NDA 020505/S-062
NDA 020844/S-053

SUPPLEMENT APPROVAL

Janssen Pharmaceuticals, Inc.
Attention: Tamara Mazza, PhD
Director, Global Regulatory Affairs
1125 Trenton-Harbourton Road
Titusville, NJ 08560

Dear Dr. Mazza:

Please refer to your supplemental new drug applications (sNDAs) dated and received October 26, 2020, and your amendments, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Topamax (topiramate) tablet and sprinkle capsule.

We acknowledge receipt of your major amendment dated July 29, 2021, which extended the goal date by three months.

These Prior Approval sNDAs provide for revisions to the Prescribing Information (PI) and Medication Guide (MG) to reflect safety outcomes from study TOPMATEPY4067 titled, "A Randomized, Active-controlled, Open-label, Flexible-dose Study to Assess the Safety and Tolerability of Topiramate as Monotherapy Compared with Levetiracetam as Monotherapy in Pediatric Subjects with New or Recent-onset Epilepsy," which was conducted to fulfill Postmarketing Requirement (PMR) 1800-1. The revisions to the PI provided for with these sNDAs include revisions in the Warnings and Precautions section [Metabolic Acidosis (5.4); Decrease in Bone Mineral Density (5.9); Negative Effects on Growth (Height and Weight) (5.10); Kidney Stones (5.13)], the Use in Specific Populations section [Pediatric Use (8.4)] and the Patient Counseling Information section (17). Revisions to the MG correspond to the new information in the PI.

APPROVAL & LABELING

We have completed our review of these applications, as amended. They are approved, effective on the date of this letter, for use as recommended in the enclosed agreed-upon labeling.

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.[1] 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.

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*.[2]

The SPL will be accessible from publicly available labeling repositories.

Also within 14 days, amend all pending supplemental applications that include labeling changes for these NDAs, 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 these supplemental applications, 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).

FULFILLMENT OF POSTMARKETING REQUIREMENT

We have received your submission dated October 26, 2020, containing the final report for the following postmarketing requirement listed in the July 15, 2011, approval letter:

1800-1 A one year prospective, randomized, parallel, active-control arm trial to complare the safety of Topamax (topiramate) with regard to metabolic acidosis, renal stone formation, bone mineral density, and development (i.e. height, weight and sexual) with that of an alternate treatment in pediatric patients ages 2 to 15 years.

Final Protocol Submission:	07/2012
Study/Trial Completion:	03/2018
Final Report Submission:	09/2018

[1] http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm
[2] 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.

We have reviewed your submission and conclude that the above requirement has been fulfilled.

We remind you that there is a postmarketing requirement listed in the June 7, 2021, postapproval postmarketing requirement letter that is still open.

PROMOTIONAL MATERIALS

You may request advisory comments on proposed introductory advertising and promotional labeling. For information about submitting promotional materials, see the final guidance for industry *Providing Regulatory Submissions in Electronic and Non-Electronic Format-Promotional Labeling and Advertising Materials for Human Prescription Drugs.*[3]

You must submit final promotional materials and Prescribing Information, accompanied by a Form FDA 2253, at the time of initial dissemination or publication [21 CFR 314.81(b)(3)(i)]. Form FDA 2253 is available at FDA.gov.[4] Information and Instructions for completing the form can be found at FDA.gov.[5]

All promotional materials that include representations about your drug product must be promptly revised to be consistent with the labeling changes approved in this supplement, including any new safety information [21 CFR 314.70(a)(4)]. The revisions in your promotional materials should include prominent disclosure of the important new safety information that appears in the revised labeling. Within 7 days of receipt of this letter, submit your statement of intent to comply with 21 CFR 314.70(a)(4).

REPORTING REQUIREMENTS

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

[3] For the most recent version of a guidance, check the FDA guidance web page at https://www.fda.gov/media/128163/download.
[4] http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM083570.pdf
[5] http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM375154.pdf

If you have any questions, email Alina Walizada, Regulatory Project Manager, at alina.walizada@fda.hhs.gov.

Sincerely,

{See appended electronic signature page}

Alice T.D. Hughes, MD
Deputy Director for Safety
Division of Neurology 2
Office of Neuroscience
Center for Drug Evaluation and Research

ENCLOSURE(S):

- Content of Labeling
  - Prescribing Information
  - Medication Guide

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/

ALICE HUGHES
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