



NDA 208056/Original 1

**NDA APPROVAL**

Takeda Development Center Americas, Inc.  
Attention: Valerie Tews, RAC  
Manager, Global Regulatory Affairs  
One Takeda Parkway  
Deerfield, IL 60015

Dear Ms. Tews:

Please refer to your New Drug Application (NDA) dated March 26, 2015, received March 26, 2015, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Dexilant SoluTab (dexlansoprazole delayed-release orally disintegrating tablet), 30 mg.

NDA 208056 provides for the use of Dexilant SoluTab (dexlansoprazole delayed-release orally disintegrating tablet), 30 mg for the following indication (b) (4)

- NDA 208056/Original 1 – indicated for adults a) to maintain healing of erosive esophagitis (EE) and relief of heartburn, and b) for the treatment of heartburn associated with symptomatic non-erosive gastroesophageal reflux disease (GERD). (b) (4)

The subject of this action letter is NDA 208056/Original 1. (b) (4)

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 agreed-upon labeling text and with the minor editorial revisions listed below.

### **Prescribing Information**

Highlights, Dosage and Administration

1. Remove bolding from subheading “Recommended Adult Dosage”

Section 5.8 (Warnings and Precautions, Interaction with Methotrexate):

2. Remove vertical line in the left margin

#### Section 7 Drug Interactions, Table 4

3. Underline the antiretrovirals in the “Intervention” row (i.e., Rilpivirine-containing products, Atazanavir, Nelfinavir, Saquinavir, and Other antiretrovirals).

#### Section 8.1 (Use in Specific Populations; Pregnancy, Data, Animal Data)

4. Revise “nine” to “9” (i.e., ...approximately 9 ~~nine~~ times the maximum recommended human dexlansoprazole dose [60 mg/day] based on body surface area...)

#### Section 13.1 (Nonclinical Toxicology; Carcinogenesis, Mutagenesis, Impairment of Fertility)

5. Revise “one” to 1 (i.e., ... about 1 ~~one~~ to 40 times the exposure on a body surface (mg/m<sup>2</sup>) basis of a 50 kg person of average height...)
6. Revise “two” to “2” (i.e., ... lansoprazole doses of 15 to 600 mg/kg/day, 2 ~~two~~ to 80 times the recommended human lansoprazole dose based on BSA.

#### Medication Guide

7. The following was revised for consistency with language used in patient labeling: “DEXILANT is not effective for symptoms of GERD in children under (b) (4) 1 year of age.”
8. The following was revised to allow for patient-friendly language: “If you take too much DEXILANT (b) (4) call your doctor or your poison control center at 1-800-222-1222 right away or go to the nearest hospital emergency room.” The language (b) (4) is only necessary for the Prescribing Information and not for the Medication Guide.
9. The spacing was revised in the text box that contains: “What are the ingredients in DEXILANT capsules and DEXILANT SoluTab?”

#### **WAIVER OF HIGHLIGHTS SECTION**

We are waiving the requirements of 21 CFR 201.57(d)(8) regarding the length of Highlights of prescribing information. This waiver applies to all future supplements containing revised labeling unless we notify you otherwise.

#### **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 <http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm>. Content of labeling must be identical to, except with the revisions listed, the enclosed labeling (text for the prescribing information and Medication Guide). 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*, available at <http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf>.

The SPL will be accessible via publicly available labeling repositories.

### **CARTON AND IMMEDIATE CONTAINER LABELS**

We acknowledge your November 5, 2015, submission containing final printed carton and container labels.

### **REQUIRED PEDIATRIC ASSESSMENTS**

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients, new indications, new dosage forms, new dosing regimens, or new routes of administration are required to contain an assessment of the safety and effectiveness of the product for the claimed indication(s) in pediatric patients unless this requirement is waived, deferred, or inapplicable.

We are waiving the pediatric study requirement for pediatric patients from birth to less than 1 month of age for the indication of maintaining healing of all grades of erosive esophagitis (EE) because the necessary studies are impossible or highly impracticable. This is because the incidence of EE in infants from birth to less than one month of age is low.

We are waiving the pediatric study requirement for pediatric patients less than 12 months of age for the indications of treatment of heartburn associated with symptomatic non-erosive GERD. There is evidence strongly suggesting that the drug would be ineffective in this pediatric age group and that conservative treatment of signs and symptoms associated with non-erosive GERD is the recommended approach.

We are deferring submission of your pediatric studies for ages 1 year to 17 years for treatment of heartburn associated with symptomatic non-erosive GERD and maintaining healing of all grades of erosive esophagitis (EE) for this application because this product is ready for approval for use in adults and the pediatric studies have not been completed.

