NDA 214679

NDA APPROVAL

Azurity Pharmaceuticals, Inc.
Attention: Michael Beckloff
Chief Development Officer
13160 Foster Street, Suite 190
Overland Park, KS 66213

Dear Mr. Beckloff:

Please refer to your new drug application (NDA) dated and received October 6, 2020, and your amendments, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Eprontia (topiramate) oral solution.

We acknowledge receipt of your major amendment dated May 28, 2021, which extended the goal date by three months.

This NDA provides for the use of Eprontia (topiramate) oral solution for the following:

- Monotherapy Epilepsy: initial monotherapy for the treatment of partial-onset or primary generalized tonic-clonic seizures in patients 2 years of age and older
- Adjunctive Therapy Epilepsy: adjunctive therapy for the treatment of partial-onset seizures, primary generalized tonic-clonic seizures, and seizures associated with Lennox-Gastaut syndrome in patients 2 years of age and older
- Migraine: preventive treatment of migraine in patients 12 years of age and older

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.

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) as well as annual reportable changes not included in the enclosed labeling. Information on submitting SPL files using eLIST

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

may be found in the guidance for industry *SPL Standard for Content of Labeling Technical Qs and As.*[2]

The SPL will be accessible via publicly available labeling repositories.

CARTON AND CONTAINER LABELING

Submit the final printed container label that is identical to the container label submitted on October 29, 2021, as soon as it is available, but no more than 30 days after it is printed. Please submit this label electronically according to the guidance for industry *Providing Regulatory Submissions in Electronic Format — Certain Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications*. For administrative purposes, designate this submission "**Final Printed Container Label for approved NDA 214679**." Approval of this submission by FDA is not required before the labeling is used.

DATING PERIOD

Based on the stability data submitted to date, the expiry dating period for Eprontia (topiramate) oral solution shall be 21 months from the date of manufacture when stored at 20°C – 25°C.

REQUIRED PEDIATRIC ASSESSMENTS

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients (which includes new salts and new fixed combinations), 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 in pediatric patients unless this requirement is waived, deferred, or inapplicable.

We are waiving the pediatric study requirement for partial-onset seizures in children less than 1 month of age because necessary studies are impossible or highly impracticable. This is because of difficulty in diagnostic certainty in this age group and the small number of available patients.

We are waiving the pediatric study requirement for primary generalized tonic-clonic seizures in children less than 2 years of age because necessary studies are impossible or highly impracticable. This is because of difficulty in diagnostic certainty in this age group and the small number of available patients.

[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 are waiving the pediatric study requirement for the preventive treatment of migraine in children 5 years of age and younger because the necessary studies are impossible or highly impracticable. This is because very few children of this age can be definitively diagnosed with migraine and even fewer would be candidates for preventive therapy.

We are deferring submission of your pediatric studies for:

1. Partial-onset seizures in patients 1 month to less than 2 years of age because this formulation is ready for approval and the pediatric studies in this age group have not been completed. The labeled partial-onset seizures indications are the same as the Listed Drug in children 2 years of age and older.

2. The preventive treatment of migraine in patients 6 to less than 12 years of age because this product is ready for approval and the pediatric studies for the preventive treatment of migraine in this age group have not been completed. The labeled preventive treatment of migraine indication is the same as the Listed Drug in children 12 years of age and older.

Your deferred pediatric studies required by section 505B(a) of the Federal Food, Drug, and Cosmetic Act are required postmarketing studies. The status of these postmarketing studies must be reported annually according to 21 CFR 314.81 and section 505B(a)(4)(C) of the Federal Food, Drug, and Cosmetic Act. These required studies are listed below.

4169-1 A randomized, double-blind, placebo-controlled efficacy and safety study under PREA to evaluate topiramate oral solution for the preventive treatment of migraine in children 6 through 11 years of age. This efficacy study must be designed to demonstrate superiority of topiramate oral solution over placebo.

Final Protocol Submission:	03/2022
Study Completion:	06/2025
Final Report Submission:	12/2025

4169-2 A pharmacokinetic analysis to determine the dosing regimen that provides similar drug exposures (at levels demonstrated to be effective in adults with partial-onset seizures) in pediatric patients 1 month to less than 2 years of age and in adult patients. This analysis will require pharmacokinetic data from both the adult and pediatric (1 month to less than 2 years of age) populations.

Final Protocol Submission:	04/2022
Study Completion:	04/2025
Final Report Submission:	10/2025

4169-3 A long-term open-label safety study in pediatric patients 1 month up to 2 years of age maintained at topiramate concentrations demonstrated to be therapeutic for partial-onset seizures for a minimum of 6 months of exposure.

Final Protocol Submission:	04/2022
Study Completion:	04/2025
Final Report Submission:	10/2025

FDA considers the term *final* to mean that the applicant has submitted a protocol, the FDA review team has sent comments to the applicant, and the protocol has been revised as needed to meet the goal of the study or clinical trial.[3]

Submit the protocols to your IND 139533, with a cross-reference letter to this NDA. Reports of these required pediatric postmarketing studies must be submitted as an 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. 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.*[4]

As required under 21 CFR 314.81(b)(3)(i), you must submit final promotional materials, and the Prescribing Information, at the time of initial dissemination or publication, accompanied by a Form FDA 2253. Form FDA 2253 is available at FDA.gov.[5] Information and Instructions for completing the form can be found at FDA.gov.[6]

[3] See the guidance for Industry *Postmarketing Studies and Clinical Trials—Implementation of Section 505(o)(3) of the Federal Food, Drug, and Cosmetic Act (October 2019).* https://www.fda.gov/RegulatoryInformation/Guidances/default.htm.

[4] For the most recent version of a guidance, check the FDA guidance web page at https://www.fda.gov/media/128163/download.

[5] http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM083570.pdf

[6] http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM375154.pdf

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, email Alina Walizada, Regulatory Project Manager, at alina.walizada@fda.hhs.gov.

Sincerely,

{See appended electronic signature page}

Nick Kozauer, MD
Director
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/

NICHOLAS A KOZAUER
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