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FDA Advertising and Promotion Enforcement Activities: Update

July 18, 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 May and June, the Office of Prescription Drug Promotion (OPDP) posted the following untitled letters on FDA's website:

- Untitled Letter to VIVUS, Inc. re: NDA 022580 QSYMIA (phentermine and topiramate extended-release) capsules, for oral use, CIV MA 414 (May 22, 2019) ("Qsymia Untitled Letter")
- Untitled Letter to Aclaris Therapeutics, Inc. re: NDA 209305 ESKATA® (hydrogen peroxide) topical solution MA 56 (June 14, 2109) ("Eskata Untitled Letter")

The Qsymia and Eskata Untitled Letters are the second and third 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 April through June 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)

Qsymia Untitled Letter (May 2019)

OPDP states that Qsymia, a weight-management prescription drug product, is misbranded under section 502(a) of the FDCA by the product's consumer website homepage[1] because the website makes false or misleading claims and/or representations about the efficacy of and risks associated with Qsymia. OPDP notes that the webpage is "especially concerning from a public health perspective because it creates a misleading impression regarding the overall effect a

[1] https://qsymia.com (last accessed by FDA May 22, 2019).

patient may expect as a result of Qsymia treatment and deemphasizes the risks associated with taking the drug."

False or Misleading Claims About Efficacy

OPDP alleges the webpage misbrands Qsymia by: (1) misleadingly suggesting Qsymia can help patients lose weight three times faster than diet and exercise alone, (2) omitting material information from the full indication and the relative effect of diet and exercise; and (3) selectively presenting results data without contextual information regarding baseline weight, baseline waist circumference, and patients who withdrew from the studies.

First, OPDP alleges that the webpage misleadingly suggests Qsymia can help patients lose weight three times faster than diet and exercise alone. The webpage includes the following claims (bolded emphasis in original, underlined emphasis added by OPDP):

- "**On average, prescription Qsymia can help you lose weight 3 times <u>faster</u> than diet and exercise alone.**[2,3]"
- "**3X**

  <u>FASTER</u> WEIGHT LOSS"

OPDP states that the cited references do not support the suggestion that Qsymia can help patients lose weight three times faster than diet and exercise alone and that it is unaware of data to support these claims. With regard to the cited references, OPDP states that the "studies were designed to evaluate the <u>amount</u> of weight loss and cannot be used to support claims regarding the <u>rate</u> of weight loss" (emphasis in original).

Second, OPDP alleges that the webpage omits material information from the full indication and about the relative effect of diet and exercise. The webpage presents the following claims (emphasis in original):

- "For patients with a body mass index (BMI)* of 30+† or 27 kg/mg^2 or greater (overweight) in the presence of at least one weight-related medical condition.

  Lose weight and keep it off with Qsymia[2,3]

  ...

  12 Weeks

  Your first milestone

  15-19 Pounds of weight loss 2-3 Inches off your waist

  28 Weeks

  Stay motivated

  22-29 Pounds of weight loss 3-4 Inches off your waist

[2] Qsymia Full Prescribing Information. Campbell, CA: VIVUS, Inc; 2018
[3] Data on File. VIVUS. Inc.

56 Weeks

Maintain progress

24-32 Pounds of weight loss 4-5 Inches off your waist"

According to the prescribing information ("PI") for Qsymia, "Qsymia is indicated as an adjunct to a reduced-calorie diet and increased physical activity for chronic weight management...." OPDP alleges that the above claims from the Qsymia webpage "omit material information ... about the relative effect of diet and exercise," and that "the webpage ... illustrations showing an exercise bike, a bag of groceries, and a capsule ... are not adequate to convey to the viewer that both exercise and diet are necessary in achieving the benefits ... of Qsymia...." OPDP also states that omitting the results for the placebo group is misleading "because it suggests that these results [stated on the webpage] are or can be attributable to Qsymia alone."

Third, OPDP states that the above presentation is misleading with regard to efficacy of Qsymia because it selectively presents results data without necessary context. Specifically, OPDP alleges that the above presentation "selectively presents the more favorable absolute amount of weight loss and reduction in waist circumference" (emphasis in original) without accounting for an individual's baseline weight and waist circumference. OPDP alleges that "this presentation misleadingly implies that all patients, no matter their baseline weight or waist circumference, should expect to achieve results similar to the absolute amounts presented on the webpage..." (emphasis in original). Additionally, OPDP alleges that the presentation fails to account for the "substantial percentage" of patients who withdrew from the studies. OPDP states that failing to present such contextual information "overstates the efficacy of the product and misleadingly implies all patients who received Qsymia remained on treatment."

False or Misleading Risk Presentation

OPDP also alleges that the webpage misbrands Qsymia because it "fails to present information relating to contraindications, warnings, precautions, and adverse reactions for Qsymia with a prominence and readability reasonably comparable with the presentation of information relating to the benefits of Qsymia." Specifically, "benefit claims for Qsymia are presented in conjunction with colorful graphics and large bolded headlines, with significant white space." In contrast, "risk information is relegated to the bottom of the webpage in paragraph format and is not easily accessible to viewers who must 'scroll' down the webpage past the entire benefit presentation." OPDP adds that "the webpage does not present any significant signal to alert the viewer that important risk information follows the presentation of benefit information."

Eskata Untitled Letter (June 2019)

OPDP states that Eskata, a topical treatment for raised seborrheic keratoses ("SK"), is misbranded under sections 502(a) and (n) of the FDCA by a direct-to-consumer video[4] of an interview featuring a physician who is a paid Aclaris spokesperson ("Physician Spokesperson") regarding Eskata, as well as the corresponding script for the video. OPDP states that the video makes false or misleading representations about the risks associated with Eskata and about the efficacy of Eskata. OPDP notes that the video is

> especially concerning from a public health perspective because it fails to include information regarding the serious risks associated with Eskata, which bears warnings and precautions related to the risks of serious eye disorders (such as permanent eye injury including blindness) in the case of exposure to the eye and severe skin reactions including scarring.

