NDA 203441/S-023

SUPPLEMENT APPROVAL

Takeda Pharmaceuticals U.S.A., Inc.
Attention: Ankith Devunapalli
Director
500 Kendall Street
Cambridge, MA 02142

Dear Ankith Devunapalli:

Please refer to your supplemental new drug application (sNDA) dated February 14, 2025, received February 14, 2025, and your amendments, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Gattex (teduglutide) for injection.

This Prior Approval supplemental new drug application provides for proposed modifications to the approved Gattex Risk Evaluation and Mitigation Strategy (REMS). This supplement is in response to our December 17, 2024, REMS Modification Notification letter.

We have completed our review of this supplemental application, as amended. It is approved, effective on the date of this letter.

RISK EVALUATION AND MITIGATION STRATEGY (REMS) REQUIREMENTS

The REMS for Gattex was originally approved on December 21, 2012, and the most recent REMS modification was approved on February 11, 2021. The REMS consists of elements to assure safe use and a timetable for submission of assessments of the REMS.
In order to ensure the benefits of Gattex outweigh its risks, we determined that you were required to make the REMS modifications outlined in our REMS Modification letter dated December 17, 2024.
Your proposed modified REMS, submitted on February 14, 2025, amended and appended to this letter, is approved.

The timetable for submission of assessments of the REMS remains the same as that approved on December 21, 2012.

The revised REMS assessment plan must include, but is not limited to, the following:

For each metric provide the two previous, current, and cumulative reporting periods (if applicable), unless otherwise noted.

Program Outreach and Communication

1. Communication Activities:
    a. Total number of Dear Healthcare Professional letters sent

        i. Total number of Dear Healthcare Professional letters sent to prescribers identified as untrained, stratified by initial outreach, 12-month outreach and 24-month outreach

        ii. Total number of Dear Healthcare Professional letters sent to trained prescribers who have not written a prescription for Gattex within 12 months of completing the REMS training

        iii. Number of mailings returned

        iv. Sources of the recipient lists

Program Implementation and Operations

2. Utilization
    a. A report of the number of Gattex prescriptions dispensed
    b. A report of the number of patients who were dispensed Gattex

3. Healthcare Professional (HCP) Training
    a. Number of HCPs who have been trained (completed the Post-Training Knowledge Assessment Questions)

    b. Number of HCPs who have prescribed Gattex

    c. Number of HCPs who have completed training within the reporting period and prescribed Gattex in the same reporting period

    d. Demographics of HCPs (by specialty type) that completed the Post-Training Knowledge Assessment Questions, to the extent possible

    e. Number and percent of HCPs who completed the Post-Training Knowledge Assessment Questions by method of completion (on-line, fax/mail)

    f. Number of HCPs who completed each knowledge assessment question correctly and the number of HCPs who did not complete each post training knowledge assessment question correctly

    g. Number of HCPs who were retrained provided as a percentage of all HCPs contacted for retraining

h. Number of HCPs identified through specialty pharmacy dispensing data to have a prescription dispensed to a patient when the HCP had not completed the Post-Training Knowledge Assessment Questions.

i. Number of HCPs who did not complete the Post-Training Knowledge Assessment Questions who were contacted and then, who completed the Post-Training Knowledge Assessment Questions

j. The following metrics will be presented in a tabular format:

   i. Number of HCPs who wrote their first prescription for Gattex

   ii. Number of HCPs who were trained at the time their first prescription was written, as a percentage of all HCPs who have written their first prescription

   iii. Number of HCPs who were untrained* at the time their first prescription was written, as a percentage of all HCPs who have written their first prescription

   iv. Number of HCPs whose first prescription was dispensed to a patient

   v. Number of HCPs who were trained at the time their first prescription was dispensed, as a percentage of all HCPs whose first prescription was dispensed

   vi. Number of HCPs who were untrained* at the time their first prescription was dispensed, as a percentage of all HCPs who have written their first prescription

*Untrained=Had not completed the Post-Training Knowledge Assessment Questions

Knowledge

4. Knowledge surveys (to be conducted every two years, with the next knowledge survey to be included with the Assessment Report due in December 2026).

   a. Knowledge surveys of prescribers', patients', and caregivers' understanding of the risks (possible acceleration of neoplastic growth and enhancement of gastric, small intestinal (duodenum, ileum, and jejunum), and colon polyp growth, gastrointestinal obstruction, and biliary and pancreatic disorders) associated with use of Gattex for Short Bowel Syndrome and their understanding of the recommended monitoring during treatment with Gattex.

Health Outcomes and/or Surrogates of Health Outcomes

5. An analysis of the following U.S. adverse events of interest: acceleration of neoplastic growth and enhancement of gastric, small intestinal (duodenum,

ileum, and jejunum), and colon polyp growth, gastrointestinal obstruction, and biliary and pancreatic disorders. Your analysis should include a distribution of cases and should inform any changes to known incidence, severity, and frequency of the risks. As part of your analysis, include the following for the current reporting period and cumulatively (if cumulative data are available):

a. The number of events identified for the risks listed above during the reporting period, stratified by the risk of interest.

b. The source(s) of the findings (e.g., postmarketing adverse event reports, published literature, clinical studies and trials, and solicited reports).

Overall Assessment of REMS Effectiveness

6. The requirements for assessments of an approved REMS under section 505-1(g)(3) include with respect to each goal included in the strategy, an assessment of the extent to which the approved strategy, including each element of the strategy, is meeting the goal or whether one or more such goals or such elements should be modified.

