ANDA 209450

**ANDA TENTATIVE APPROVAL**

Amneal Pharmaceuticals LLC
50 Horseblock Road
Brookhaven, NY 11719
Attention: Candis Edwards
Senior Vice President, Regulatory Affairs

Dear Madam:

This letter is in reference to your abbreviated new drug application (ANDA) received for review on December 28, 2016, submitted pursuant to section 505(j) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) for Lubiprostone Capsules, 8 mcg and 24 mcg.

Reference is also made to the tentative approval letter issued by this office on June 19, 2019, 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 meets the requirements for approval under the FD&C Act. We have determined your Lubiprostone Capsules, 8 mcg and 24 mcg, to be bioequivalent and therapeutically equivalent to the reference listed drug (RLD), Amitiza Capsules, 8 mcg and 24 mcg, of Sucampo Pharma Americas LLC (Sucampo).

However, we are unable to grant final approval to your ANDA at this time because of the exclusivity 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.

The RLD upon which you have based your ANDA, Sucampo's Amitiza Capsules, 8 mcg and 24 mcg, is subject to periods of patent protection. The following patents and expiration dates are currently listed in the Agency's publication titled *Approved Drug Products with Therapeutic Equivalence Evaluations* (the "Orange Book"):

| U.S. Patent Number | Expiration Date |
|---|---|
| 6,982,283 (the '283 patent) | December 4, 2022 (24 mcg strength only) |
| 7,064,148 (the '148 patent) | August 30, 2022 |
| 7,795,312 (the '312 patent) | September 17, 2024 (8 mcg strength only) |
| 8,026,393 (the '393 patent) | October 25, 2027 |
| 8,097,653 (the '653 patent) | November 14, 2022 (24 mcg strength only) |
| 8,338,639 (the '639 patent) | January 23, 2027 |
| 8,389,542 (the '542 patent) | November 14, 2022 (24 mcg strength only) |
| 8,748,481 (the '481 patent) | September 1, 2025 |
| 8,779,187 (the '187 patent) | January 23, 2027 |

With respect to the '312 and '481 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 or other condition of use for which you are seeking approval under your ANDA.

With respect to the '283, '148, '393, '653, '639, '542, and '187 patents, 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 Lubiprostone Capsules, 8 mcg and 24 mcg, under this ANDA. You have notified the Agency that Amneal Pharmaceuticals of New York, LLC (Amneal) complied with the requirements of section 505(j)(2)(B) of the FD&C Act. Litigation was initiated within the statutory 45-day period against Amneal for infringement of the '283, '393, '653, '639, and '542 patents in the United States District Court for the District of New Jersey [Sucampo AG, Sucampo Pharmaceuticals, Inc., Sucampo Pharma, LLC, Takeda Pharmaceutical Company Limited, Takeda Pharmaceuticals USA, Inc., and Takeda Pharmaceuticals America, Inc. v. Amneal Pharmaceuticals LLC, Civil Action No. 17-02577]. You have also notified the Agency that this case was dismissed.

However, we are unable to grant final approval to your ANDA at this time. Prior to the submission of your ANDA, another applicant or applicants submitted a substantially complete ANDA providing for Lubiprostone Capsules, 8 mcg and 24 mcg, and containing a paragraph IV certification. Your ANDA will be eligible for final approval on the date that is 180 days after the commercial marketing date identified in section 505(j)(5)(B)(iv) of the FD&C Act.

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 3 months for Agency review. Accordingly, such a request for final approval should be submitted no later than 3 months 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 related to amendments under the generic drug user fee program to determine the duration of Agency review needed to review the changes submitted. As part of this consideration, applicants should monitor any changes to the RLD that occur after tentative approval, including changes in labeling, patent or exclusivity information, or marketing status. 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.

**ANNUAL FACILITY FEES**

The Generic Drug User Fee Amendments of 2012 (GDUFA) (Public Law 112-144, Title III) established certain provisions[1] 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 1st 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 or active pharmaceutical ingredients 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.

For further information on the status of this ANDA or upon submitting an amendment to the ANDA, please contact Dawn Kimble-Vance, Regulatory Project Manager, at (240) 402-5831.

Sincerely yours,

*{See appended electronic signature page}*

For Edward M. Sherwood
Director
Office of Regulatory Operations
Office of Generic Drugs
Center for Drug Evaluation and Research

[1] Some of these provisions were amended by the Generic Drug User Fee Amendments of 2017 (GDUFA II) (Public Law 115-52, Title III).

Catherine Poole

Digitally signed by Catherine Poole
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