OPDP also notes that it had issued advisory comments on March 29, 2018, that "recommended that Aclaris revise proposed presentations" that bore "certain similarities to the video" described in the untitled letter. OPDP states that it had recommended that Aclaris revise those presentations "so that they did not omit material information regarding the risks associated with Eskata or otherwise misrepresent important risk information," and "so that they did not overstate the efficacy of Eskata." OPDP explains that it is "concerned that Aclaris is promoting Eskata in a manner that fails to adequately present the serious risks of the drug or describe the efficacy of the drug in a truthful and non-misleading manner despite this direction from OPDP."

False or Misleading Risk Presentation

OPDP alleges the video misbrands Eskata because it "fails to include prominent, balancing risk information about Eskata." Specifically, OPDP states that the video (1) "fails to reveal the serious risks that are reflected in the warnings and precautions for the drug," and (2) "create[s] misleading impressions regarding Eskata treatment and the safety profile of the product."

First, OPDP alleges that the video fails to reveal the serious risks that are reflected in the warnings and precautions for Eskata and are intended to be communicated to patients as described in the PI and patient information. OPDP states that this omission is not mitigated by the Physician Spokesperson referring consumers to Eskata.com for more information or the inclusion of superimposed text ("SUPERs") listing the drug's most common side effects and directing consumers to Eskata.com for full safety and PI.

Second, OPDP alleges the claims and presentations in the video with respect to Eskata's common adverse reactions create a misleading impression that patients will experience only stinging as Eskata is applied with no other local adverse reactions during or after application of Eskata. OPDP cites the following claims and images:

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[4] The Eskata Untitled Letter states the video was available on the internet at https://youtu.be./QncHius7UAU (last accessed June 14, 2019). The video was originally broadcast on ABC's *The View* on September 19, 2018, and could also be accessed through the Eskata Facebook page and the Aclaris LinkedIn page (both last accessed June 14, 2019).

- The Physician Spokesperson makes the following claim: "And, typically in one or two treatments the lesions go away, they resolve, and that's the end of it." (emphasis added by FDA).
- This claim is followed by side-by-side images of two patients with SKs "BEFORE," at "3 WEEKS," and on "DAY 106 (Final Result)" of ESKATA treatment.
- As the "before" and "after" images are presented, the following exchange takes place:
  - Interviewer: "Does it burn as you're doing it?"
  - Physician Spokesperson: "It can sting as you apply it."

OPDP alleges it is misleading for the Physician Spokesperson to state that patients can experience stinging upon application without disclosing the other most common local adverse reactions, such as erythema, edema, scaling, crusting and pruritus. OPDP also states it is misleading for the Physician Spokesperson to suggest that typically after one to two treatments, "that's the end of it," because many patients experience local adverse reactions at a longer interval after the application of Eskata, including 15 weeks after the initial treatment. OPDP states that this misleading impression is not sufficiently mitigated by presentation of SUPERs that list the most common side effects because the SUPERs are presented with a large amount of unrelated information (e.g., efficacy information, attention-grabbing photographs, and Physician Spokesperson statements) at a fast pace over approximately 10 seconds, all of which compete for the consumer's attention.

False or Misleading Claims About Efficacy

OPDP also alleges that the video misbrands Eskata because (1) it misleadingly represents that the typical patient treated with Eskata will experience complete clearance of all treated SK lesions, and (2) it suggests that more patients will achieve complete clearance of their SK lesions than has been demonstrated.

First, OPDP cites the following Physician Spokesperson claims and presentations that allegedly misleadingly represent that the typical patient treated with Eskata will experience complete clearance of all treated SK lesions:

- "And, typically in one or two treatments the lesions go away, they resolve, and that's the end of it." (emphasis added by FDA)
- "So, you can see from the before and after, what it looks like."
- The claims are followed by presentations of side-by-side, before and after, visual images of two patients, both of which have no visible lesions in the "after" photographs that illustrate the final results at Day 106.

OPDP states that the CLINICAL STUDIES section of the PI states that only 4% and 8% of subjects treated with Eskata achieved clearance of four out of four SK lesions at Day 106 in clinical studies 1 and 2, respectively. OPDP states that the misleading impression is not sufficiently mitigated by the concurrently presented SUPER (described above), which includes the proportion of patients treated with Eskata versus vehicle who achieved clearance of three out of four lesions at Day 106 and discloses that individual results will vary. OPDP reiterates that the SUPER is presented with a large amount of unrelated information at a fast pace that competes for the consumer's attention.

Second, OPDP alleges that the claims and presentations suggest that more patients will achieve complete clearance of their SK lesions than has been demonstrated. OPDP cites the following SUPER, which is presented in conjunction with the before and after images of patients depicting complete clearance of their SK lesions:

- "18% of patients experienced clearance of 3 out of 4 raised SKs treated with ESKATA vs 0% with vehicle (Day 106 end of study)."

OPDP states that "[p]resenting images of patients depicting complete clearance, in conjunction with data for clearance of at least 3 out of 4 lesions, while omitting data for clearance of 4 out of 4 lesions, misleadingly suggests that these data apply to the results seen in the 'before' and 'after' images when this is not the case." OPDP points to the PI, which states that only 4% and 8% of subjects treated with Eskata achieved clearance of four out of four SK lesions at Day 106 in clinical studies 1 and 2, respectively.

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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