We remind you that in addition to the REMS assessments submitted according to the timetable in the approved REMS, you must include an adequate rationale to support a proposed REMS modification for the addition, modification, or removal of any goal or element of the REMS, as described in section 505-1(g)(4) of the FDCA.

We also remind you that you must submit a REMS assessment when you submit a supplemental application for a new indication for use, as described in section 505-1(g)(2)(A) of the FDCA. This assessment should include:

a) An evaluation of how the benefit-risk profile will or will not change with the new indication;

b) A determination of the implications of a change in the benefit-risk profile for the current REMS;

c) *If the new indication for use introduces unexpected risks*: A description of those risks and an evaluation of whether those risks can be appropriately managed with the currently approved REMS.

d) *If a REMS assessment was submitted in the 18 months prior to submission of the supplemental application for a new indication for use*: A statement about whether the REMS was meeting its goals at the time of that last assessment and if any modifications of the REMS have been proposed since that assessment.

e) *If a REMS assessment has not been submitted in the 18 months prior to submission of the supplemental application for a new indication for use:* Provision of as many of the currently listed assessment plan items as is feasible.

f) *If you propose a REMS modification based on a change in the benefit-risk profile or because of the new indication of use, submit an adequate rationale to support the modification, including*: Provision of the reason(s) why the proposed REMS modification is necessary, the potential effect on the serious risk(s) for which the REMS was required, on patient access to the drug, and/or on the burden on the health care delivery system; and other appropriate evidence or data to support the proposed change. Additionally, include any changes to the assessment plan necessary to assess the proposed modified REMS. *If you are not proposing REMS modifications*, provide a rationale for why the REMS does not need to be modified.

If the assessment instruments and methodology for your REMS assessments are not included in the REMS supporting document, or if you propose changes to the submitted assessment instruments or methodology, you should update the REMS supporting document to include specific assessment instrument and methodology information at least 90 days before the assessments will be conducted. Updates to the REMS supporting document may be included in a new document that references previous REMS supporting document submission(s) for unchanged portions. Alternatively, updates may be made by modifying the complete previous REMS supporting document, with all changes marked and highlighted.

Prominently identify the submission containing the assessment instruments and methodology with the following wording in bold capital letters at the top of the first page of the submission:

> **NDA 203441 REMS ASSESSMENT METHODOLOGY**
> **(**insert concise description of content in bold capital letters, e.g.,
> **ASSESSMENT METHODOLOGY, PROTOCOL, SURVEY METHODOLOGIES, AUDIT PLAN, DRUG USE STUDY)**

An authorized generic drug under this NDA must have an approved REMS prior to marketing. Should you decide to market, sell, or distribute an authorized generic drug under this NDA, contact us to discuss what will be required in the authorized generic drug REMS submission.

We remind you that section 505-1(f)(8) of FDCA prohibits holders of an approved covered application with elements to assure safe use from using any element to block or delay approval of an application under section 505(b)(2) or (j). A violation of this provision in 505-1(f) could result in enforcement action.

Prominently identify any submission containing the REMS assessments or proposed modifications of the REMS with the following wording in bold capital letters at the top of the first page of the submission as appropriate:

NDA 203441 REMS ASSESSMENT

or

NEW SUPPLEMENT FOR NDA 203441/S-000
CHANGES BEING EFFECTED IN 30 DAYS
PROPOSED MINOR REMS MODIFICATION

or

NEW SUPPLEMENT FOR NDA 203441/S-000
PRIOR APPROVAL SUPPLEMENT
PROPOSED MAJOR REMS MODIFICATION

or

NEW SUPPLEMENT FOR NDA 203441/S-000
PRIOR APPROVAL SUPPLEMENT
PROPOSED REMS MODIFICATIONS DUE TO SAFETY LABELING CHANGES SUBMITTED IN SUPPLEMENT XXX

or

NEW SUPPLEMENT (NEW INDICATION FOR USE)
FOR NDA 203441/S-000
REMS ASSESSMENT
PROPOSED REMS MODIFICATION (if included)

Should you choose to submit a REMS revision, prominently identify the submission containing the REMS revisions with the following wording in bold capital letters at the top of the first page of the submission:

REMS REVISIONS FOR NDA 203441

To facilitate review of your submission, we request that you submit your proposed modified REMS and other REMS-related materials in Microsoft Word format. If certain documents, such as enrollment forms, or website screenshots are only in PDF format, they may be submitted as such, but Word format is preferred.

SUBMISSION OF REMS DOCUMENT IN SPL FORMAT

As soon as possible, but no later than 14 days from the date of this letter, submit the REMS document in Structured Product Labeling (SPL) format using the FDA automated drug registration and listing system (eLIST). Content of the REMS document must be identical to the approved REMS document. The SPL will be publicly available.

Information on submitting REMS in SPL format may be found in the guidance for industry *Providing Regulatory Submission in Electronic Format – Content of the Risk Evaluation and Mitigation Strategies Document Using Structured Product Labeling.*

For more information on submitting REMS in SPL format, please email FDAREMSwebsite@fda.hhs.gov.

REPORTING REQUIREMENTS

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

If you have any questions, contact Jacqueline LeeHoffman, Safety Regulatory Project Manager, at (240) 402-8689 or Jacqueline.leehoffman@fda.hhs.gov.

Sincerely,

{See appended electronic signature page}

Joyce Korvick, M.D., M.P.H.
Deputy Director for Safety
Division of Gastroenterology (DG)
Office of Immunology and Inflammation (OII)
Center for Drug Evaluation and Research

ENCLOSURE(S):
- REMS

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/

JACQUELINE D LEEHOFFMAN
08/12/2025 04:19:41 PM

JOYCE A KORVICK
08/13/2025 11:28:09 PM