DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration Silver Spring, MD 20993

Ann Robards
Manager
Eli Lilly and Company
Lilly Corporate Center
Indianapolis, Indiana 46285

RE: BLA 125469
TRULICITY® (dulaglutide) injection, for subcutaneous use
MA 1035

Dear Ms. Ann Robards:

The Office of Prescription Drug Promotion (OPDP) of the U.S. Food and Drug Administration (FDA) has reviewed the promotional communication, a social media post, "Trulicity 2020 Instagram Ad – 10,080 Minutes" (PP-DG-US-3210) for TRULICITY® (dulaglutide) injection, for subcutaneous use (Trulicity) submitted by Eli Lilly and Company (Lilly) under cover of Form FDA 2253. The FDA Bad Ad Program also received a complaint regarding this post[1] and other posts with similar claims and presentations as the ones discussed in this letter. This post makes false or misleading claims and representations about the benefits and risks of Trulicity. Thus, the post misbrands Trulicity within the meaning of the Federal Food, Drug and Cosmetic Act (FD&C Act), making its distribution violative. 21 U.S.C. 352(a), (n); 321(n), 331(a). *See* 21 CFR 202.1 (e)(3)(i); (e)(5); (e)(7)(viii). These violations are especially concerning from a public health perspective because the promotional communication creates a misleading impression regarding the safety and effectiveness of Trulicity, which is a drug with multiple serious, potentially life-threatening risks, including a boxed warning for the risk of thyroid C-cell tumors. Type 2 diabetes mellitus is a significant public health concern that affects millions of adults in the United States and is associated with numerous co-morbidities. Consumers and patients who seek assistance with managing their type 2 diabetes mellitus should receive truthful and non-misleading information regarding the serious risks, and expected benefits associated with the use of a type 2 diabetes prescription drug product, such as Trulicity.

Background

Below are the indication and summary of the most serious and most common risks associated with the use of Trulicity.[2] According to the FDA-approved product labeling (PI)[3]:

TRULICITY® is indicated

[1] Trulicity_us Instagram post, at https://www.instagram.com/p/CDyrU-6Hz0C/ (Last accessed, January 18, 2022)
[2] This information is for background purposes only and does not necessarily represent the risk information that should be included in the promotional piece(s) cited in this letter.
[3] The version of the Trulicity PI referred to in this letter is dated February 2020.

- as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.
- to reduce the risk of major adverse cardiovascular events (cardiovascular death, non-fatal myocardial infarction, or non-fatal stroke) in adults with type 2 diabetes mellitus who have established cardiovascular disease or multiple cardiovascular risk factors.

Limitations of Use

- TRULICITY has not been studied in patients with a history of pancreatitis. Consider other antidiabetic therapies in patients with a history of pancreatitis.
- TRULICITY should not be used in patients with type 1 diabetes mellitus or for the treatment of diabetic ketoacidosis. TRULICITY is not a substitute for insulin.
- TRULICITY has not been studied in patients with severe gastrointestinal disease, including severe gastroparesis. The use of TRULICITY is not recommended in patients with pre-existing severe gastrointestinal disease

The PI for Trulicity contains a boxed warning regarding the risk of thyroid C-cell tumors. Trulicity is contraindicated in patients with a personal or family history of medullary thyroid carcinoma (MTC) or in patients with Multiple Endocrine Neoplasia syndrome type 2 (MEN 2); and in patients with a prior serious hypersensitivity reaction to dulaglutide or to any of the product components. In addition, the PI for Trulicity includes warnings and precautions regarding pancreatitis, hypoglycemia with concomitant use of insulin secretagogues or insulin, hypersensitivity reactions, acute kidney injury, severe gastrointestinal disease, and diabetic retinopathy complications in patients with a history of diabetic retinopathy. The most common adverse reactions reported with Trulicity were nausea, diarrhea, vomiting, abdominal pain, and decreased appetite.

Prior Communications

OPDP notes that our advisory comments dated September 16, 2014, April 6, 2015, January 30, 2018, and February 12, 2019, to Lilly (b) (4) We are concerned that Lilly is promoting Trulicity without presenting the benefits and serious risks of the drug in a truthful and non-misleading manner, despite concerns previously expressed by OPDP.

