



Jenny McNeil, PharmD, Regulatory Affairs Associate
Exeltis USA Inc.
180 Park Avenue, Suite 101
Florham Park, NJ 07932

RE: NDA 211367
SLYND (drospirenone) tablets, for oral use
MA 40

Dear Dr. McNeil:

As part of its monitoring and surveillance program, the Office of Prescription Drug Promotion (OPDP) of the U.S. Food and Drug Administration (FDA) has reviewed a promotional communication, a social media sponsored post (EXS-22-64 R00) (post), for SLYND (drospirenone) tablets, for oral use (Slynd).¹ The post makes false or misleading claims and representations about the risks and efficacy of Slynd. Thus, the post misbrands Slynd within the meaning of the Federal Food, Drug, and Cosmetic Act (FD&C Act) and makes its distribution violative. 21 U.S.C. 352(a), (n); 321(n); 331(a). See 21 CFR 202.1(e)(5). In addition, this material was not submitted at the time of initial dissemination or publication as required by 21 CFR 314.81(b)(3)(i). These violations are concerning from a public health perspective because the promotional communication fails to include any risk information, which creates a misleading impression about the expected benefits and safety of Slynd.

Background

Below are the indication and summary of the most serious and most common risks associated with the use of Slynd.² According to the INDICATIONS AND USAGE section of the FDA-approved prescribing information (PI)³:

SLYND is a progestin indicated for use by females of reproductive potential to prevent pregnancy.

Slynd is contraindicated in females with renal impairment; adrenal insufficiency; presence or history of cervical cancer or progestin sensitive cancers; liver tumors, benign or malignant, or hepatic impairment; and undiagnosed abnormal uterine bleeding. The PI for Slynd includes warnings and precautions regarding hyperkalemia, thromboembolic disorders, bone loss, cervical cancer, liver disease, ectopic pregnancy, risk of hyperglycemia in patients with diabetes, bleeding irregularities and amenorrhea, and depression. The most common adverse reactions reported with Slynd were acne, metrorrhagia, headache, breast pain,

¹ This post was last viewed and documented from Facebook's newsfeed on August 5, 2023, at 3:50 PM (EDT).

² This information is for background purposes only and does not necessarily represent the risk information that should be included in the promotional communication(s) cited in this letter.

³ The version of the Slynd PI referred to in this letter is dated May 2019.

weight increase, dysmenorrhea, nausea, vaginal hemorrhage, libido decreased, breast tenderness, and menstruation irregular[ity].

False or Misleading Risk Presentation

Prescription drug advertisements and labeling (promotional communications) misbrand a drug if they are false or misleading with respect to risk. The determination of whether a promotional communication is misleading includes, among other things, not only representations made or suggested in the promotional communication, but also the extent to which the promotional communication fails to reveal facts material in light of the representations made or with respect to consequences that may result from the use of the drug as recommended or suggested in the promotional communication.

The post, titled “Slynd® (drospirenone),” is misleading because it presents claims and representations about the benefits of Slynd but fails to communicate **any** risk information. By omitting the risks associated with Slynd, the post fails to provide material information about the consequences that may result from the use of Slynd and creates a misleading impression about the drug’s safety.

False or Misleading Claims about Efficacy

Promotional communications misbrand a drug if they are false or misleading with respect to efficacy. The determination of whether a promotional communication is misleading includes, among other things, not only representations made or suggested in the promotional communication, but also the extent to which the promotional communication fails to reveal facts material in light of the representations made or with respect to consequences that may result from the use of the drug as recommended or suggested in the promotional communication.

The post includes the following claim (emphasis original):

- **“Offer your patients estrogen-free birth control with periods on a schedule.”**

This claim is misleading because it overstates the efficacy of Slynd by claiming patients will have a “period,” or bleeding, that is predictable and “on a schedule” when this has not been demonstrated. We note that, according to the CLINICAL STUDIES section of the Slynd PI, in Study CF111/303, 81.2% of patients had scheduled⁴ bleeding in Cycle 1. However, this **decreased** to 26.4% after 13 cycles of treatment with Slynd. Similarly, in Study CF111/304, scheduled bleeding also **decreased** over time from 98.0% in Cycle 1 to 28.4% in Cycle 13. Thus, the majority of patients did **not** experience “periods on a schedule” over the duration of treatment with Slynd. Rather, “periods on a schedule” decreased. In addition, Slynd is associated with bleeding irregularities and amenorrhea. According to the WARNINGS AND PRECAUTIONS section of the Slynd PI, “Females using SLYND may

