



ANDA 206098

**ANDA TENTATIVE APPROVAL**

INC Research, LLC  
U.S. Agent for Alembic Pharmaceuticals Limited  
4800 Falls of Neuse Rd., Suite 600  
Raleigh, NC 27609  
Attention: Shawna Richards

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 tentative approval letters issued by this office on February 12, 2016 and June 8, 2017, and to your amendments received on June 9, 2016, May 5, 2017, May 10, 2017, June 1, 2017, June 21, 2017, and July 6, 2017.

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. 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).

However, we are unable to grant final approval to your ANDA at this time because of the patent issue noted below. Therefore, the ANDA is **tentatively approved**. This determination is based upon information available to the Agency at this time (e.g., information in your ANDA and the status of current good manufacturing practices (cGMPs) of the facilities used in the manufacturing and testing of the drug product). This determination is subject to change on the basis of new information that may come to our attention. This letter does not address issues related to the 180-day exclusivity provisions under section 505(j)(5)(B)(iv) of the FD&C Act.

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 (U-326: Method of treating schizophrenia, U-1960, U-1961, and U-1962 only) and '358 (U-1064: Treatment of schizophrenia, U-1960, U-1961, and U-1962 only) patents, your ANDA contains statements under section 505(j)(2)(A)(viii) of the FD&C Act that these are method of use patents that do not claim any indication for which you are seeking approval under your ANDA.

With respect to the '476 (excluding U-326: Method of treating schizophrenia, U-1960, U-1961, and U-1962), '358 (excluding U-1064: Treatment of schizophrenia, U-1960, U-1961, and U-1962) and '228 patents,<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 Alembic Pharmaceuticals Limited (Alembic) 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 Alembic for infringement of the '476 patent in the United States District Court for the District of Delaware [Forest Laboratories, LLC and Forest Laboratories Holdings, Ltd. v. Alembic Pharmaceuticals Ltd., Alembic Global Holding SA, and Alembic Pharmaceuticals, Inc., Civil Action No. 1:14-cv-01119]. You have also notified the Agency that on June 30, 2017, the court rendered a decision in favor of Forest finding that claims 1, 2, 4, 5, 6, 9, and 10 of the '476 patent are valid. Therefore, according to the final judgment of the court and in accordance with 35 U.S.C. 271(e)(4)(A), the effective date of approval by the FDA of Alembic's ANDA 206098 is to be a date not earlier than the date of expiration of the '476 patent, currently December 9, 2020 (with pediatric exclusivity added).

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.

## **RESUBMISSION**

To request final approval, please submit an amendment titled "FINAL APPROVAL REQUESTED" with enough time to permit FDA review prior to the date you believe that your ANDA will be eligible for final approval. A request for final approval that contains no new data, information, or other changes to the ANDA generally requires a period of 90 days for Agency review. Accordingly, such a request for final approval should be submitted no later than 90 days prior to the date on which you seek approval. A request for final approval that contains substantive changes to this ANDA or changes in the status of the manufacturing and testing facilities' compliance with cGMPs will be classified and reviewed according to OGD policy in effect at the time of receipt. Applicants should review available agency guidance for industry

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<sup>1</sup> The Agency notes that 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.

related to amendments under the generic drug user fee program to determine the duration of Agency review needed to review the changes submitted. The submission of multiple amendments prior to final approval may also result in a delay in the issuance of the final approval letter.

The amendment requesting final approval should provide the legal/regulatory basis for your request for final approval and should include a copy of a court decision, settlement or licensing agreement, or other information described in 21 CFR 314.107, as appropriate. It should also identify changes, if any, in the conditions under which the ANDA was tentatively approved, e.g., updated information such as final-printed labeling, chemistry, manufacturing, and controls data as appropriate. This amendment should be submitted even if none of these changes were made, and it should be designated clearly in your cover letter as a “FINAL APPROVAL REQUESTED.”

In addition to the amendment requested above, the Agency may request, at any time prior to the date of final approval, that you submit an additional amendment containing information as specified by the Agency. Failure to submit either or, if requested, both types of amendments described above may result in a delay in the issuance of the final approval letter.

This drug product may not be marketed without final Agency approval under section 505(j) of the FD&C Act. The introduction or delivery for introduction into interstate commerce of this drug product before the final approval date is prohibited under section 301 of the FD&C Act. Also, until the Agency issues the final approval letter, this drug product will not be deemed approved for marketing under section 505(j) of the FD&C Act, and will not be listed in the Orange Book. Should you believe that there are grounds for issuing the final approval letter prior to December 9, 2020, you should amend your ANDA accordingly.

### **ANNUAL FACILITY FEES**

The Generic Drug User Fee Amendments of 2012 (GDUFA) (Public Law 112-144, Title III) established certain provisions 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.

In addition, we note that GDUFA requires that certain non-manufacturing sites and organizations listed in generic drug submissions comply with the self-identification requirement. The failure of any facility, site, or organization to comply with its obligation to self-identify and/or to pay

fees when due may raise significant concerns about that site or organization and is a factor that may increase the likelihood of a site inspection prior to approval. FDA does not expect to give priority to completion of inspections that are required simply because facilities, sites, or organizations fail to comply with the law requiring self-identification or fee payment.

Additionally, we note that the failure of any facility referenced in the application to self-identify and pay applicable fees means that FDA will not consider the GDUFA application review goal dates to apply to that application.

The Electronic Common Technical Document (eCTD) is CDER's standard format for electronic regulatory submissions. Beginning May 5, 2017, ANDAs must be submitted in eCTD format and beginning May 5, 2018, drug master files must be submitted in eCTD format. Submissions that do not adhere to the requirements stated in the eCTD Guidance will be subject to rejection. For more information please visit: [www.fda.gov/ectd](http://www.fda.gov/ectd).

For further information on the status of this ANDA or upon submitting an amendment to the ANDA, please contact Jasmeet Kaur, Regulatory Project Manager, at (240) 402-2735.

Sincerely yours,

*{See appended electronic signature page}*

For Vincent Sansone, PharmD  
Acting Deputy Director  
Office of Regulatory Operations  
Office of Generic Drugs  
Center for Drug Evaluation and Research



Priya  
Shah

Digitally signed by Priya Shah  
Date: 8/11/2017 10:39:04AM  
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