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FDA Advertising and Promotion Enforcement Activities: Update

September 12, 2019

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 July and August, the Office of Prescription Drug Promotion (OPDP) posted the following enforcement letters on FDA's website:

- Untitled Letter to CooperSurgical, Inc. re: NDA 018680 ParaGard® T380A INTRAUTERINE COPPER CONTRACEPTIVE, MA 578 (July 25, 2019) ("ParaGard Untitled Letter")
- Warning Letter to Metuchen Pharmaceuticals, LLC re: NDA 202276 STENDRA® (avanafil) tablets, for oral use, MA 169, 182, 187 (Aug. 16, 2019) ("Stendra Warning Letter")

The ParaGard Untitled Letter and the Stendra Warning Letter are the fourth and fifth enforcement letters OPDP has issued this year. 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 July or August of this year. FDA's Advertising and Promotional Labeling Branch (APLB) in the Office of Compliance and Biologics Quality (OCBQ) has not posted 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)

ParaGard Untitled Letter (July 2019)

OPDP's untitled letter to CooperSurgical states that a direct-to-consumer (DTC) television ad for ParaGard, an intrauterine contraceptive, misbrands ParaGard under section 502(n) of the FDCA because it misleadingly minimizes the risks associated with the use of ParaGard. OPDP's letter further states that this misbranding is "especially problematic from a public health perspective given the serious and potentially life-threatening risks associated with the drug." FDA received a complaint about the advertisement through its Bad Ad Program.

False or Misleading Risk Presentation

OPDP alleges the ad minimizes the risks associated with ParaGard by: (1) failing to include important risk information, (2) undermining the presentation of certain risk information, (3) communicating important risk information in only the visual, and not the audio, portion of the ad, (4) presenting unrelated risk and benefit information in competing modalities, and (5) misleadingly suggesting that ParaGard does not have the potential negative health effects of hormone contraceptives.

First, OPDP alleges that the ad is misleading because it includes claims and representations about the uses and benefits of ParaGard but fails to include important risk information, thereby "misleadingly suggest[ing] that ParaGard is safer than has been demonstrated." Specifically, OPDP states that the ad:

- includes the statement as onscreen superimposed text (SUPER), "Don't use Paragard *[sic]* if you have certain cancers" but fails to include any of the other contraindications;
- includes the statement as an audio voice-over (VO), "If you experience pain, pelvic infection . . . call your healthcare provider," but fails to adequately communicate that ParaGard is associated with an increased risk of pelvic inflammatory disease (PID) and that PID can have serious consequences; and
- omits the warning for "expulsion of the product" (the product falling out of the uterus).

Second, OPDP alleges that the presentation of the "major statement," via audio and SUPERs, is undermined by the simultaneous presentation of fast-paced visuals featuring choreographed dancing to background music and multiple scene changes. OPDP states that these "compelling and attention-grabbing visuals" are "unrelated to the risk message presented" and compete for the consumers' attention. As a result, consumers may have difficulty "adequately process[ing] and comprehend[ing] the risk information, resulting in a misleading impression of the drug's risk."

Third, OPDP alleges that the ad is misleading because it communicates contraindications for certain cancers, as well as a precaution for vaginal bleeding, only as SUPERs. Citing FDA regulations at 21 C.F.R. section 202.1(e)(1), however, OPDP's letter states that television ads are required to include information relating to major side effects and contraindications in the audio (or audio and visual) part(s) of an advertisement.

Fourth, OPDP alleges that the ad minimizes the presentation of risk information by presenting unrelated risk and benefit information in "competing modalities." Specifically, OPDP alleges that the ad:

- (a) discloses in a SUPER important risk information about the contraindication for certain cancers but (b) does so simultaneously with audio containing unrelated risk information about calling a healthcare provider for pain, pelvic infection, or missed period; and
- (a) discloses in a SUPER important risk information about the precaution for vaginal bleeding but (b) does so simultaneously with unrelated audio and visual benefit claims that ParaGard is 100% hormone free and over 99% effective at preventing pregnancy.

Fifth, OPDP alleges that the ad further minimizes the risks associated with ParaGard by including claims and presentations that misleadingly suggest that ParaGard does not have the

potential negative health effects of hormone contraceptives. Specifically, the ad includes the following claims and presentations (emphasis in original):

- "No hormones! I found a birth control with no hormones! Paragard's *[sic]* 100% hormone-free ...!" (VO)
- "No hormones not an ounce! With an ingredient I can pronounce." (VO)
- "**100% HORMONE FREE**" (background visuals and SUPER)
- "**1 SIMPLE ACTIVE INGREDIENT**" (background visuals and SUPER)

OPDP acknowledges that ParaGard is hormone-free but explains that "the totality of the overwhelming, repetitive nature of the claims . . . along with the misleading omission and presentational elements of the TV ad . . . create a misleading impression of the safety profile of the drug." "In fact," OPDP notes, "ParaGard is associated with many of the same serious risks as other [long-acting reversible contraceptive] products," as well as additional risks, "some of which may be fatal."

Stendra Warning Letter (August 2019)

OPDP's warning letter to Metuchen Pharmaceuticals states that a DTC print ad and display banners misbrand Stendra, a phosphodiesterase 5 (PDE5) inhibitor for the treatment of erectile dysfunction. OPDP states that the print ad suggests a new use for which Stendra lacks approval and for which the labeling does not provide adequate directions for use. It further states that both the print ad and the banners make false or misleading claims and/or representations about the risks associated with, and the efficacy of, Stendra.

