COVINGTON

COVINGTON & BURLING LLP

# E-ALERT | Food & Drug

January 29, 2014

## SUMMARY OF FDA ADVERTISING AND PROMOTION ENFORCEMENT ACTIVITIES

## DECEMBER 2013

This e-alert is part of a series of monthly 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 2013, FDA's Office of Prescription Drug Promotion (OPDP) posted the following enforcement letters on FDA's website[1]:

- Untitled letter to Covis Pharmaceuticals re: NDA #020405 LANOXIN® (digoxin) tablets, for oral use MA #534 (December 9, 2013) ("Covis Untitled Letter")
- Untitled letter to Amarin Pharmaceuticals Ireland LTD, re: VASCEPA® (icosapent ethyl) capsules, for oral use MA #63 (December 16, 2013) ("Amarin Warning Letter")
- Untitled letter to Pernix Therapeutics Holdings, Inc. re: NDA #050685, 050686 CEDAX® (ceftibuten) capsules and oral suspension MA #241, 211 (December 20, 2013) ("Pernix Untitled Letter")

The Office of Compliance and Biologics Quality (OCBQ) in FDA's Center for Biologics Evaluation and Research (CBER) and the Office of Compliance in FDA's Center for Devices and Radiological Health (CDRH) did not post any enforcement letters relating to advertising and promotion on FDA's website.

***This alert merely summarizes the allegations contained in FDA's letters. It does not contain any analysis, 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.***

## LETTERS ISSUED BY OFFICE OF PRESCRIPTION DRUG PROMOTION (OPDP)

### Covis Untitled Letter

OPDP alleged that a physician letter regarding Lanoxin tablets was misleading because it omitted and minimized risk information, made misleading superiority claims, and suggested that the drug is useful in a broader range of patients or conditions than has been approved.[2]

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[1] Only enforcement letters posted to FDA's website in December 2013 are included herein. Letters issued in December but not posted to the website by December 30, 2013 will be summarized in our alerts for the months in which those letters are posted.

[2] OPDP also alleged that the letter was disseminated with an outdated version of the product label in violation of 21 C.F.R. § 201.100(d).

*Omission and Minimization of Risk Information:* According to OPDP, the physician letter omitted all information from the CONTRAINDICATIONS section of the approved prescribing information, as well as important risk information from the WARNINGS and PRECAUTIONS and ADVERSE REACTIONS sections. Although OPDP acknowledged that the physician letter contained some information regarding risks and common adverse events, OPDP claimed the physician letter failed to include material safety information, including information regarding symptoms of digoxin toxicity and other serious adverse reactions such as cardiac toxicity. OPDP stated that including a reference to the full prescribing information did not mitigate the misleading omission of important risk information from the body of the letter. Further, OPDP alleged that Covis minimized risk information by placing the included safety information on the back side of the physician letter after the signature block and in small print, while efficacy claims were prominently displayed in bold font on the front side.

*Misleading Superiority Claims:* The physician letter included the following claims:

- "Physicians, like yourself, have many options when choosing a medication to treat their patients, including prescribing a brand or a generic. With some medications the difference may have no impact. But with others, such as narrow therapeutic index products, you may want to consider all your options."
- "Branded **Lanoxin** has been manufactured by the same organization for over 78 years, and has been made at the same plant for over 30 years with no disruption to supply due to any manufacturing concerns. It is critical to insure that Lanoxin/digoxin tablets are manufactured to specific tolerances so that the patient does not receive either too much or too little of the drug. In fact, in the past 5 years there have been two manufacturers that have left the digoxin market because of manufacturing issues and one company has suspended manufacturing."[3]

OPDP alleged that the above claims implied that Lanoxin is superior to generic formulations of digoxin, which FDA considers therapeutically equivalent to Lanoxin. OPDP stated that unless FDA's determination that generic formulations are therapeutically equivalent to Lanoxin is changed or reversed, "any promotion suggesting a lack of equivalence between Lanoxin and products deemed to be therapeutically equivalent are (sic) considered false or misleading."

*Broadening of Patient Population or Condition:* The physician letter included the following claim:

- "**Lanoxin** is indicated . . . for the control of ventricular response rate in patients with chronic atrial fibrillation."[4]

According to OPDP, the above claim suggested that Lanoxin is useful in treating all patients with chronic atrial fibrillation, even though Lanoxin's approved indication is limited to adult patients. The prescribing information also states that "[t]he safety and effectiveness of LANOXIN in the control of ventricular rate in children with atrial fibrillation . . . have not been established." Thus, OPDP alleged that the statement above provides evidence that Lanoxin is intended for a new use for which it lacks approval.

## Amarin Untitled Letter

OPDP contended that a print invitation for a webcast series related to Vascepa presented efficacy claims but failed to provide necessary risk information.

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[3] Emphasis in original and citations omitted.
[4] Emphasis in original.

*Omission of Risk Information:* OPDP alleged that the print invitation contained efficacy claims, including the complete indications and limitations of use for the product, as well as the following:

- "**VASCEPA (incosapent ethyl).** . . [j]oin us to learn more about lowering triglyceride (TG) levels in adult patients with very high TG, including a review of key clinical data for VASCEPA. . . ."[5]

According to OPDP, the statements above constituted efficacy claims, requiring Amarin to present serious and frequently occurring risks associated with the drug in the print invitation as well. OPDP stated that although the print invitation referenced attached prescribing information, this did not mitigate the omission of risk information from the body of the invitation.

## Pernix Untitled Letter

OPDP alleged that a product information webpage for Cedax was misleading because it omitted risks and material facts.[6]

*Omission of Risk Information/Omission of Material Facts:* The webpage contained portions of Cedax's indication. According to OPDP, Pernix was thus required to provide risk information associated with Cedax. In addition, OPDP contended that Cedax's indication was presented with "images of children who clearly appear to be under 12 years of age," and thus Pernix was required to provide "material facts about the instructions for use of the product" with children. OPDP alleged that Pernix should have explained that the prescribing information allegedly only provides dosage information for the treatment of acute bacterial exacerbations of chronic bronchitis in patients 12 years of age and older; that there are limitations regarding dosage for pediatric patients with pharyngitis, tonsillitis, or acute bacterial otitis media; and that Cedax must be administered at least two hours before, or one hour after, a meal.

OPDP also claimed that Pernix was required to provide information in the NOTE portions of the INDICATIONS and USAGE section of the prescribing information. OPDP alleged that the website described Cedax's indication for acute bacterial otitis media, but failed to disclose that efficacy against the pathogen *Streptococcus pneumonia* was 23% less than control, as described in the NOTE portion of the prescribing information.

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If you have any questions concerning the material discussed in this client alert, please contact the following members of our Food & Drug Practice Group:


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[5] Emphasis in print invitation.
[6] OPDP also alleged that Pernix failed to submit a completed transmittal Form FDA-2253 at the time of initial publication in violation of 21 C.F.R. § 314.81(b)(3)(i).