DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 022117/S-020
022117/S-021

SUPPLEMENT APPROVAL/
FULFILLMENT OF POSTMARKETING COMMITMENT

Forest Laboratories, LLC
Attention: Nadia C. Success
Manager, Regulatory Affairs
Harborside Financial Center, Plaza V
Suite 1900
Jersey City, NJ 07311

Dear Ms. Success:

Please refer to your Supplemental New Drug Applications (sNDAs) dated and received March, 14, 2016 (S-020) and March 18, 2016 (S-021), and your amendments, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Saphris (asenapine) Sublingual Tablets 2.5 mg, 5 mg, and 10 mg.

These Prior Approval supplemental new drug applications propose the following changes:

S-020: Updates to labeling to reflect efficacy and safety results from the following maintenance study in adult patients:

Study P06384: A double-Blind, Placebo-Controlled Trial of Asenapine in the Prevention of Recurrence of a Mood Episode After Stabilization of an Acute Manic/Mixed Episode in Subjects With Bipolar 1 Disorder (Phase 3B)

S-021: Updates to labeling to reflect lower starting dose of 5 mg twice daily in adult patients:

Study P05591: A Phase 3b, Multicenter, Double-Blind, Fixed-Dose, Parallel-Group, Three Week Placebo Controlled Trial Evaluating the Safety and Efficacy of Asenapine in Subjects with Bipolar 1 disorder Experiencing an Acute Manic or Mixed Episode

APPROVAL & LABELING

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

WAIVER OF HIGHLIGHTS SECTION

Please note that we have previously granted a waiver of the requirements of 21 CFR 201.57(d)(8) regarding the length of Highlights of prescribing information.

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), 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).

FULFILLMENT OF POSTMARKETING COMMITMENTS

Additionally, we note that supplemental applications 022117/S-020 and 022117/S-021 contained the final reports for the following postmarketing commitments listed in the August 13, 2009 letter:

1496-5 To conduct an adequate and well-controlled long-term maintenance study to evaluate the efficacy and safety of asenapine in the treatment of adults with acute manic or mixed episodes associated with bipolar I disorder. The maintenance study should be appropriately designed to assess the efficacy of asenapine in preventing all types of mood episodes associated with bipolar disorder (depression, mania, and mixed episodes).

1496-6 It is not apparent from the studies you have conducted in bipolar mania that the lowest effective dose of asenapine has been identified. We request that you further characterize

the utilization of asenapine in the treatment of adults with acute manic or mixed episodes associated with bipolar I disorder with a dose lower than 10 mg twice daily (e.g. 5 mg twice daily) through an adequate and well controlled trial.

We have reviewed your submissions and conclude that the above commitments were fulfilled.

This completes all of your postmarketing requirements and postmarketing commitments acknowledged in our August 13, 2009 approval letter.

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).

You must submit final promotional materials and package insert(s), 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 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, contact Danbi Lee, Regulatory Project Manager, at danbi.lee@fda.hhs.gov.

Sincerely,

{See appended electronic signature page}

Mitchell V. Mathis, MD
Director
Division of Psychiatry 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/

MITCHELL V Mathis
01/13/2017