DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Silver Spring, MD 20993

Kimmy Dovan
Regulatory Ad Promo Manager
Neurocrine Biosciences, Inc
6027 Edgewood Bend Court
San Diego, CA 92130

RE: NDA 209241
INGREZZA® (valbenazine) capsules, for oral use
MA 1086

Dear Kimmy Dovan:

The U.S. Food and Drug Administration (FDA) has reviewed the promotional communication, a direct-to-consumer broadcast advertisement (TV ad), titled "TakING on TD Pool Out 1" (CP-VBZ-US-3838) for INGREZZA® (valbenazine) capsules, for oral use (Ingrezza) submitted by Neurocrine Biosciences, Inc. (Neurocrine) under cover of Form FDA 2253. FDA has determined that the TV ad is false or misleading. Thus, the TV ad misbrands Ingrezza and makes the distribution of the drug in violation of the Federal Food, Drug, and Cosmetic Act (FD&C Act).

The TV ad begins with the protagonists at their respective workplaces showing obvious uncontrollable movements, indicative of tardive dyskinesia (TD). These movements affected their work. The TV ad then has a lengthy post-treatment segment in which the protagonists continue their work without showing involuntary movements that are easily noticed by the viewer. These presentations misleadingly suggest that Ingrezza provides a greater magnitude of benefit in the treatment of TD than has been demonstrated. According to the CLINICAL STUDIES section of the FDA-approved prescribing information (PI), the primary endpoint of the clinical study was the mean change from baseline in the Abnormal Involuntary Movement Scale (AIMS)[1] total score at week 6. The mean AIMS total score in all treatment and placebo groups ranged from 9.8 to 10.4 at baseline. Table 4 in the PI shows that the change from baseline to week 6 in the study was -1.8 relative to placebo for Ingrezza 40 mg and -3.1 for Ingrezza 80 mg (i.e., -1.9 and -3.2 units for the Ingrezza 40 mg and 80 mg arms, respectively, compared with -0.1 units for placebo). Of note, the Ingrezza 40 mg dose was not statistically significantly different from placebo after adjusting for multiplicity. These results do not correlate with the near-complete resolution of symptoms portrayed in the post-treatment portion of the TV ad.

[1] The AIMS is a 12-item clinician-rated scale; items 1 to 7 assess the severity of involuntary movements across body regions, and these items were used in the studies. The AIMS total score (sum of items 1 to 7) can range from 0 to 28, with a score of 0 representing no involuntary movements and 28 representing severe involuntary movements in all body regions assessed.

The TV ad includes the following claims:

- Narrator: "…quickly reducing TD movements by greater than 5 times at 2 weeks."
- Text-graphic: "ReducING TD Movements >5X at 2 WEEKS vs placebo."
- SUPER: "In a 6-week clinical trial, reductions based on average change from baseline to Week 2 on an uncontrollable movement severity scale for INGREZZA (40 mg and 80 mg combined) -1.7 vs placebo -0.3."

These claims misleadingly suggest that patients will experience improvement in TD symptoms earlier than was demonstrated in the clinical trial. As stated previously, the primary endpoint was measured at six weeks. The change from baseline to week 2 was included in the trial as an exploratory endpoint (i.e., hypothesis-generating), therefore, it is not known whether this result represents a false positive finding that occurred by chance alone. Claims that draw conclusions from exploratory endpoints are misleading.

The TV ad includes the following claims:

- Narrator: "98% of people were still satisfied with INGREZZA after 2 years."
- Text-graphic: "Long-LastING Satisfaction >98% still satisfied after 2 YEARS."
- SUPER: "55 of 56 patients in a rollover study of patients taking INGREZZA for 48 weeks after completing long-term KINECT 3 & KINECT 4 studies. Based on Patient Satisfaction Questionnaire [(PSQ)] given to patients at beginning and end of treatment."

This claims misleadingly suggest that almost all patients who take Ingrezza are satisfied with their treatment. However, this does not account for the potential that patients from the long-term KINECT 3 or KINECT 4 study may not enroll in the rollover study if they had an unfavorable response to treatment with Ingrezza. Also, patients who are not satisfied with their treatment during the rollover study may stop taking the drug before the end of the study. Such patients would not complete the PSQ.[2] Therefore, it is misleading to suggest that the PSQ results from this enriched patient population represent the general experience expected in patients who take Ingrezza.

Conclusion and Requested Action

For the reasons described above, the TV ad misbrands Ingrezza and makes the distribution of the drug in violation of the FD&C Act.

This letter notifies you of our concerns and provides you with an opportunity to address them. FDA requests that Neurocrine take immediate action to address any violations (including, for example, ceasing and desisting promotional communications that are misleading as

[2] Lindenmayer J-P, Verghese C, Marder SR, Burke J, Jimenez R, Siegert S, Liang GS, and O'Brien CF (2021). A long-term, open-label study of valbenazine for tardive dyskinesia. CNS Spectrums 26(4), 345–353. https://doi.org/10.1017/S109285292000108X

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 Ingrezza that contain representations like those described above, and explaining your plan for the discontinuation of such communications, or for ceasing distribution of Ingrezza.

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 1086 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. Additionally, the response submission should be coded as an Amendment to eCTD Sequence 5337 under NDA 209241. Questions related to the submission of your response letter should be emailed to 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 05:08:55 PM
On behalf of George Tidmarsh, M.D., Ph.D