DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Silver Spring, MD 20993

Rebekah Snyder Logan, V.P. of U.S. Regulatory Affairs
Lundbeck Seattle Biopharmaceuticals, Inc.
6 Parkway North, Suite 400
Deerfield, IL 60015

RE: BLA 761119
Vyepti® (eptinezumab-jjmr) injection, for intravenous use
MA 684

Dear Rebekah Snyder Logan:

The U.S. Food and Drug Administration (FDA) has reviewed the promotional communication, the "Efficacy and 2-year patient outcomes" and "Real VYEPTI experience" webpages[1] of the Healthcare Provider Branded Website (EPT-B-101196v4) (webpages) for Vyepti® (eptinezumab-jjmr) injection, for intravenous use (Vyepti) submitted by Lundbeck Seattle Biopharmaceuticals, Inc. (Lundbeck) under cover of Form FDA 2253. FDA has determined that the webpages are false or misleading. Thus, the webpages misbrand Vyepti and make the distribution of the drug in violation of the Federal Food, Drug, and Cosmetic Act (FD&C Act).

The "Efficacy and 2-year patient outcomes" webpage includes claims and presentations based on the results of the PREVAIL trial[2], an open-label, single arm trial, a post-hoc analysis of the PREVAIL trial[3], and a post-hoc analysis of the PROMISE trials[4]. We note several significant limitations to the cited references that preclude the drawing of conclusory claims regarding the benefits of Vyepti.

Specifically, the "Efficacy and 2-year patient outcomes" webpage includes the following claims and presentations (emphasis original):

- "During a 6-month chronic migraine pivotal study, **40%** of patients treated with VYEPTI 300 mg were **100%** migraine free for a month or more vs 22% with

[1] The "Efficacy and 2-year patient outcomes" webpage located at https://www.vyeptihcp.com/efficacy-and-patient-outcomes and "Real VYEPTI experience" webpage located at https://www.vyeptihcp.com/real-vyepti-experience (last accessed June 24, 2026).
[2] Kudrow D, Cady R, Allan B, et al., 2021, Long-term safety and tolerability of eptinezumab in patients with chronic migraine: a 2-year, open-label, phase 3 trial, BMC Neurology, 21(126):1-12.
[3] Blumenfeld A, Ettrup A, Hirman J, et al., 2022, Long-term reductions in disease impact in patients with chronic migraine following preventive treatment with eptinezumab, BMC Neurology, 22(251):1-9.
[4] Winner P, McAllister P, Cady R, et al, 2019, Migraine-free months in patients with episodic or chronic migraine treated with eptinezumab: results from the PROMISE-1 and PROMISE-2 trials, Poster presented at: 61st Annual Scientific Meeting of the American Headache Society (AHS), Philadelphia, PA.

placebo" in conjunction with a prominent graphic of a woman standing in front of a large **100%** image.

- **"Give your patients the chance for 100% migraine freedom for a month or more"**
- "During the same period, 35% of patients treated with VYPETI 100 mg were 100% migraine free for a month or more vs 22% with placebo."

These claims and presentations create the misleading impression that patients treated with Vyepti will be 100% migraine-free for a month or more, when this has not been demonstrated. The webpage cites the post-hoc analysis of the data from PROMISE-1 and PROMISE-2 in support of these claims. However, because these analyses were conducted post hoc and there was no prespecified statistical procedure controlling for type 1 error rate (false positive rate), it is not possible to ascertain whether the findings were attributable to treatment with Vyepti, or merely due to chance. As a result, these findings are exploratory (i.e., hypothesis-generating). Therefore, claims that draw conclusions based on these data suggesting a substantial treatment benefit of "100% migraine freedom" in patients are not supported and are misleading. We acknowledge the statement, "Post hoc analysis" is included as a less prominent footnote for these claims. However, this does not mitigate the misleading impression.

The "Efficacy and 2-year patient outcomes" webpage also includes the following claims and presentations (emphasis original):

- "**Reduce the impact of migraine for your patients**"
- "**Meaningful improvement in migraine severity**"
  - "**Patients on VYEPTI 300 mg experienced SUSTAINED REDUCTION** in average headache **pain severity** over 2 years"
  - A graph depicting the mean change in MIDAS headache pain severity for patients receiving Vyepti 300 mg from week 0 to week 104.
- **">70% of patients on VYEPTI 300 mg reported their migraine symptoms were MUCH IMPROVED or VERY MUCH IMPROVED through 2 years**"
  - A graph depicting the "Reported improvement through 2 years based on PGIC" for patients receiving Vyepti 300 mg from week 0 to week 104
- "**Increase potential for patient productivity and engagement in everyday life**"
- **">60% of patients on VYEPTI 300 mg reported IMPROVEMENT IN MIGRAINE-ASSOCIATED DISABILITY through 2 years**"
  - A graph depicting the percent improvement in MIDAS score for patients receiving Vyepti 300 mg from week 0 to week 104
- "Patients saw improvement in disability from first dose through 2 years, which resulted in more engagement at home, work, and in their social life"

These claims and presentations create a misleading impression that Vyepti has demonstrated a benefit on patient reported outcomes (PROs), such as long-term improvement in migraine severity, migraine-associated disability, and Health Related Quality of Life (HRQoL), when this is not the case. Specifically, while the PROs for migraine severity, migraine-related disability, and HRQoL were included in PREVAIL as outcomes, there was no alpha-allocation to these outcomes. Since there was no alpha-allocation and, therefore, no

specified false positive error rate, these data are considered exploratory (i.e., hypothesis generating) and it is not known whether the outcome data were due to chance. Additionally, because PREVAIL was an open-label, single arm trial, it did not establish that any of the PRO outcomes seen were attributable to the effect of the drug.