False or Misleading Benefit Presentation

Prescription drug advertisements and labeling (promotional communications) misbrand a drug if they are false or misleading with respect to benefits. 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 is misleading because the video portion of the post prominently communicates that Trulicity can help "lower A1C along with diet and exercise," but it fails to adequately communicate Trulicity's FDA-approved indication and the limitations of use. Specifically, the "**What is TRULICITY?**" section of the Medication Guide states the following (in pertinent part, underlined emphasis added):

- TRULICITY is an injectable prescription medicine that is used:
    - along with diet and exercise to improve blood sugar (glucose) in <u>adults with type 2 diabetes mellitus.</u>

. . . .

- <u>It is not known if TRULICITY can be used in people who have had pancreatitis.</u>
- <u>TRULICITY is not a substitute for insulin and is not for use in people with type 1 diabetes or people with diabetic ketoacidosis.</u>
- <u>TRULICITY is not recommended for use in people with severe stomach or intestinal problems.</u>

By failing to adequately communicate the indication and limitations of use associated with Trulicity, the post creates a misleading impression about the scope of the FDA-approved indication. This is particularly concerning given the serious risks of this product and the suggestion that Trulicity will help "lower A1C" in all patients, when this has not been demonstrated. OPDP notes that the indication and the limitations of use are presented only in small, fast-paced scrolling font in a small window below the video, relegated to the bottom of the post, competing for the consumer's attention with several distracting video elements (fast-paced visuals, frequent scene changes, busy scenes, large-moving superimposed text, and a strong fast-moving musical beat) that detract from the communication of the indication and limitations of use. Therefore, this presentation does not mitigate the misleading impression created by the post.

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.

Promotional materials are misleading if they fail to present information relating to risks associated with the drug with a prominence and readability reasonably comparable with the presentation of information relating to the benefits of the drug. The post prominently presents benefit claims and representations about Trulicity emphasized by colorful, compelling, and attention-grabbing fast-paced visuals that take up the majority of the post in a video with frequent scene changes, busy scenes, and large-moving superimposed text along with other competing modalities such as the strong, fast-moving musical beat. In contrast, the risk information is in a small window relegated to the bottom of the post and is presented using fast-paced, scrolling, small font that is difficult to read and cannot be adequately processed or comprehended by consumers.

In addition, this presentation fails to include material information from the warning and precaution for hypoglycemia with concomitant use of insulin secretagogues or insulin. Specifically, the "**What are the possible side effects of TRULICITY?**" section of the Medication Guide states the following (in pertinent part; bolded emphasis original; underlined emphasis added):

- **Low blood sugar (hypoglycemia).** Your risk for getting low blood sugar may be higher if you use TRULICITY with another medicine that can cause low blood sugar, such as a sulfonylurea or insulin.

By omitting this material information about this risk, the post creates a misleading impression about the drug's safety.

The overall effect of this presentation undermines the communication of the important risk information and thereby misleadingly minimizes the risks associated with the use of Trulicity. The presentation in the post is especially problematic from a public health perspective given the serious risks associated with the drug.

Conclusion and Requested Action

For the reasons discussed above, the post misbrands Trulicity 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)(3)(i); (e)(5); (e)(7)(viii).

This letter notifies you of our concerns and provides you with an opportunity to address them. OPDP requests that Lilly 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 promotional communications (with the 2253 submission date) for Trulicity that contain representations described above, and explaining any plan for discontinuing use of such communications, or for ceasing distribution of Trulicity. If you believe that your product is 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.

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 Ammendale Road, Beltsville, Maryland 20705-1266**. A courtesy copy can be sent by facsimile to (301) 847-8444. To ensure timely delivery of your submissions, please use the full address above and include a prominent directional notation (e.g., a sticker) to indicate that the submission is intended for OPDP. Please refer to MA 1035 in addition to the BLA 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.

Sincerely,

{See appended electronic signature page}

Samantha Bryant, PharmD, BCPS
Regulatory Review Officer
Division of Advertising & Promotion Review 2
Office of Prescription Drug Promotion

{See appended electronic signature page}

Melinda Wilson, PharmD, MPH, BCPS, RAC
Team Leader
Division of Advertising & Promotion Review 2
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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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