



ANDA 206107

**ANDA APPROVAL**

Sigmapharm Laboratories, LLC  
3375 Progress Drive  
Bensalem, PA 19020  
Attention: Shilpa Dangeti  
Director, Regulatory Affairs

Dear Madam:

This letter is in reference to your abbreviated new drug application (ANDA) received for review on August 13, 2013, submitted pursuant to section 505(j) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) for Asenapine Sublingual Tablets, 5 mg and 10 mg.

Reference is also made to the complete response letter issued by this office on April 4, 2018, and to any amendments thereafter.

We have completed the review of this ANDA and have concluded that adequate information has been presented to demonstrate that the drug is safe and effective for use as recommended in the submitted labeling. Accordingly, the ANDA is **approved**, effective on the date of this letter. The Office of Bioequivalence has determined your Asenapine Sublingual Tablets, 5 mg and 10 mg, to be bioequivalent and, therefore, therapeutically equivalent to the reference listed drug (RLD), Saphris Sublingual Tablets, 5 mg and 10 mg, of Forest Laboratories, LLC (Forest).

The RLD upon which you have based your ANDA, Forest's Saphris Sublingual Tablets, 5 mg and 10 mg, is subject to periods of patent protection. The following patents and expiration dates (with pediatric exclusivity added) are currently listed in the Agency's publication titled *Approved Drug Products with Therapeutic Equivalence Evaluations* (the "Orange Book"):

<u>U.S. Patent Number</u>	<u>Expiration Date</u>
5,763,476 (the '476 patent)	December 9, 2020
7,741,358 (the '358 patent)	October 6, 2026
8,022,228 (the '228 patent)	October 6, 2026

With respect to the '476 patent insofar as it pertains to U-326 (Method of treating schizophrenia), U-1960 (Use of the atypical antipsychotic asenapine for treatment of schizophrenia in adults), U-1961 (Use of the atypical antipsychotic asenapine for treatment of manic or mixed episodes of bipolar I disorder: acute monotherapy of manic or mixed episodes (ages 10 to adult)), and U-1962 (Use of the atypical antipsychotic asenapine for treatment of manic or mixed episodes of bipolar I disorder: maintenance monotherapy in adults), your ANDA contains statements under section 505(j)(2)(A)(viii) of the FD&C Act that this is a method-of-use patent that does not claim any indication for which you are seeking approval under your ANDA.

With respect to the '358 patent insofar as it pertains to U-1064 (Treatment of schizophrenia), U-1960 (Use of the atypical antipsychotic asenapine for treatment of schizophrenia in adults), U-1961 (Use of the atypical antipsychotic asenapine for treatment of manic or mixed episodes of bipolar I disorder: acute monotherapy of manic or mixed episodes (ages 10 to adult)), and U-1962 (Use of the atypical antipsychotic asenapine for treatment of manic or mixed episodes of bipolar I disorder: maintenance monotherapy in adults), your ANDA contains statements under section 505(j)(2)(A)(viii) of the FD&C Act that this is a method-of-use patent that does not claim any indication for which you are seeking approval under your ANDA.

With respect to: 1) the '476 patent (excluding U-326 (Method of treating schizophrenia), U-1960 (Use of the atypical antipsychotic asenapine for treatment of schizophrenia in adults), U-1961 (Use of the atypical antipsychotic asenapine for treatment of manic or mixed episodes of bipolar I disorder: acute monotherapy of manic or mixed episodes (ages 10 to adult)), and U-1962 (Use of the atypical antipsychotic asenapine for treatment of manic or mixed episodes of bipolar I disorder: maintenance monotherapy in adults)), 2) the '358 patent (excluding U-1064 (Treatment of schizophrenia), U-1960 (Use of the atypical antipsychotic asenapine for treatment of schizophrenia in adults), U-1961 (Use of the atypical antipsychotic asenapine for treatment of manic or mixed episodes of bipolar I disorder: acute monotherapy of manic or mixed episodes (ages 10 to adult)), and U-1962 (Use of the atypical antipsychotic asenapine for treatment of manic or mixed episodes of bipolar I disorder: maintenance monotherapy in adults)), and 3) the '228 patent,<sup>1</sup> your ANDA contains paragraph IV certifications under section 505(j)(2)(A)(vii)(IV) of the FD&C Act stating that the patents are invalid, unenforceable, or will not be infringed by your manufacture, use, or sale of Asenapine Sublingual Tablets, 5 mg and 10 mg, under this ANDA. You have notified the Agency that Sigmapharm Laboratories, LLC (Sigmapharm) complied with the requirements of section 505(j)(2)(B) of the FD&C Act and that litigation was initiated within the statutory 45-day period against Sigmapharm for infringement of the '476 and '358 patents in the United States District Court for the District of Delaware [Forest Laboratories, LLC and Forest Laboratories Holdings, Ltd. v. Sigmapharm Laboratories, LLC, Civil Action No. 14-01119]. You have notified the Agency that litigation with respect to the '358 patent has been dismissed. With respect to the '476 patent, though litigation remains ongoing, the 30-month period identified in section 505(j)(5)(B)(iii) of the FD&C Act, during which FDA was precluded from approving your ANDA, has expired.

