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FDA Advertising and Promotion Enforcement Activities: Update

December 20, 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 November, the Office of Prescription Drug Promotion (OPDP) posted the following enforcement letters on FDA's website:

- Untitled Letter to Nascent Biotech, Inc. re: Pritumumab, MA 1 (Nov. 1, 2019) ("Pritumumab Untitled Letter")
- Untitled Letter to Rockwell Medical, Inc. re: NDA 206317; NDA 208551 TRIFERIC® (ferric pyrophosphate citrate) solution and TRIFERIC® (ferric pyrophosphate citrate) powder packet for addition to bicarbonate concentration, MA 26; MA 22 ("Triferic Untitled Letter")

The Pritumumab Untitled Letter and the Triferic Untitled Letter are the eighth and ninth 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 October or November 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)

Pritumumab Untitled Letter (November 2019)

OPDP's untitled letter to Nascent Biotech states that the company's website[1] misbrands pritumumab, an investigational new drug for the treatment of brain cancer, under section

[1] The letter cites https://www.nascentbiotech.com/ (last accessed by OPDP October 31, 2019) and https://www.nascentbiotech.com/products/pritumumab (last accessed by OPDP October 31, 2019). Both pages are no longer active.

502(f)(1) of the Food, Drug, and Cosmetic Act (FDCA) and violates section 301(k) of the FDCA by representing the drug as safe and effective for the purpose for which it is being investigated. OPDP states that the claims made on the website "represent the drug as having an established role in the treatment of brain cancer, when pritumumab has not been proven safe and effective within the meaning of the [FDCA] and has not been approved as a drug under that authority for any use."

Misbranding of an Investigational Drug

OPDP alleges that the Nascent Biotech website misbrands pritumumab by describing pritumumab for the use for which it is being investigated, i.e., to treat brain cancer. Under section 502(f)(1), a drug is misbranded unless its labeling bears "adequate directions for use." By regulation, however, an investigational drug is exempt from such requirement if it "complies with section 505(i) [of the FDCA] … and regulations thereunder." 21 CFR 201.115(b). Among these regulations, "[a] sponsor or investigator … shall not represent in a promotional context that an investigational new drug is safe or effective for the purposes for which it is under investigation or otherwise promote the drug." 21 CFR 312.7(a). OPDP alleges that Nascent Biotech's website fails to comply with the requirements for this exemption because it makes claims that promote pritumumab as safe and effective for the purpose for which it is being investigated or that otherwise promote the drug when it has not been approved by FDA for any use.

Specifically, OPDP cites the following claims (emphasis by OPDP):

- "Pritumumab has **cured a rare form of brain cancer**"
- "Delivering human antibodies for the treatment of cancer"
- "After 5 years, patients treated with pritumumab have an overall survival rate of 25-30%, compared to 3% standard therapy, **demonstrating antibodies are safe and effective**"

OPDP alleges that these claims "make numerous conclusory statements" and "are extremely concerning given the lack of adequate safety and efficacy data for pritumumab." OPDP further alleges that the above claims "are concerning given the seriousness of this disease and the relatively few available treatment options." OPDP states that the first claim, that pritumumab has "cured a rare form of brain cancer," is "especially troubling given that brain cancer in general is a disease associated with a poor prognosis (i.e., decreased overall survival)."

Finally, OPDP states that the website does not clearly indicate that pritumumab is an investigational new drug that has not been approved for commercial distribution in the United States.

Triferic Untitled Letter (November 2019)

OPDP's untitled letter to Rockwell Medical states that a portion of the company's webpage[2] misbrands Triferic, a product indicated for the treatment of iron deficiency in patients with hemodialysis-dependent chronic kidney disease (HDD-CKD), under sections 502(a) and 502(n) of the FDCA, and 21 CFR 202.1(e)(3)(ii) and 202.1(e)(5). Specifically, OPDP alleges that the

[2] The letter cites https://www.rockwellmed.com/bio-pharma-development/triferic/ (last accessed by OPDP November 18, 2019). That webpage is no longer active.

webpage provides information about the drug's benefits without communicating the associated risks, makes false or misleading claims about the risks and efficacy associated with Triferic, and omits other material facts.

OPDP's letter further states that the alleged violations "are concerning from a public health perspective because patients with [HDD-CKD] are a vulnerable patient population at increased risk of medical complications and adverse outcomes."

False or Misleading Risk and Benefit Presentations

OPDP alleges that the webpage includes claims and/or representations about Triferic's benefits, but does not offer "**any** risk information about the product" (emphasis by OPDP). As a result, the webpage "creates a misleading impression about the safety of Triferic."

OPDP alleges that the claims on the webpage "suggest Triferic is safer and more effective than other IV iron replacement products, when this has not been demonstrated." In particular, the webpage makes the following claims:

- Unlike current nurse IV iron administration, Triferic is seamlessly administered via dialysate directly to the bone marrow, delivering iron in a physiologic manner avoiding iron storage in the liver or reticuloendothelial system.
- Triferic improves the effectiveness of iron delivery for the majority of dialysis patients and prevents iron induced liver damage, especially for those patients with known concomitant liver disease.
- Released clinical trial data along with real world usage have shown that small, frequent doses of Triferic, as compared to the current administration of large, infrequent doses of IV iron, is safer and more effective in delivering and maintaining optimal iron balance.

OPDP states the webpage does not cite any references, and the Agency is not aware of data, to support these claims.

OPDP acknowledges that Triferic is the sole FDA-approved iron replacement product administered by hemodialysate, but "once inside the blood stream, iron delivered by Triferic is used by the body in the same manner as other currently approved iron replacement products." Regarding comparative "iron storage" claims, the Agency notes that the studies supporting approval of Triferic did not include liver iron testing. Furthermore, "[t]hese studies were also neither designed to assess the benefit of Triferic in patients with known concomitant liver disease nor sized to quantitatively evaluate the risk of hepatotoxicity compared to IV iron."

Omission of Material Facts

OPDP alleges that the webpage fails to communicate material information about the product's full FDA-approved indication and its limitations of use.

The FDA-approved labeling states that Triferic is intended for use "in adult patients with hemodialysis-dependent chronic kidney disease (HDD-CKD)" (emphasis by OPDP). The labeling also provides the following "limitations of use" (emphasis omitted):

- Triferic is not intended for use in patients receiving peritoneal dialysis.
- Triferic has not been studied in patients receiving home hemodialysis.

OPDP alleges that in omitting this information the webpage creates a misleading impression about the FDA-approved indication for Triferic. Moreover, OPDP alleges that broad claims such as "Triferic improves the effectiveness of iron delivery for the majority of dialysis patients . . ." (emphasis by OPDP) are "particularly concerning" because they suggest that Triferic is indicated for patients receiving any type of dialysis.

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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