⁴ Scheduled bleeding was defined as any bleeding or spotting that occurred during hormone-free intervals (days 25 to 28±1 day) and continued for up to eight consecutive days (i.e., a “period”, vaginal bleeding during a menstrual cycle).

experience unscheduled (breakthrough or intracyclic) bleeding and spotting, especially during the first three months of use.” In fact, a large proportion of patients (40.3% and 52.2% in Studies CF111/303 and CF111/304, respectively) still reported unscheduled⁵ bleeding after 13 cycles of treatment. Thus, “periods” and other occurrences of bleeding were **not** “on a schedule.” Therefore, due to the majority of patients not experiencing scheduled bleeding (as would be expected during a menstrual cycle) during treatment with Slynd and the large proportion of patients still experiencing breakthrough bleeding, claims regarding Slynd patients experiencing predictable or “scheduled periods” are not supported by the data. If you have information or data to support periods occurring on a schedule, please submit to FDA for review.

Failure to Submit Under Form FDA-2253

FDA regulations require any labeling or advertising devised for promotion of the drug product to be submitted at the time of initial dissemination of the labeling and at the time of initial publication of the advertisement for a prescription drug product. Each submission is required to be accompanied by a completed transmittal Form FDA-2253 (Transmittal of Advertisements and Promotional Labeling for Drugs for Human Use) and is required to include a copy of the product’s current professional labeling. A copy of the post was not submitted to OPDP under cover of Form FDA-2253 at the time of initial publication as required by 21 CFR 314.81(b)(3)(i).

Conclusion and Requested Action

For the reasons discussed above, the post misbrands Slynd within the meaning of the FD&C Act and make its distribution violative. 21 U.S.C. 352(a), (n); 321(n); 331(a). See 21 CFR 202.1(e)(5). Furthermore, Exeltis did not comply with 21 CFR 314.81(b)(3)(i).

This letter notifies you of our concerns and provides you with an opportunity to address them. OPDP requests that Exeltis cease any violations of the FD&C Act. Please submit a written response to this letter within 15 working days from the date of receipt, addressing the concerns described in this letter, listing all other promotional communications (with the 2253 submission date) for Slynd that contain representations such as those described above, and explaining any plan for discontinuing use of such communications, or for ceasing distribution of Slynd.

If you believe that your products are not in violation of the FD&C Act, please include in your submission to us your reasoning and any supporting information for our consideration within 15 working days from the date of receipt of this letter.

The concerns discussed in this letter do not necessarily constitute an exhaustive list of potential violations. It is your responsibility to ensure compliance with each applicable requirement of the FD&C Act and FDA implementing regulations.

⁵ Unscheduled bleeding was defined as bleeding or spotting that occurred while taking active hormones (days 2 to 23), except days which were classified as scheduled bleeding days.

Please direct your response to the undersigned at the **Food and Drug Administration, Center for Drug Evaluation and Research, Office of Prescription Drug Promotion, 5901-B Amundson Avenue, Beltsville, Maryland 20705-1266**. A courtesy copy can be sent by facsimile to (301) 847-8444. Please refer to MA 40 in addition to the NDA number in all future correspondence relating to this particular matter. All correspondence should include a subject line that clearly identifies the submission as a Response to Untitled Letter. You are encouraged, but not required, to submit your response in eCTD format. All correspondence submitted in response to this letter should be placed under eCTD Heading 1.15.1.6. Questions related to the submission of your response letter should be emailed to the OPDP RPM at CDER-OPDP-RPM@fda.hhs.gov.

Sincerely,

{See appended electronic signature page}

Elvy Varghese, PharmD.
Regulatory Review Officer
Division of Advertising & Promotion Review 2
Office of Prescription Drug Promotion

James Dvorsky, PharmD., MPH
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This is a representation of an electronic record that was signed electronically. Following this are manifestations of any and all electronic signatures for this electronic record.

/s/

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08/11/2023 11:05:43 AM

JAMES S DVORSKY
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