Furthermore, PREVAIL collected PRO data utilizing the Headache Impact Test (HIT-6) and the Migraine Disability Assessment (MIDAS). However, the HIT-6 is a questionnaire developed for use in general headache patients and is not specific to migraine headaches; therefore, this tool lacks content validity for the purpose of evaluating outcomes in migraine patients. The HIT-6 also fails to specify a recall period in the instrument instructions, and without a standard recall period, results will yield inconsistent, inaccurate, and unpredictable data. The MIDAS, which measures HRQoL, utilizes a recall period of 3 months, rendering it prone to recall bias and errors related to number of headache days, average severity of headaches, and number of days absent/present at work. This limitation of the MIDAS impacts the interpretability of the results. Lastly, the Patient Global Impression of Change (PGIC) is also prone to recall bias as a patient is expected to compare their current state to a baseline months or years prior. Depending on the length of the recall period, recent events may have a disproportionate influence.

Therefore, due to the limitations and biases described above regarding the PRO data from PREVAIL and, consequently, its associated post-hoc analysis, conclusory claims and presentations based on these data are not supported and are misleading[5].

The "Real VYEPTI experience" webpage includes the following claims and presentations (emphasis original):

- "**~70%** of patients reported increased satisfaction with their ability **TO PLAN, BE PRODUCTIVE, AND PARTICIPATE** in their daily lives"
    - A graph depicting patient satisfaction with impact on elements of daily living after starting Vyepti
- "After starting VYEPTI, patients reported **>2x** THE AMOUNT OF MONTHLY **GOOD DAYS**"
    - A graph depicting the mean number of good days per month before and after starting Vyepti
- "Of the 74 patients who stated they experience brain fog, **86% REPORTED IMPROVEMENT IN BRAIN FOG"**
    - A graph depicting the degree to which brain fog symptoms improved after starting Vyepti

These claims and presentations are presented in conjunction with attention-grabbing, colorful, bold graphics and charts with large font. These claims and presentations create a misleading impression that Vyepti has demonstrated a benefit on PROs such as patient

[5] We note that FDA encourages thoughtful inclusion of patient-reported outcomes in the design and conduct of clinical trials, where appropriate. See, for example, FDA's Guidance for Industry: Patient-Reported Outcome Measures: Use in Medical Product Development to Support Labeling Claims; FDA Patient-Focused Drug Development Guidance Series for Enhancing the Incorporation of the Patient's Voice in Medical Product Development and Regulatory Decision Making; and the Draft Guidance for Industry: Core Patient-Reported Outcomes in Cancer Clinical Trials.

satisfaction with daily living, increased number of “good days,” and improved “brain fog,” when this is not the case. Similar to the discussion above, we note significant limitations to the REVIEW study[6], an observational, single-arm trial, which precludes the drawing of conclusions regarding Vyepti’s benefits related to these PROs. Specifically, this study has inherent selection bias due to the study inclusion criteria. We note that the protocol required patients to have completed ≥ 2 consecutive Vyepti infusion cycles (≥ 6 months exposure) in order to be included in the study. Requiring patients to have successfully completed 2 cycles of Vyepti treatment, in addition to the lack of an active control arm, may have created a favorable bias in the results, as patients who discontinued treatment due to lack of efficacy or adverse events were systematically excluded.

In addition to the above concern, the REVIEW study’s chosen endpoints (i.e., patient satisfaction, “good days,” and “brain fog”) are associated with interpretational limitations and a lack of validity evidence. For example, the clinical meaningfulness of the scale (e.g., higher, much higher, about the same, etc.) used to measure social and functional domains is unclear due to a lack of standardized definitions. “Brain fog” and “good days” also lack standardized definitions and have no objective correlates, which can lead to inconsistencies in how patients perceive and report these symptoms. Additionally, due to the lack of an active control arm, it cannot be established if improvements in these PRO measures are attributable to treatment with Vyepti. It also cannot be established if improvements on any of these PRO outcomes resulted from confounding factors unrelated to the drug’s effectiveness, including patient expectations or socioeconomic variables, rather than true clinical benefit. Furthermore, the REVIEW study required patients to retrospectively recall symptoms from several months before treatment initiation, with some patients recalling experiences from 15 or more months prior, raising concerns about recall bias. Lastly, inconsistent data collection methods across sites created additional variability that was not evaluated in terms of its potential impact on data quality or study outcomes. Therefore, due to these limitations to the REVIEW study, conclusory claims regarding PROs such as patient satisfaction with daily living, increased number of “good days,” and improved “brain fog” are not supported and are misleading.

Conclusion and Requested Action

For the reasons described above, the webpages misbrand Vyepti 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 Lundbeck 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 Vyepti that contain representations like those described above, and explaining your plan for the discontinuation of such communications, or for ceasing distribution of Vyepti.

[6] Argoff C, Herzog SP, Smith RM, Kotak SV, Sopina L, et al., 2024, Real-world effectiveness and satisfaction with intravenous eptinezumab treatment in patients with chronic migraine: REVIEW, an observational, multi-site, US-based study, J Headache Pain, 25:65:1-13.

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 684 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. 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 0807 under BLA 761119. 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}

Taylor Burnett Mmagu, PharmD, RAC
Team Lead
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/

TAYLOR B BURNETT MMAGU
06/24/2026 12:55:00 PM