DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Silver Spring, MD 20993

Nada Glavan
Senior Director, Regulatory
Eisai Inc.
100 Tice Boulevard
Woodcliff Lake, NJ 07677

RE: NDA 202834; 208277
Fycompa® (perampanel) tablets, for oral use, CIII
Fycompa® (perampanel) oral suspension, CIII
MA 352; MA 78

Dear Ms. Glavan:

The Office of Prescription Drug Promotion (OPDP) of the U.S. Food and Drug Administration (FDA) has become aware of oral statements made by an Eisai Inc. (Eisai) sales representative on (b) (4) in his capacity as an employee of Eisai. According to a report submitted as a part of a complaint to the OPDP Bad Ad Program, the statements were made to healthcare professionals, regarding Fycompa® (perampanel) tablets, for oral use, and oral suspension, CIII (Fycompa). Per the report, the Eisai sales representative made statements that provide evidence that Fycompa is intended for new uses for which it lacks approval, and for which its labeling does not provide adequate directions for use. Thus, this promotional activity misbrands Fycompa in violation of the Federal Food, Drug, and Cosmetic Act (FD&C Act), and makes its distribution violative. 21 U.S.C. 352(f)(1); 331(a); *see* 21 CFR 201.5; 201.100; 201.115; 201.128. These statements are especially concerning from a public health perspective because they misleadingly suggest that Fycompa is safe and effective for (b) (4) In addition, the sales representative's statements are false and misleading because they minimize the serious risks associated with Fycompa, which bears a Boxed Warning due to serious, life-threatening risks, including psychiatric and behavioral reactions, as well as numerous warnings.

Background

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

According to the FDA-approved product labeling (PI)[2], Fycompa is indicated for the treatment of partial-onset seizures (POS) with or without secondarily generalized seizures in patients

[1] This information is for background purposes only and does not necessarily represent the risk information that should be included in the promotional activity cited in this letter.
[2] The version of the Fycompa PI referred to in this letter, dated July 2017, is the one that was approved at the time the promotional activity at issue occurred. However, a new version of the PI was approved on September 27, 2018.

with epilepsy 12 years of age and older, and as adjunctive therapy for the treatment of primary generalized tonic-clonic (PGTC) seizures in patients with epilepsy 12 years of age and older.

The PI for Fycompa contains a Boxed Warning regarding serious psychiatric and behavioral reactions. In addition, the WARNINGS AND PRECAUTIONS section includes risk information regarding: suicidal behavior and ideation; neurologic effects; falls; drug reaction with eosinophilia and systemic symptoms (DRESS)/multiorgan hypersensitivity; and withdrawal of antiepileptic drugs. The most common adverse reactions associated with Fycompa are dizziness, somnolence, fatigue, irritability, falls, nausea, weight gain, vertigo, ataxia, headache, vomiting, contusion, abdominal pain, and anxiety.

Lack of Adequate Directions for Use

On (b) (4), a sales representative from Eisai gave a lunch presentation to the (b) (4) During this presentation, the sales representative stated in word or substance that Eisai had (b) (4) The representative (b) (4) In addition, the sales representative stated that (b) (4)

At the time of the presentation, (b) (4) We acknowledge that FDA approved Fycompa for the treatment of POS with or without secondarily generalized seizures in patients with epilepsy four years of age and older on September 27, 2018. (b) (4) Thus, the labeling (b) (4)

In sum, the sales representative's statements provide evidence that Fycompa is intended for new uses for which it lacks approval, and for which its labeling does not provide adequate directions for use. These claims, which misleadingly suggest that Fycompa is safe and effective for uses for which it is not approved, are especially concerning from a public health perspective (b) (4)

Additionally, during the presentation, the sales representative minimized serious, life-threatening, risks associated with Fycompa. Specifically, while the sales representative acknowledged the Boxed Warning risk of homicidal ideations and aggressive behavior, the representative downplayed these risks by suggesting the healthcare practitioners should not worry about it. Although the members of the audience asked for more information about the serious psychiatric and behavioral reactions, especially the homicidal ideations, the representative further downplayed the risk of Fycompa with anecdotal claims regarding the age of pediatric patients who experienced serious psychiatric and behavioral reactions. To further downplay this risk, the sales representative also noted that other epilepsy centers have this drug on formulary and were not concerned about the Boxed Warning. The presentation minimizes the serious risks associated with Fycompa and misleadingly suggests the drug is safer than has been demonstrated.

Conclusion and Requested Action

For the reasons discussed above, the presentation described above provides evidence that Fycompa is intended for new uses for which it lacks approval, and for which its labeling does not provide adequate directions for use, and minimizes the risks of Fycompa, which renders Fycompa misbranded within the meaning of the FD&C Act and makes its distribution violative. 21 U.S.C. 352(f)(1); 331(a); *see* 21 CFR 201.5; 201.100; 201.115; 201.128.

OPDP requests that Eisai immediately cease violating the FD&C Act, as discussed above. Please submit a written response to this letter on or before October 25, 2018, stating whether you intend to comply with this request, listing all promotional materials (with the 2253 submission date) for Fycompa that contain violations such as those described above, and explaining your plan for discontinuing use of such violative materials. If you believe that your products are not in violation of the FD&C Act, include your reasoning and any supporting information for our consideration.

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 352 and MA 78 in addition to the NDA 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. 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 Fycompa comply with each applicable requirement of the FD&C Act and FDA implementing regulations.

Sincerely,

{See appended electronic signature page}

Dhara Shah, PharmD, RAC
Regulatory Review Officer
Division of Advertising & Promotion Review 1
Office of Prescription Drug Promotion

{See appended electronic signature page}

Aline Moukhtara, RN, MPH
Acting Team Leader
Division of Advertising & Promotion Review 1
Office of Prescription Drug Promotion

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/

DHARA SHAH
10/11/2018

ALINE M MOUKHTARA
10/11/2018