With respect to 180-day generic drug exclusivity, we note that Sigmapharm was one of the first ANDA applicants for Asenapine Sublingual Tablets, 5 mg and 10 mg, to submit a substantially complete ANDA with a paragraph IV certification. Therefore, with this approval, Sigmapharm may be eligible for 180 days of shared generic drug exclusivity for Asenapine Sublingual Tablets, 5 mg and 10 mg. The Agency notes that Sigmapharm failed to obtain tentative approval of its ANDA within 30 months after the date on which the ANDA was filed. See section 505(j)(5)(D)(i)(IV) of the FD&C Act (forfeiture of exclusivity for failure to obtain tentative approval). The Agency is not, however, making a formal determination at this time of Sigmapharm's eligibility for 180-day generic drug exclusivity.

At least one first applicant remains eligible for 180-day generic drug exclusivity for Asenapine Sublingual Tablets, 5 mg and 10 mg.<sup>2</sup> This exclusivity, which is provided for under section 505(j)(5)(B)(iv) of the FD&C Act, will begin to run from the date of the commercial marketing by any first applicant, as identified in section 505(j)(5)(B)(iv). Please submit correspondence to this ANDA notifying the Agency within 30 days of the date of the first commercial marketing of this drug product or the RLD. If you do not notify the Agency within 30 days, the date of first

commercial marketing will be deemed to be the date of the drug product's approval. See 21 CFR 314.107(c)(2).

Under section 506A of the FD&C Act, certain changes in the conditions described in this ANDA require an approved supplemental application before the change may be made.

Please note that if FDA requires a Risk Evaluation and Mitigation Strategy (REMS) for a listed drug, an ANDA citing that listed drug also will be required to have a REMS. See section 505-1(i) of the FD&C Act.

### **REPORTING REQUIREMENTS**

Postmarketing reporting requirements for this ANDA are set forth in 21 CFR 314.80-81 and 314.98 and at section 506I of the FD&C Act. The Agency should be advised of any change in the marketing status of this drug or if this drug will not be available for sale after approval. In particular, under section 506I(b) of the FD&C Act, you are required to notify the Agency in writing within 180 days from the date of this letter if this drug will not be available for sale within 180 days from the date of approval. As part of such written notification, you must include (1) the identity of the drug by established name and proprietary name (if any); (2) the ANDA number; (3) the strength of the drug; (4) the date on which the drug will be available for sale, if known; and (5) the reason for not marketing the drug after approval.

### **PROMOTIONAL MATERIALS**

You may request advisory comments on proposed introductory advertising and promotional labeling materials prior to publication or dissemination. Please note that these submissions are voluntary. 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 (PI), Medication Guide, and patient PI (as applicable) 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

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 also 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>.

## **ANNUAL FACILITY FEES**

The Generic Drug User Fee Amendments of 2012 (GDUFA) (Public Law 112-144, Title III) established certain provisions<sup>3</sup> with respect to self-identification of facilities and payment of annual facility fees. Your ANDA identifies at least one facility that is subject to the self-identification requirement and payment of an annual facility fee. Self-identification must occur by June 1<sup>st</sup> of each year for the next fiscal year. Facility fees must be paid each year by the date specified in the *Federal Register* notice announcing facility fee amounts.

All finished dosage forms (FDFs) or active pharmaceutical ingredients (APIs) manufactured in a facility that has not met its obligations to self-identify or to pay fees when they are due will be deemed misbranded. This means that it will be a violation of federal law to ship these products in interstate commerce or to import them into the United States. Such violations can result in prosecution of those responsible, injunctions, or seizures of misbranded products. Products misbranded because of failure to self-identify or pay facility fees are subject to being denied entry into the United States.

## **CONTENT OF LABELING**

As soon as possible, but no later than 14 days from the date of this letter, submit, using the FDA automated drug registration and listing system (eLIST), the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format, as described at <http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm>, that is identical in content to the approved labeling (including the package insert, and any patient package insert and/or Medication Guide that may be required). 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 via publicly available labeling repositories.

Sincerely yours,

*{See appended electronic signature page}*

For Vincent Sansone, Pharm.D.  
Deputy Director  
Office of Regulatory Operations  
Office of Generic Drugs  
Center for Drug Evaluation and Research

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<sup>1</sup> The Agency notes the '228 patent was submitted to the Agency after submission of your ANDA. Litigation, if any, with respect to this patent would not create a statutory stay of approval.

<sup>2</sup> See also draft guidance for industry on *180-Day Exclusivity: Questions and Answers*, Q. 42, at 26 (Jan. 2017).

<sup>3</sup> Some of these provisions were amended by the Generic Drug User Fee Amendments of 2017 (GDUFA II) (Public Law 115-52, Title III).



Sarah  
Kurtz

Digitally signed by Sarah Kurtz

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