DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Silver Spring, MD 20993

Nikki Hill, PharmD
Head of Regulatory Affairs, U.S. Advertising and Promotion
AbbVie, Inc.
1 N. Waukegan Road, Dept. PA95, Bldg. ABV1
North Chicago, IL 60064

RE: BLA 761105; 761262
SKYRIZI® (risankizumab-rzaa) injection, for subcutaneous or intravenous use
MA 2876; 1060

Dear Dr. Hill:

The U.S. Food and Drug Administration (FDA) has reviewed the promotional communication, the "SKYRIZI VS STELARA (ustekinumab)" webpage (webpage)[1] on the Healthcare Provider Branded Website (US-SKZG-241257) (website) for SKYRIZI® (risankizumab-rzaa) injection, for subcutaneous or intravenous use (Skyrizi) submitted by AbbVie, Inc., under cover of Form FDA 2253. FDA has determined that the website is false or misleading. Thus, the website misbrands Skyrizi and makes the distribution of the drug in violation of the Federal Food, Drug, and Cosmetic Act (FD&C Act).

The top of the webpage includes the following prominent headline claim (emphasis original):

- "**SKYRIZI vs STELARA® (ustekinumab)**[;] **SKYRIZI ACHIEVED SUPERIORITY ACROSS SEVERAL RANKED ENDPOINTS IN A HEAD-TO-HEAD STUDY**"

When users scroll down the webpage past the above headline claim, they can view the following claims (emphasis original; in pertinent part):

- "**FIRST APPROVED CROHN'S DISEASE THERAPY THAT MET ENDOSCOPIC SUPERIORITY ENDPOINTS IN A HEAD-TO-HEAD TRIAL**[;] **Skyrizi® risankizumab-rzaa vs STELARA® ustekinumab**"
- **"PRIMARY ENDPOINTS EVALUATED:** . . .
  - Superiority Endpoint: ENDOSCOPIC REMISSION† (SES-CD ≤4) AT WEEK 48‡, Endpoint Met"
- "**~2X MORE PATIENTS ON SKYRIZI DEMONSTRATED ENDOSCOPIC REMISSION VS STELARA AT WEEK 48**"

[1] The "SKYRIZI VS STELARA (ustekinumab)" webpage is accessed from the "SKYRIZI VS STELARA (ustekinumab)" menu item under the "EFFICACY" sub-navigation menu of the website: https://www.skyrizihcp.com/gastroenterology/crohns-disease/efficacy/skyrizi-vs-stelara (last accessed September 8, 2025)

As users continue down the webpage, they can view the additional following claims under different subsections of the section "ENDOSCOPIC DATA" (emphasis original; in pertinent part).

Under the subsection "ENDOSCOPIC RESPONSE":

- "**SUPERIORITY MET ACROSS ENDOSCOPIC OUTCOMES**[;] **Endoscopic Response at Week 24 and Week 48 (Ranked Secondary Endpoints, NRI-MI)**"
- "**MORE PATIENTS ON SKYRIZI EXPERIENCED ENDOSCOPIC RESPONSE VS STELARA AT WEEKS 24 AND 48**"

Under the subsection "ENDOSCOPIC REMISSION":

- "**SUPERIORITY MET ACROSS ENDOSCOPIC OUTCOMES**[;] **Endoscopic Remission at Week 48 (Primary Endpoint, NRI-MI)**"
- "**~2X MORE PATIENTS ON SKYRIZI DEMONSTRATED ENDOSCOPIC REMISSION VS STELARA AT WEEK 48**"

Under the subsection "STEROID-FREE ENDOSCOPIC REMISSION":

- "**SUPERIORITY MET ACROSS ENDOSCOPIC OUTCOMES**[;] **Steroid-Free Endoscopic Remission at Week 48 (Ranked Secondary Endpoint, NRI-MI)**"
- "**~2X MORE PATIENTS ON SKYRIZI WERE IN ENDOSCOPIC REMISSION WITHOUT STEROIDS (STEROID-FREE ENDOSCOPIC REMISSION) VS STELARA AT WEEK 48**"

We also note that data under these subsections, as well as under the sections, "PRIMARY ENDPOINTS" and "CLINICAL REMISSION DATA," are presented in conjunction with claims that Skyrizi "MET SUPERIORITY" and statistically significant p-values.