Lack of Adequate Directions for Use

OPDP alleges that the print ad misbrands Stendra because it suggests that Stendra may be used for reducing the risk of heart failure, but Stendra is not approved for such use, nor does its labeling contain adequate directions for such use. Specifically, the print ad includes the following headline claim (emphasis in original): "**Treat ED and Reduce Risk of Heart Failure with a PDE-5 Inhibitor**."

OPDP states that the claim, for which the sponsor allegedly has provided no supporting evidence, is "especially concerning from a public health perspective given that the PI contains a warning and precaution regarding cardiovascular risks, and specifically states that Stendra is not recommended for patients with New York Heart Association Class 2 or greater congestive heart failure."

False or Misleading Risk Presentations

OPDP alleges that the print ad and banners misbrand Stendra because they (1) omit risk information, (2) misleadingly suggest that Stendra can safely be used at any time, (3) misleadingly suggest that Stendra is safe for all patients with heart disease, (4) misleadingly suggest that Stendra is safer or more effective than its competitors, and (5) fail to present risk information with reasonably comparable prominence and readability as effectiveness information.

First, OPDP alleges that the print ad and each of the banners omit information regarding the risks associated with use of Stendra, thereby creating a misleading impression about the drug's safety. Specifically, OPDP alleges:

- The print ad includes several efficacy claims, but it fails to disclose any of the contraindications or warnings and precautions other than warnings regarding alcohol use and the most common side effects.
- One of the banners includes the claims "**Get Hard & Stay Hard**" (emphasis in original) and "Indulge in life's sweetest pleasures whenever you want" but fails to include any risk information. OPDP states that the first of these claims "further exacerbate[s]" the misleading safety impression created by the banner because Stendra's labeling includes a warning and precaution regarding prolonged erection.
- The other banner includes several claims but fails to include any of the contraindications or warnings and precautions associated with the drug, except for a statement about common side effects. Specifically, the banner makes the following claims (emphasis in original):
  - Version A: "**The ED Pill For Your Lifestyle**" and "Stendra prescriptions can be taken with or without food and alcohol."
  - Version B: "**The Fast-Acting ED Prescription**" and "Stendra can be effective in as little as 15 minutes, with or without food."

  OPDP alleges that the claim in Version A that "Stendra prescriptions can be taken with or without food and alcohol" "further exacerbate[s]" the misleading safety impression because the banner fails to disclose that there is a specific risk related to drinking too much alcohol when taking Stendra. OPDP states that the omission of such material information in the banner is not mitigated by the Clinical Studies section of the PI, which states that food and alcohol intake was not restricted during the studies.

OPDP states that the omission of such risk information is "especially problematic from a public health perspective due to the multiple serious risks associated with the drug." Moreover, OPDP states that such omissions are not mitigated by the statements included in the print ad and banners, to "Ask your doctor for more information" (capitalized emphasis omitted by OPDP) and, "Learn more at BIT.LY/STENDRA."

Second, OPDP alleges that one of the banners misleadingly suggests that Stendra can be used at any time. Specifically, OPDP states that the banner claim "Indulge in life's sweetest pleasures whenever you want" misleadingly suggests that Stendra is effective "whenever" a patient wants. Instead the PI recommends a maximum dosing frequency of once a day and provides that efficacy beyond 2 hours of administration is inconclusive. OPDP states that it is not aware of data to support Stendra's efficacy outside of 15 minutes to 2 hours after dosing, which was the period studied in the Stendra development program.

Third, OPDP alleges that the print ad falsely or misleadingly suggests that Stendra is safe for all patients with heart disease, including all patients with heart failure, by including the following claims (bolded emphasis original, underlined emphasis by OPDP):

- "**TREAT ED and <u>Reduce Risk of Heart Failure</u> with a PDE-5 Inhibitor**"
- "Stendra (Avanafil) is . . . safe and effective for those with <u>heart disease</u> . . . ."

OPDP acknowledges that "there is evidence that PDE-5 inhibitors, including Stendra, may be safe and effective for men with **some** types of heart disease" (emphasis in original). OPDP goes on to state, however, that "the PI for Stendra contains a warning and precaution for

cardiovascular risks associated with the drug" and is not recommended for use in patients with certain heart diseases or conditions.

Fourth, OPDP alleges that the print ad misleadingly suggests that Stendra is safer and more effective than its competitors by referring to it as "**the next-generation, PDE-5 inhibitor that improves erectile function**" (bolded emphasis original, underlined emphasis by OPDP). OPDP alleges that no references were cited in support of this claim and that it is not aware of evidence to support the suggestion that Stendra is safer or more effective than its competitors.

Fifth, OPDP alleges that the print ad minimizes the risks associated with Stendra by failing to present risk information with reasonably comparable prominence and readability as compared to effectiveness information. Specifically, OPDP states that whereas efficacy claims are presented "in large, bolded font size and colorful text and graphics surrounded by a significant amount of white space," the "limited risk information is presented in much smaller font size, surrounded by little white space, and in single-spaced format at the bottom of the ad."

False or Misleading Claims about Efficacy

OPDP alleges that one of the banner ads misleadingly suggests that Stendra is safe and effective as an aid to achieve and maintain an erection for people without erectile dysfunction. Specifically, OPDP points to the following claims (emphasis in original):

- "**Get Hard & Stay Hard**"
- "Indulge in life's sweetest pleasures whenever you want."

OPDP states that the banner is misleading because it fails to communicate that Stendra is indicated "for the treatment of erectile dysfunction." OPDP states that "[t]he omission of the indication is particularly concerning from a public health perspective due to the serious health risks associated with Stendra."

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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