

NDA 20406-S94  
NDA 21428-S41

## SUPPLEMENT APPROVAL

Takeda Pharmaceuticals U.S.A., Inc.  
Attention: Cristiane Kohiyama  
Associate Director, Global Regulatory Affairs Marketed Products  
95 Hyden Avenue  
Lexington, MA 02421

Dear Ms. Kohiyama:

Please refer to your supplemental new drug application (sNDA) dated December 21, 2021, and your amendments, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Prevacid (lansoprazole) delayed-release capsules and Prevacid SoluTab (lansoprazole) delayed-release orally disintegrating tablets.

We also refer to our letter dated November 22, 2021, notifying you, under Section 505(o)(4) of the FDCA, of new safety information that we believe should be included in the labeling for following risks:

- hypocalcemia and hypokalemia in patients treated with PPIs for at least three months.
- severe cutaneous adverse reactions which includes, acute generalized exanthematous pustulosis (AGEP) and drug reaction with eosinophilia and systemic symptoms (DRESS).
- hyponatremia.

This supplemental new drug application provides for revisions to the labeling for Prevacid. The agreed upon changes to the language included in our November 22, 2021, letter are as follows (additions are noted by underline and deletion are noted by ~~strike~~through).

### 5.8 Hypomagnesemia and Mineral Metabolism

Hypomagnesemia, symptomatic and asymptomatic, has been reported rarely in patients treated with PPIs for at least three months, in most cases after a year of therapy. Serious adverse reactions include tetany, arrhythmias, and seizures. Hypomagnesemia may lead to hypocalcemia and/or hypokalemia and may exacerbate underlying hypocalcemia in at-risk patients. In most patients, treatment of hypomagnesemia required magnesium replacement and discontinuation of the PPI. (b) (4)

(b) (4)

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For patients expected to be on prolonged treatment or who take PPIs with medications such as digoxin or drugs that may cause hypomagnesemia (e.g., diuretics), health care professionals may consider monitoring magnesium levels prior to initiation of PPI treatment and periodically [see Adverse Reactions (6.2)].

Consider monitoring magnesium and calcium levels prior to initiation of PREVACID or PREVACID SoluTab and periodically while on treatment in patients with a preexisting risk of hypocalcemia (e.g., hypoparathyroidism). Supplement with magnesium and/or calcium as necessary. If hypocalcemia is refractory to treatment, consider discontinuing the PPI.

## **APPROVAL & LABELING**

We have completed our review of this application, as amended. It is approved, effective on the date of this letter, for use as recommended in the enclosed agreed-upon labeling with minor editorial revisions listed below and reflected in the enclosed labeling.

- Added “PREVACID SoluTab” in Section 5.4 Severe Cutaneous Adverse Reactions.
- Added “PREVACID or PREVACID SoluTab” in Section 17 Patient Counseling Information to subsection “Severe Cutaneous Adverse Reactions”.
- Added “and/or” in Section 17 to subsection “Hypomagnesemia and Mineral Metabolism” where describing symptoms.

## **CONTENT OF LABELING**

As soon as possible, but no later than 14 days from the date of this letter, submit the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format using the FDA automated drug registration and listing system (eLIST), as described at FDA.gov.<sup>1</sup> Content of labeling must be identical to the enclosed labeling (text for the Prescribing Information, and Medication Guide), with the addition of any labeling changes in pending “Changes Being Effected” (CBE) supplements, as well as annual reportable changes not included in the enclosed labeling.

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<sup>1</sup> <http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm>

Information on submitting SPL files using eList may be found in the guidance for industry *SPL Standard for Content of Labeling Technical Qs and As*.<sup>2</sup>

The SPL will be accessible from publicly available labeling repositories.

Also within 14 days, amend all pending supplemental applications that include labeling changes for this NDA, including CBE supplements for which FDA has not yet issued an action letter, with the content of labeling [21 CFR 314.50(l)(1)(i)] in Microsoft Word format, that includes the changes approved in this supplemental application, as well as annual reportable changes. To facilitate review of your submission(s), provide a highlighted or marked-up copy that shows all changes, as well as a clean Microsoft Word version. The marked-up copy should provide appropriate annotations, including supplement number(s) and annual report date(s).

## **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, call Jay Fajiculay, Pharm.D., Regulatory Project Manager, at (301) 796-9007.

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 (OI)  
Center for Drug Evaluation and Research

### **ENCLOSURE(S):**

- Content of Labeling
  - Prescribing Information
  - Medication Guide
  - Instructions for Use

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<sup>2</sup> We update guidances periodically. For the most recent version of a guidance, check the FDA Guidance Documents Database <https://www.fda.gov/RegulatoryInformation/Guidances/default.htm>.

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**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.**  
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/s/  
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