



ANDA 214293

ANDA APPROVAL

Amneal Pharmaceuticals of New York, LLC
50 Horseblock Road
Brookhaven, NY 11719
Attention: Janie M. Gwinn
Senior Director, Regulatory Affairs

Dear Janie M. Gwinn:

This letter is in reference to your abbreviated new drug application (ANDA) received for review on January 6, 2020, submitted pursuant to section 505(j) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) for Estradiol and Progesterone Capsules, 1 mg/100 mg.

Reference is also made to the tentative approval letter issued by this office on November 9, 2021, 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. Accordingly, the ANDA is **approved**, effective on the date of this letter. We have determined your Estradiol and Progesterone Capsules, 1 mg/100 mg, to be bioequivalent and therapeutically equivalent to the reference listed drug (RLD), Bijuva Capsules, 1 mg/100 mg, of TherapeuticsMD, Inc. (TherapeuticsMD).

The RLD upon which you have based your ANDA, TherapeuticsMD's Bijuva Capsules, 1 mg/100 mg, 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>U.S. Patent Number</u>	<u>Expiration Date</u>
8,633,178 (the '178 patent)	November 21, 2032
8,846,648 (the '648 patent)	November 21, 2032
8,846,649 (the '649 patent)	November 21, 2032
8,987,237 (the '237 patent)	November 21, 2032
8,993,548 (the '548 patent)	November 21, 2032

8,993,549 (the '549 patent)	November 21, 2032
9,006,222 (the '222 patent)	November 21, 2032
9,114,145 (the '145 patent)	November 21, 2032
9,114,146 (the '146 patent)	November 21, 2032
9,301,920 (the '920 patent)	November 21, 2032
10,052,386 (the '386 patent)	November 21, 2032
10,206,932 (the '932 patent)	November 21, 2032
10,639,375 (the '375 patent)	November 21, 2032
10,675,288 (the '288 patent)	November 21, 2032
10,806,740 (the '740 patent)	November 21, 2032
11,033,626 (the '626 patent)	November 21, 2032
11,103,513 (the '513 patent)	November 21, 2032
11,103,516 (the '516 patent)	November 21, 2032
11,110,099 (the '099 patent)	November 21, 2032

Your ANDA contains paragraph IV certifications to each of the patents¹, 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 Estradiol and Progesterone Capsules, 1 mg/100 mg, 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 '178, '648, '649, '237, '548, '549, '222, '145, '146, '920, '386, and '932 patents in the United States District Court for the District of New Jersey [TherapeuticsMD, Inc. v. Amneal Pharmaceuticals, Inc., Amneal Pharmaceuticals, LLC, and Amneal Pharmaceuticals of New York, LLC, Civil Action No. 20-05256]. You have also notified the Agency that this case was dismissed.

With respect to 180-day generic drug exclusivity, we note that Amneal was the first ANDA applicant to submit a substantially complete ANDA with a paragraph IV certification for Estradiol and Progesterone Capsules, 1 mg/100 mg. Therefore, with this approval, Amneal is eligible for 180 days of generic drug exclusivity for Estradiol and Progesterone Capsules, 1 mg/100 mg. FDA notes that after issuance of this

approval letter, eligibility for 180-day exclusivity is subject to future events that may result in forfeiture of exclusivity under section 505(j)(5)(D) of the FD&C Act. 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 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: <https://www.fda.gov/media/128163/download>).

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: <https://www.fda.gov/media/73013/download>. Information and Instructions for completing the form can be found at: <https://www.fda.gov/media/132152/download>. For more information about submission of promotional materials to the Office of Prescription Drug Promotion (OPDP), see: <https://www.fda.gov/about-fda/center-drug-evaluation-and-research-cder/opdp-ectd>.

ANNUAL FACILITY FEES

The Generic Drug User Fee Amendments of 2012 (GDUFA) (Public Law 112-144, Title III) established certain provisions² 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.

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: <https://www.fda.gov/media/71211/download>. The SPL will be accessible via publicly available labeling repositories.

We remind you that you must continually monitor available labeling resources such as DRUGS@FDA for changes to your RLD's labels and labeling and make any necessary revisions to your labels and labeling. More information on post-approval labeling changes may be found in the guidance for industry titled "Changes to an Approved NDA or ANDA" at: <https://www.fda.gov/media/71846/download>.

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 The Agency notes that the '375, '288, '740, '626, '513, '516, and '099 patents were submitted to the Agency after submission of your ANDA. Litigation, if any, with respect to these patents would not create a statutory stay of approval.

² 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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