DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Silver Spring, MD 20993

Malyha Mannan, Director, Regulatory Affairs
Amgen Inc.
One Amgen Center Drive
Thousand Oaks, CA 91320-1799

RE: BLA 761344
IMDELLTRA™ (tarlatamab-dlle) for injection, for intravenous use
MA 54

Dear Malyha Mannan:

The U.S. Food and Drug Administration (FDA) has reviewed the promotional communication, the "ORR" webpage (webpage) on the IMDELLTRA Healthcare Provider Branded Website (USA-757-80287) (website) for IMDELLTRA™ (tarlatamab-dlle) for injection, for intravenous use (Imdelltra), submitted by Amgen Inc., (Amgen) under cover of Form FDA 2253. FDA has determined that the webpage is false or misleading. Thus, the webpage misbrands Imdelltra and makes the distribution of the drug in violation of the Federal Food, Drug, and Cosmetic Act (FD&C Act).

The "ORR" webpage, under the "Clinical Results" sub-navigation menu of the website for Imdelltra, includes a section titled "Efficacy, Depth of response" under which a waterfall plot titled, "Tumor change from baseline with IMDELLTRA®" is presented. The waterfall plot includes different colored bars to illustrate "CR" (complete response), "PR" (partial response), "SD" (stable disease), "PD" (progressive disease), and "NE" (not evaluable). This presentation makes the promotional communication misleading by suggesting that Imdelltra improves "depth of response" in patients with extensive stage small cell lung cancer (ES-SCLC) with disease progression on or after platinum-based chemotherapy for all response types included in the waterfall plot, including SD, when the study from which the presentation is drawn could not demonstrate this. Imdelltra was approved based on an effect shown on overall response rate (ORR) and duration of response endpoints in DeLLphi-301, a single arm trial. In DeLLphi-301, the endpoint of ORR was comprised of PR + CR, as defined by Response Evaluation Criteria in Solid Tumors (RECIST) v 1.1.[1] Because DeLLphi-301 was designed as a single arm trial, the study did not establish that the SD result was attributable to the effect of the drug; for example, the result may instead reflect the natural history of the

[1] Response was measured using the Response Evaluation Criteria in Solid Tumors (RECIST) v 1.1., which defines the evaluation of target lesions as the following: Complete Response (CR): Disappearance of all target lesions. Partial Response (PR): At least a 30% decrease in the sum of diameters of target lesions, taking as reference the baseline sum diameters. Progressive Disease (PD): At least a 20% increase in the sum of diameters of target lesions, taking as reference the smallest sum on study. In addition to the relative increase of 20%, the sum must also demonstrate an absolute increase of at least 5 mm. Stable Disease (SD): Neither sufficient shrinkage to qualify for PR nor sufficient increase to qualify for PD, taking as reference the smallest sum diameters while on study. See: https://ctep.cancer.gov/protocoldevelopment/docs/recist guideline.pdf.

disease. An assessment of delay in time to disease progression in patients treated with Imdelltra (i.e., an assessment of SD) would need to be based on the results of a randomized controlled trial.

In support of these representations, you cite a publication and its supplement by Ahn, M-J et al. (2023), which include results from DeLLphi-301.[2,3] However, it is misleading to include in promotional materials representations or suggestions that rely on a study or studies whose design is not capable of supporting such representations or suggestions. Here, as already noted, since DeLLphi-301 was a *single-arm trial*, it is not known whether the data on SD are attributable to treatment with Imdelltra. Consequently, the presentation of the "depth of response" achieved by patients treated with Imdelltra, which includes SD data, is not supported by the data cited. Your presentation of the SD data as part of the "depth of response" conveys to the audience of the website that the data are relevant to their understanding of the efficacy of Imdelltra notwithstanding the limitations in the study.

We acknowledge the following text appears below the waterfall plot: "Tarlatamab-dlle was studied in a single-arm trial, which did not establish that SD was attributable to the effect of the drug. The results may instead reflect the natural history of the disease. An assessment of delay in time to disease progression in patients treated with tarlatamab-dlle (ie, an assessment of SD) would need to be based on the results of a randomized controlled trial." However, for the reasons discussed above, this promotional communication makes misleading representations or suggestions about the efficacy of Imdelltra through the presentation of SD data that are based on DeLLphi-301, which, as a single-arm trial, is not capable of supporting such representations or suggestions. The disclosures of the study's limitations (noted above) in this promotional communication do not correct or mitigate the misleading representations or suggestions of the presentation.

Conclusion and Requested Action

For the reasons discussed above, the website misbrands Imdelltra within the meaning of the FD&C Act and makes its distribution violative. 21 U.S.C. 352(a), (n); 321(n); 331(a). *See* 21 CFR 202.1(e)(5).

This letter notifies you of our concerns and provides you with an opportunity to address them. FDA requests that Amgen 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 Imdelltra that contain representations like those described above, and explaining your plan for the discontinuation of such communications, or for ceasing distribution of Imdelltra.

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[2] Ahn M-J, et al., 2023, Tarlatamab for Patients with Previously Treated Small-Cell Lung Cancer, New England Journal of Medicine, 389:2063-2075.
[3] Ahn M-J, et al., Tarlatamab for Patients with Previously Treated Small-Cell Lung Cancer, New England Journal of Medicine, 389(suppl):2063-2075.

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 54 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 6054 under BLA 761344. 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 05:13:38 PM
On behalf of George Tidmarsh, M.D., Ph.D