



ANDA 205256

APPROVAL

Amneal Pharmaceuticals
85 Adams Avenue
Hauppauge, NY 11788
Attention: Alpesh Patel
Vice President, Global Regulatory Affairs

Dear Sir:

This is in reference to your abbreviated new drug application (ANDA) dated January 2, 2013, submitted pursuant to section 505(j) of the Federal Food, Drug, and Cosmetic Act (the Act), for Estradiol Vaginal Inserts USP, 10 mcg.

Reference is made to the Complete Response Letter issued by this office on November 19, 2014, and to your amendment dated January 28, 2015.

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 Division of Bioequivalence has determined your Estradiol Vaginal Inserts USP, 10 mcg, to be bioequivalent and, therefore, therapeutically equivalent to the reference listed drug (RLD), Vagifem Tablets of Novo Nordisk Inc. (Novo). Your dissolution testing should be incorporated into the stability and quality control program using the same method proposed in your ANDA.

The RLD upon which you have based your ANDA, Novo's Vagifem Tablets, 10 mcg, is subject to periods of patent protection. As noted in the agency's publication titled Approved Drug Products with Therapeutic Equivalence Evaluations (the "Orange Book"), U.S. Patent Nos. 5,860,946 (the '946 patent) and 7,018,992 (the '992 patent) are scheduled to expire on July 1, 2017, and September 17, 2022, respectively.

Your ANDA contains paragraph IV certifications to each of the patents under section 505(j)(2)(A)(vii)(IV) of the Act stating that the patents are invalid, unenforceable, or will not be infringed by your manufacture, use, or sale of Estradiol Vaginal Inserts USP, 10 mcg, under this ANDA. You have notified the agency that Amneal Pharmaceuticals (Amneal) complied with the requirements of section 505(j)(2)(B) of the Act, and that litigation was initiated against Amneal for infringement of the '992 patent within the statutory 45-day period in the United States District Court for the District of New Jersey [Novo Nordisk Inc. and Novo Nordisk Femcare AG, v. Amneal Pharmaceuticals, LLC and Amneal Pharmaceuticals of New York, LLC, Civil Action No. 3:2013-cv-04915-MAS-DEA]. You have notified the agency that on June 23, 2014, the court dismissed the litigation.

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 Vaginal Inserts USP, 10 mcg. Therefore, with this approval, Amneal is eligible for 180 days of generic drug exclusivity for Estradiol Vaginal Inserts USP, 10 mcg. This exclusivity, which is provided for under section 505(j)(5)(B)(iv) of the 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 informing the agency of the date the exclusivity begins to run.

Under section 506A of the 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 & 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 Act.

Postmarketing reporting requirements for this ANDA are set forth in 21 CFR 314.80-81 and 314.98. The Office of Generic Drugs should be advised of any change in the marketing status of this drug.

Promotional materials may be submitted to FDA for comment prior to publication or dissemination. Please note that these submissions are voluntary. If you desire comments on proposed launch promotional materials with respect to compliance with applicable regulatory requirements, we recommend you submit, in draft or mock-up form, two copies of both the promotional materials and package insert(s) directly to:

Food and Drug Administration
Center for Drug Evaluation and Research
Office of Prescription Drug Promotion
5901-B Ammendale Road
Beltsville, MD 20705

We call your attention to 21 CFR 314.81(b)(3) which requires that all promotional materials be submitted to the Office of Prescription Drug Promotion with a completed Form FDA 2253 at the time of their initial use.

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 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.

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,

For Carol A. Holquist, RPh
Acting Deputy Director
Office of Regulatory Operations
Office of Generic Drugs
Center for Drug Evaluation and Research