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E-ALERT | Food & Drug

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SUMMARY OF FDA ADVERTISING AND PROMOTION ENFORCEMENT ACTIVITIES

FEBRUARY 2014

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 February 2014, FDA's Office of Prescription Drug Promotion (OPDP) posted the following enforcement letter on FDA's website[1]:

- Untitled letter to Mission Pharmacal Company, re: NDA #021618 Tindamax® (tinidazole) tablets for oral use MA #45 (January 23, 2014) ("Mission Untitled Letter")

The Office of Compliance (OC) in FDA's Center for Devices and Radiological Health (CDRH) and the Office of Compliance and Biologics Quality (OCBQ) in FDA's Center for Biologics Evaluation and Research (CBER) 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.

LETTER ISSUED BY OFFICE OF PRESCRIPTION DRUG PROMOTION (OPDP)

Mission Untitled Letter

OPDP alleged that a professional sales sheet for Tindamax was misleading because it omitted risk information, broadened the patient population and condition for the drug, made unsubstantiated superiority claims, omitted material facts, and made an unsubstantiated claim.

Omission of Risk Information: OPDP contended that although the sales sheet included the drug's boxed warning and selected risk information with promotional statements, it should have included the drug's full contraindications, warnings regarding neurological adverse reactions and blood dyscrasias, and common adverse reactions.

Broadening of Patient Population or Condition: OPDP alleged that the sales sheet failed to present the full approved indication of Tindamax and thus broadened its patient population or condition. The sales sheet included the following statements:

[1] Only enforcement letters posted to FDA's website in February 2014 are included herein. Letters issued in February but not posted to the website by February 28, 2014 will be summarized in our alerts for the months in which those letters are posted.

- "For short, affordable treatment of bacterial vaginosis (BV)…"
- "**TINDAMAX (tinidazole tablets) is the one and only treatment for BV that gives . . .**"[2]

The INDICATIONS AND USAGE section of the approved product label states that "Tinidazole is indicated for the treatment of bacterial vaginosis in non-pregnant women."[3] The approved label also states that the drug is contraindicated for women in their first trimester of pregnancy. According to OPDP, the statements above imply that the drug is approved for the treatment of BV in all women, when this has not been supported by clinical trials. OPDP stated that the presentation was "especially concerning" because "the sales sheet include[d] images of women of child-bearing age and omit[ted] the drug's contraindication related to use in pregnant women."

Unsubstantiated Superiority Claims: The sales sheet stated, "**TINDAMAX (tinidazole tablets) is the one and only treatment that gives your patients . . . better tolerability –** than metronidazole, with minimal risk of GI side effects."[4] OPDP contended this statement was misleading because it suggested that Tindamax is superior to metronizadole in the treatment of BV based on its risk profile, when this is not supported by substantial evidence. OPDP acknowledged that the sales sheet cited published studies and data on file that include adverse events data on subjects treated with tinidazole or metronidazole for trichomoniasis and other conditions aside from BV. However, OPDP alleged that since none of these data involved BV patients, used FDA-approved dosing regiments of Tindamax for BV, or were based on head-to-head clinical studies between Tindamax for BV, the data did not constitute substantial evidence.

The sales sheet also stated, "**shorter dosing** – 2-day or 5-day options streamline recovery vs 7-day metronidazole therapy."[5] OPDP acknowledged that the 2-day or 5-day dosing options approved for Tindamax are shorter in duration than the 7-day regimen approved for metronidazole. FDA stated, however, that this does not support a claim that Tindamax "streamlines recovery" from BV.

In addition, the sales sheet stated that Tindamax provided "**targeted efficacy** – with lower risk of secondary candidiasis infection (4.7%)."[6] According to OPDP, this claim suggests that patients on Tindamax have a lower rate of vaginal candidiasis as compared to patients taking metronidazole, when this is not supported by substantial evidence. OPDPD alleged that there was no information in Tindamax's approved product label to support a decreased risk of secondary candidiasis compared to other therapies.

Omission of Material Facts: The sales sheet included the following statement: "**The July 2010 issue of Treatment Guidelines from The Medical Letter®** recommends tinidazole as a 'drug of choice' for BV and trichomoniasis."[7] OPDP contended that this statement omitted materials facts. For example, FDA alleged that the sales sheet should have included important information regarding diagnostic procedures and the need to treat sexual partners simultaneously, as stated in the INDICATIONS AND USAGE section of the product label. OPDP acknowledged that the sales sheet referenced the prescribing information and stated that the drug's "**use should be reserved for the conditions described in INDICATIONS AND USAGE**."[8] OPDP alleged, however, that this did not mitigate the misleading omission of these material facts.

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[2] Emphasis in sales sheet.
[3] Emphasis added by OPDP.
[4] Bolded emphasis in sales sheet; underlined emphasis added by OPDP.
[5] Bolded emphasis in sales sheet; underlined emphasis added by OPDP.
[6] Bolded emphasis in sales sheet; underlined emphasis added by OPDP.
[7] Bolded emphasis in sales sheet; underlined emphasis added by OPDP.
[8] Emphasis in sales sheet.

Unsubstantiated Claim: The sales sheet also included the following statement: "**Patient-friendly convenience.**"[9] OPDP alleged this claim was misleading because Tindamax requires multiple tablets to be taken with food and patients must abstain from alcoholic beverages while taking tinidazole and for three days afterwards. According to OPDP, "patient convenience" encompasses a variety of factors such as dosage and administration, all aspects of efficacy, adverse reactions, and cost.

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[9] Emphasis in sales sheet.