Your deferred pediatric studies required by section 505B(a) of the FDCA are required postmarketing studies. The status of these postmarketing studies must be reported annually according to 21 CFR 314.81 and section 505B(a)(3)(B) of the FDCA. These required studies are listed below.

- 3091-1 Deferred study under PREA to evaluate the pharmacokinetics of dexlansoprazole, maintenance of healing, and symptoms of endoscopy-proven erosive esophagitis (EE) in patients 1 year to 11 years of age.

Final Protocol Submission:	10/2020
Study Completion:	10/2024
Final Report Submission:	10/2025

3091-2 Deferred study under PREA to evaluate the pharmacokinetics of dexlansoprazole, maintenance of healing, and symptoms of endoscopy-proven erosive esophagitis (EE) in patients 12 years to 17 years of age.

Final Protocol Submission:	10/2016
Study Completion:	10/2018
Final Report Submission:	10/2019

3091-3 Deferred pediatric study under PREA for treating heartburn associated with non-erosive gastroesophageal reflux disease (GERD) in pediatric patients aged 1 year to 11 years.

Final Protocol Submission:	10/2020
Study Completion:	10/2024
Final Report Submission:	10/2025

3091-4 Deferred pediatric study under PREA for treating heartburn associated with non-erosive gastroesophageal reflux disease (GERD) in pediatric patients aged 12 year to 17 years.

Final Protocol Submission:	10/2016
Study Completion:	10/2018
Final Report Submission:	10/2019

3091-5 Deferred study under PREA to evaluate the long-term safety of dexlansoprazole for the maintenance of healing of erosive esophagitis (EE) in pediatric patients 1 month through 11 months of age, who require chronic treatment with dexlansoprazole due to underlying conditions that predispose to chronic gastroesophageal reflux disease (GERD) and relapsing EE.

Final Protocol Submission:	08/2022
Study Completion:	08/2028
Final Report Submission:	02/2029

3091-6 Deferred study under PREA to evaluate the long-term safety of dexlansoprazole for the maintenance of healing of erosive esophagitis (EE) in pediatric patients 1 year through 17 years of age, who require chronic treatment with dexlansoprazole due to underlying conditions that predispose to chronic gastroesophageal reflux disease (GERD) and relapsing EE.

Final Protocol Submission:	08/2022
Study Completion:	08/2028
Final Report Submission:	02/2029

Submit the protocols to your IND 106858, with a cross-reference letter to this NDA.

Reports of these required pediatric postmarketing studies must be submitted as a new drug application (NDA) or as a supplement to your approved NDA with the proposed labeling changes you believe are warranted based on the data derived from these studies. When submitting the reports, please clearly mark your submission "**SUBMISSION OF REQUIRED PEDIATRIC ASSESSMENTS**" in large font, bolded type at the beginning of the cover letter of the submission.

### **PROMOTIONAL MATERIALS**

You may request advisory comments on proposed introductory advertising and promotional labeling. To do so, submit, in triplicate, a cover letter requesting advisory comments, the proposed materials in draft or mock-up form with annotated references, and the package insert to:

OPDP Regulatory Project Manager  
Food and Drug Administration  
Center for Drug Evaluation and Research  
Office of Prescription Drug Promotion  
5901-B Ammendale Road  
Beltsville, MD 20705-1266

Alternatively, you may submit a request for advisory comments electronically in eCTD format. For more information about submitting promotional materials in eCTD format, see the draft Guidance for Industry (available at:

<http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM443702.pdf> ).

As required under 21 CFR 314.81(b)(3)(i), you must submit final promotional materials, and the package insert, at the time of initial dissemination or publication, accompanied by a Form FDA 2253. Form FDA 2253 is available at

<http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM083570.pdf>.

Information and Instructions for completing the form can be found at

<http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM375154.pdf>. For more information about submission of promotional materials to the Office of Prescription Drug Promotion (OPDP), see <http://www.fda.gov/AboutFDA/CentersOffices/CDER/ucm090142.htm>.

### **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 Maureen Dewey, Senior Regulatory Project Manager,  
at (301) 796-0845.

Sincerely,

*{See appended electronic signature page}*

Andrew E. Mulberg, M.D., FAAP, CPI  
Deputy Director  
Division of Gastroenterology and Inborn Errors  
Products  
Office of Drug Evaluation III  
Center for Drug Evaluation and Research

Enclosures:  
Content of Labeling

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**This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.**  
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/s/  
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ANDREW E MULBERG  
01/26/2016