DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 22416/S-009

SUPPLEMENT APPROVAL
FULFILLMENT OF POSTMARKETING REQUIREMENTS
RELEASE FROM POSTMARKETING REQUIREMENTS

Sunovion Pharmaceutical Inc.
Attention: Kimberly Parthum, Ph.D.
Director, Global Regulatory Affairs
84 Waterford Drive
Marlborough, MA 01752

Dear Dr. Parthum:

Please refer to your Supplemental New Drug Application (sNDA) dated March 13, 2017, and received March 13, 2017, and your amendments, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Aptiom (eslicarbazepine acetate) tablets, 200 mg, 400 mg, 600 mg, and 800 mg.

This Prior Approval supplemental new drug application provides for a change to the indicated patient population for Aptiom used as treatment of partial-onset seizures. Specifically, the indication for Aptiom is being expanded to include pediatric patients 4 years of age and older. In addition, this application provides for a 7 tablet professional sample for the 200 mg strength of Aptiom tablets.

APPROVAL & LABELING

We have completed our review of this supplemental application, as amended. It is approved, effective on the date of this letter, for use as recommended in the enclosed, agreed-upon labeling text.

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 the enclosed labeling (text for the package insert, 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 titled "SPL Standard for Content of Labeling Technical Qs and As" at http://www.fda.gov/downloads/DrugsGuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf.

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 MS Word format, that includes the changes approved in this supplemental application, as well as annual reportable changes and annotate each change. To facilitate review of your submission, 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).

CARTON AND IMMEDIATE CONTAINER LABELS

Submit final printed carton and immediate container labels that are identical to the carton and immediate-container labels submitted on March 13, 2017, as soon as they are available, but no more than 30 days after they are printed. Please submit these labels electronically according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format — Certain Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications (May 2015, Revision 3)*. For administrative purposes, designate this submission "**Final Printed Carton and Container Labels for approved NDA 22416/S-009**." Approval of this submission by FDA is not required before the labeling is used.

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.

Because none of these criteria apply to your application, you are exempt from this requirement.

FULFILLMENT OF POSTMARKETING REQUIREMENTS

We have received your submission dated March 13, 2017, reporting on the following postmarketing requirements listed in our November 8, 2013, approval letter for NDA 22416:

2099-3 A prospective, randomized, controlled, double-blind, efficacy and safety study of eslicarbazepine acetate in children ages 12 years to <18 years for the adjunctive the treatment of partial onset seizures. The primary efficacy endpoint must examine seizure frequency based upon diary data. Safety must be evaluated.

Subgroup analyses of the effect of the concomitant use of enzyme-inducing anticonvulsants (i.e., carbamazepine, phenytoin, phenobarbital or primidone) on the safety and efficacy of eslicarbazepine acetate must be performed.

2099-4 Open-label long term extension study for PMR 2099-#3 (A prospective, randomized, controlled, double- blind, efficacy and safety study of eslicarbazepine acetate in children ages 12 years to <18 years for the adjunctive the treatment of partial onset seizures). Safety must be evaluated. Subgroup analyses of the effect of the concomitant use of enzyme-inducing anticonvulsants (i.e., carbamazepine, phenytoin, phenobarbital or primidone) on the safety of eslicarbazepine acetate must be performed.

2099-5 A prospective, randomized, controlled, double-blind, efficacy and safety study of eslicarbazepine acetate in children ages 2 years to < 12 years for the adjunctive treatment of partial onset seizures. The primary efficacy endpoint during the controlled phase must examine seizure frequency based upon diary data. Safety must be evaluated during the controlled phase. Subgroup analyses of the effect of the concomitant use of enzyme-inducing anticonvulsants (i.e., carbamazepine, phenytoin, phenobarbital or primidone) on the safety and efficacy of eslicarbazepine acetate must be performed.

2099-6 Open-label long term extension study for PMR 2099-5 (A prospective, randomized, controlled, double-blind, efficacy and safety study of eslicarbazepine acetate in children ages 2 years to < 12 years for the adjunctive treatment of partial onset seizures). Safety must be evaluated. Subgroup analyses of the effect of the concomitant use of enzyme-inducing anticonvulsants (i.e., carbamazepine, phenytoin, phenobarbital or primidone) on the safety of eslicarbazepine acetate must be performed.

We have reviewed your submission and have concluded that the above requirements have been fulfilled.

Please note that all of your pediatric assessments required under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c) have not yet been fulfilled. Additional labeling changes may be deferred until results from your required pediatric clinical safety and efficacy studies have been reviewed.

RELEASE FROM POSTMARKETING REQUIREMENTS

We have received your submission dated March 13, 2017, reporting on the following postmarketing requirement listed in our August 27, 2015, approval letter for NDA 22416/S-001:

2951-1 Establish the efficacy and safety of APTIOM when used as monotherapy in the treatment of partial-onset seizures in patients 1 month to <18 years of age. This PMR may be fulfilled by a pharmacokinetic/pharmacodynamic analysis of data collected as part of studies of APTIOM as adjunctive treatment of partial-onset

seizures in adults and pediatric patients, and as monotherapy treatment in adults. However, if the data from adjunctive treatment studies are insufficient to support the efficacy and safety of APTIOM as monotherapy for partial-onset seizures in any or all pediatric age subsets, additional clinical studies may be required.

Final Protocol Submission:	09/2018
Study/Trial Completion:	05/2024
Final Report Submission:	11/2024

2951-2 An open-label, long-term safety study to evaluate the long-term safety of APTIOM when used as monotherapy for partial-onset seizures in patients 1 month to <18 years of age.

Final Protocol Submission:	09/2017
Study/Trial Completion:	09/2025
Final Report Submission:	09/2026

We have reviewed your submission and have determined that you are released from the above requirements as they are no longer needed because we have determined that it is acceptable to extrapolate the efficacy and safety of drugs approved as adjunctive therapy for the treatment of partial onset seizures to their use as monotherapy for the treatment of partial onset seizures in both adult and pediatric patients (b) (4)

(b) (4)

We remind you that there are postmarketing requirements listed in the November 8, 2013, approval letter that are still open.

PROMOTIONAL MATERIALS

You may request advisory comments on proposed introductory advertising and promotional labeling. To do so, submit the following, in triplicate, (1) a cover letter requesting advisory comments, (2) the proposed materials in draft or mock-up form with annotated references, and (3) the package insert(s) to:

OPDP Regulatory Project Manager
Food and Drug Administration
Center for Drug Evaluation and Research
Office of Prescription Drug Promotion (OPDP)
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).

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 LaShawn Dianat, PharmD, Regulatory Project Manager, at (240) 402-7713.

Sincerely,

{See appended electronic signature page}

Billy Dunn, MD
Director
Division of Neurology Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

ENCLOSURE:
Content of Labeling

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

WILLIAM H Dunn
09/13/2017