These claims misleadingly represent that Skyrizi has been shown to be superior to Stelara in the treatment of patients with moderately to severely active Crohn's disease. Specifically, they represent that Skyrizi is superior to Stelara with respect to endoscopic remission at Week 48, endoscopic response at Weeks 24 and 48, steroid-free endoscopic remission at Week 48, and clinical remission at Week 48. However, these conclusions are not supported by the results from the Phase 3b SEQUENCE study[2] and "Data on File"[3] cited in support of the above claims and presentations.

SEQUENCE was a multicenter, open-label study that evaluated the effect of Skyrizi compared to Stelara on two primary endpoints in the treatment of adult patients with moderate to severe Crohn's disease: clinical remission at week 24 and endoscopic remission at week 48. The open-label nature of the SEQUENCE study introduces bias and reduces the internal validity of the study results. First, patients' awareness of their group allocation and prior knowledge about Skyrizi and/or Stelara may have influenced their reporting of clinical

[2] Peyrin-Biroulet L, Chapman JC, Colombel J-F, et al. Risankizumab Versus Ustekinumab for Patients With Moderate to Severe Crohn's Disease: Results From the Phase 3b SEQUENCE Study. Abstract presented at: United European Gastroenterology Week (UEGW 2023); October 14-17, 2023. Abstract LB01.
[3] Data on File. ABVRRTI76928. AbbVie, Inc. 2023.

symptoms and possibly affected endoscopic outcomes as the result of a placebo effect. Second, patients' awareness of their group allocation may have influenced their decision to remain in the study, thereby limiting the interpretability of the results. Specifically, 90.2% (230/255) of patients in the Skyrizi group completed the study compared to 72.8% (193/265) of patients in the Stelara group, creating an imbalance between the study arms in patients completing the study. Additionally, for the primary endpoint of endoscopic remission at Week 48, there were missing assessments for 16% (41/255) of patients in the Skyrizi group compared to 34% (89/265) of patients in the Stelara group. Third, while the central endoscopy reader who interpreted the endoscopy results was blinded to group assignments, the endoscopist performing the procedure (who was, whenever possible, the investigator or sub-investigator) was not blinded to patients' treatment allocation; therefore, bias may have also been introduced during conduct of endoscopy.

For these reasons, SEQUENCE was inadequately designed to support conclusory representations that Skyrizi is superior to Stelara. We acknowledge that the webpage includes the following statement (emphasis original):

- "**DATA LIMITATION: The open-label nature of this study may have influenced these results**"

However, including this statement in Skyrizi promotional communications, along with misleading representations about Skyrizi's efficacy, does not render the promotional communication nonmisleading in light of the issues with SEQUENCE (explained above) that make the study incapable of supporting such conclusions.

Conclusion and Requested Action

For the reasons described above, the website misbrands Skyrizi and makes the distribution of the drug in violation of the Federal Food, Drug, and Cosmetic Act (FD&C Act).

This letter notifies you of our concerns and provides you with an opportunity to address them. FDA requests that AbbVie, Inc. take immediate action to address any violations (including, for example, ceasing and desisting promotional communications that are misleading as described above). 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 Skyrizi that contain representations like those described above, and explaining your plan for the discontinuation of such communications, or for ceasing distribution of Skyrizi.

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.

Please direct your response to 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. Please refer to MA 2876 and MA 1060 in addition to the BLA numbers 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. Additionally, the response submission should be coded as an Amendment to eCTD Sequence 7979 under BLA 761105 and eCTD Sequence 5979 under BLA 761262. 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}

George Tidmarsh, M.D., Ph.D.
Director
Center for Drug Evaluation and Research

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/

CARTER M BEACH
09/09/2025 05:10:20 PM
On behalf of George Tidmarsh, M.D., Ph.D