarized to include:
  - **Omission of material information from indication** – *See e.g.,* Qsymia Untitled Letter, issued for the weight-loss drug's consumer webpage. The efficacy presentation on the website highlighted the reduction in total weight (pounds lost) and waistline circumference (inches lost) but failed to prominently disclose that Qsymia is indicated as an *adjunct* to diet and exercise. As a result, the graphic overstated the drug's efficacy by suggesting that the weight loss depicted was due to Qsymia alone.
  - **Unsubstantiated superiority claims** - *See e.g.,* Doral Warning Letter, issued for a professional email that included the claim, "Doral is the only marketed medication for insomnia that helps with all three important components of sleep." OPDP cited this claim as false because other marketed medications are also indicated for all three components of sleep.
  - **Cherry picking data and context** – *See e.g.,* Qsymia Untitled Letter, where OPDP cited claims regarding *rate* of weight loss, such as "3X FASTER WEIGHT LOSS" and ". . . 3 times faster than diet and exercise alone." OPDP found these claims misleading because the referenced studies evaluated *amount* of weight loss but were not designed to evaluate the *rate* of weight loss over time to support a claim of "faster" weight loss. OPDP also noted that the efficacy claims failed to disclose that weight loss was measured in relation to the patient's baseline weight and circumference, misleadingly implying that all patients will lose the same number of pounds per week regardless of their baseline weight.
  - **"Before and After" photos with atypical results** – *See e.g.,* Eskata Untitled Letter, issued for a DTC video for a seborrheic keratoses (SK) drug. OPDP cited "before and after" images showing complete clearance of the patient's SK lesions. OPDP found the images misleading because the majority of patients in the trial did not achieve complete clearance. Notably, the company attempted to provide some context by disclosing the percentage of patients in the trial who achieved complete clearance and including the statement: "Individual results may vary." OPDP found these disclaimers insufficient because they were presented at a fast pace and simultaneously with other competing information, making it difficult for consumers to adequately process and comprehend the information.
- **Other notable trends in OPDP's 2019 enforcement letters include the following:**
  - **Continued focus on pre-approval promotion**: Last year, FDA continued its regular scrutiny of and enforcement against preapproval promotion of investigational drugs. *See, e.g.*, Pritumumab Untitled Letter and Sodium Acetate (C-11) Untitled Letter.
  - **Continued focus on risk presentation in consumer TV ads**: The presentation of risk information in DTC television ads continues to be an area of focus for OPDP. Since 2016, OPDP has issued 4 letters directed at DTC TV ads, including the 2019 Paragard letter. Taken together, these letters highlight 3 key concerns by OPDP related to presentation of risk information in DTC TV ads:

- Compelling and attention-grabbing visuals and other distracting elements, such as dancing and frequent scene changes, occurring during the presentation of the major statement on risks. This was a key concern in the 2019 Paragard letter. *See also*, 2016 Toujeo and Otezla Untitled Letters.
- Disclosing important risk information (such as contraindications) in superimposed text only.
- Presenting unrelated risk information in competing audio voiceovers and superimposed text, making it difficult for consumers to process and comprehend. *See e.g.*, 2017 Contrave Untitled Letter.

— **OPDP targets repeat offenders**: In three of the ten enforcement letters in 2019, OPDP indicated that the companies had previously been put on notice regarding the Agency's concerns. In the Eskata Untitled Letter, FDA noted that the company had received OPDP advisory comments for presentations that were similar to the video at issue and FDA had recommended revising the presentations so they did not misrepresent important risk information. The Doral Warning Letter for a professional email raised similar concerns to those outlined in a 2014 untitled letter to the then-sponsor of Doral – the manufacturer, Sciecure. Similarly, the Vivitrol Warning Letter cited two separate prior communications from FDA related to an important risk of the product that was omitted in the challenged ad. This underscores the importance of a promotional review and approval process and ensuring that teams are well versed on the history of the product, including previous enforcement letters, advisory comments, and formal or informal discussions with FDA regarding scope of permissible claims.

— **Reemergence of OPDP's Bad Ad program**: An interesting observation from recent OPDP letters is an apparent reemergence of OPDP's Bad Ad program as a trigger for enforcement. CDER launched the Bad Ad program in 2010, establishing a way for healthcare professionals to directly report misleading prescription drug promotion to FDA. The majority of letters triggered by Bad Ad reports occurred in the first two years of the program – between 2010 – 2011, complaints to the Bad Ad program prompted eight enforcement letters. Although none of the 2016-2017 OPDP letters included references to Bad Ad reports, three letters in 2018 and 2019 (including the 2019 Paragard letter) were initiated, at least in part, through a Bad Ad program complaint.

For your reference, we have prepared a chart that lists the ten Warning and Untitled Letters issued to pharmaceutical manufacturers for promotional violations in 2019, including summaries of the promotional violations alleged in each letter and a hyperlink to each letter and related promotional materials. The chart is available online in a searchable PDF document here. Similarly, summaries of the 2018 OPDP enforcement letters are available here.