DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Silver Spring, MD 20993

Bhupesh Desai, Ph.D.
Director, Regulatory Affairs Advertising & Promotion
Celgene Corporation
86 Morris Ave, Bldg. I, Office I-308
Summit, NJ, 07901

RE: NDA 205437
OTEZLA® (apremilast) tablets, for oral use
MA 378

Dear Dr. Desai:

The Office of Prescription Drug Promotion (OPDP) of the U.S. Food and Drug Administration (FDA) has reviewed a Direct-to-Consumer broadcast television advertisement (TV ad) entitled "Otezla PsO SHOWING 2.0 TV Spot" (USII-APR150246) for OTEZLA® (apremilast) tablets, for oral use (Otezla) submitted by Celgene Corporation (Celgene) under cover of Form FDA 2253. This TV ad makes false or misleading representations about the risks associated with Otezla. Thus, the TV ad misbrands Otezla within the meaning of the Federal Food, Drug, and Cosmetic Act (FD&C Act), and makes its distribution violative. 21 U.S.C. 352(n); 331(a). 21 CFR 202.1(e)(5). This violation is concerning from a public health perspective because it creates a misleading impression about the safety of Otezla.

Background

Below are the indication and summary of the most serious and most common risks associated with the use of Otezla.[1]

According to the FDA-approved product labeling (PI), Otezla is indicated the treatment of adult patients with active psoriatic arthritis. Otezla is also indicated for the treatment of patients with moderate to severe plaque psoriasis who are candidates for phototherapy or systemic therapy.

Otezla is contraindicated in patients with a known hypersensitivity to apremilast or to any of the excipients in the formulation. Otezla is associated with serious risks. The PI contains warnings and precautions regarding depression, weight decrease and drug interactions. The most common adverse reactions associated with Otezla are diarrhea, nausea, upper respiratory tract infection, and headache, including tension headache.

[1] This information is for background purposes only and does not necessarily represent the risk information that should be included in the promotional piece cited in this letter.

False or Misleading Risk Presentation

Promotional materials misbrand a drug if they are false or misleading with respect to risk.

The TV ad includes the following claims and presentations during the major statement of risks for Otezla:

- A scene of a couple sitting on a park bench playfully bringing their faces together as a dog licks the man's face and the man snaps a selfie along with the SUPER, "YOUR **CLOSE-UP** IS SHOWING" (emphasis original) presented in conjunction with the audio risk disclosure, "Don't take Otezla if you are allergic to any of its ingredients" (Frame 12).

- A scene where a woman is clothes shopping with two girlfriends in which the woman picks out a black dress, and enters a dressing room where she is smiling (Frames 13-15). She then tries on the dress and pulls back the dressing room curtain proudly and smiles again, twirling around to show off the dress to her girlfriends (Frames 16-18) along with the SUPER on Frame 18, "YOUR **CHECK ME OUT** IS SHOWING" (emphasis original). This scene is presented in conjunction with the audio risk disclosure, "Otezla may increase the risk of depression. Tell your doctor if you have a history of depression or suicidal thoughts, or if these feelings develop."

- A scene where a rooftop party is being set up featuring a woman who raises the music volume way up (Frames 19 and 20). The scene then cuts to a guy working on stringing some lights across the rooftop (Frame 21). The scene cuts back again to the woman who grabs her friend's hands and starts dancing with her. The scene cuts again to the man setting up the lights stops what he's doing and reacts to the dancing women with a smile (Frame 22). The woman acknowledges the attention of the man and woman who were hanging the lights as she smiles broadly while continuing to dance (Frames 23-26) along with the SUPER on Frame 26, "YOUR **LIFE OF THE PARTY** IS SHOWING" (emphasis original). This scene is presented in conjunction with the following audio risk disclosures:

  > Some people taking Otezla reported weight loss. Your doctor should monitor your weight and may stop treatment. Side effects may include diarrhea, nausea, upper respiratory tract infection and headache. Tell your doctor about all the medicines you take and if you're pregnant or planning to be.

- Throughout the TV ad, including the major statement, an instrumental version of the song, "Walking on Sunshine" is played in the background. However, during the major statement, a loud brass interjection is played over several audio risk disclosures.

The presentation of these compelling and attention-grabbing visuals and SUPERs, all of which are unrelated to the risk message, in addition to the frequent scene changes and the other competing modalities such as the musical interjections, compete for the consumers' attention. As a result, it is difficult for consumers to adequately process and comprehend the risk information. The overall effect undermines the communication of the important risk

information and thereby misleadingly minimizes the risks associated with the use of Otezla. The presentation in the video 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 TV ad misbrands Otezla within the meaning of the FD&C Act and makes its distribution violative. 21 U.S.C. 352(n); 331(a). 21 CFR 202.1(e)(5).

OPDP requests that Celgene immediately cease violating the FD&C Act, as discussed above. Please submit a written response to this letter on or before December 27, 2016, stating whether you intend to comply with this request, listing all promotional materials (with the 2253 submission date) for Otezla that contain violations such as those described above, and explaining your plan for discontinuing use of such violative materials.

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 378 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. OPDP reminds you that only written communications are considered official.

The violations discussed in this letter do not necessarily constitute an exhaustive list. It is your responsibility to ensure that your promotional materials for Otezla comply with each applicable requirement of the FD&C Act and FDA implementing regulations.

Sincerely,

{See appended electronic signature page}

Silvia Wanis, Pharm.D.
Regulatory Review Officer
Division of Advertising & Promotion Review 2
Office of Prescription Drug Promotion

{See appended electronic signature page}

Matthew J. Falter, Pharm.D.
Team Leader
Division of Advertising & Promotion Review 2
Office of Prescription Drug Promotion

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

SILVIA WANIS
12/12/2016

MATTHEW J FALTER
12/12/2016