



ANDA 202349

APPROVAL

Watson Laboratories, Inc.
311 Bonnie Circle
Corona, CA 92880
Attention: Kelly Delgado
Manager, Regulatory Affairs

Dear Madam:

This is in reference to your abbreviated new drug application (ANDA), submitted pursuant to section 505(j) of the Federal Food, Drug, and Cosmetic Act (FD&C Act), for Estradiol Valerate Tablets, 1 mg and 3 mg, Estradiol Valerate and Dienogest Tablets, 2 mg/2 mg and 2 mg/3 mg.

Reference is also made to the complete response letter issued by this office on August 26, 2014, and to your amendments dated March 27, June 11, September 4, and December 16, 2015; and March 7, 2016.

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 Estradiol Valerate Tablets, 1 mg and 3 mg, Estradiol Valerate and Dienogest Tablets, 2 mg/2 mg and 2 mg/3 mg, to be bioequivalent and, therefore, therapeutically equivalent to the reference listed drug (RLD), Natazia Tablets of Bayer HealthCare Pharmaceuticals Inc. (Bayer). 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, Bayer's Natazia Tablets, 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>
6,133,251 (the '251 patent)	October 25, 2016
6,884,793 (the '793 patent)	October 25, 2016
8,071,577 (the '577 patent)	May 13, 2026
8,153,616 (the '616 patent)	January 30, 2028

With respect to the '251, '793, and '577 patents,¹ your ANDA contains paragraph IV certifications under section 505(j)(2)(A)(vii)(IV) of the FD&C Act stating that each patent is invalid, unenforceable, or will not be infringed by your manufacture, use, or sale of Estradiol Valerate Tablets, 1 mg and 3 mg, Estradiol Valerate and Dienogest Tablets, 2 mg/2 mg and 2 mg/3 mg, under this ANDA. You have notified the agency that Watson Laboratories, Inc. (Watson) complied with the requirements of section 505(j)(2)(B) of the FD&C Act, and that no action for infringement of the '251 and '793 was brought against Watson within the statutory 45-day period. You have also notified the agency that litigation for infringement of the '577 patent was brought against Watson in the United States District Court for the District of Delaware [Bayer Healthcare v. Watson Laboratories, Inc., civil action no. 12-cv-1726] and that this litigation is ongoing.

With respect to the '616 patent, your ANDA contains a statement 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 180-day generic drug exclusivity, we note that Watson was the first ANDA applicant for Estradiol Valerate Tablets, 1 mg and 3 mg, Estradiol Valerate and Dienogest Tablets, 2 mg/2 mg and 2 mg/3 mg, to submit a substantially complete ANDA with a paragraph IV certification. Therefore, with this approval, Watson may be eligible for 180 days of generic drug exclusivity for Estradiol Valerate Tablets, 3 mg and 1 mg, Estradiol Valerate and Dienogest Tablets, 2 mg/2 mg and 2 mg/3 mg. This exclusivity, which is provided for under section 505(j)(5)(B)(iv) of the FD&C Act, would begin to run from the date of the commercial marketing identified in section 505(j)(5)(B)(iv). The agency notes that Watson failed to obtain tentative approval of this ANDA within 36² 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 Watson's eligibility for 180-day generic drug exclusivity. It will do so only if a subsequent paragraph IV applicant becomes eligible for full approval (a) within 180 days after Watson begins commercial marketing of Estradiol Valerate Tablets, 1mg and 3 mg, Estradiol Valerate and Dienogest Tablets, 2 mg/2 mg and 2 mg/3 mg, or (b) at any time prior to the expiration of

¹ The agency notes that the '577 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.

² For applications submitted between January 9, 2010, and July 9, 2012 containing a paragraph IV certification (or amended to first contain a paragraph IV certification during that period of time), and approved or tentatively approved during the period of time beginning on July 9, 2012, and ending on September 30, 2015, section 1133 of the Food and Drug Administration Safety and Innovation Act (FDASIA) (P.L. 112-144) extends this period to 40 months. For applications submitted between January 9, 2010, and July 9, 2012 (or amended to first contain a paragraph IV certification during that period of time), and approved or tentatively approved during the period of time beginning on October 1, 2015, and ending on September 30, 2016, section 1133 of FDASIA extends this period to 36 months. In addition, if an application was submitted between January 9, 2010, and July 9, 2012 containing a Paragraph IV certification (or amended to first contain a paragraph IV certification during that period of time), and FDA has not approved or tentatively approved the application but must consider whether the applicant has forfeited exclusivity because a potentially blocked application is ready for approval, FDA will apply the 36-month period if it makes the forfeiture determination between the period of time beginning on October 1, 2015, and ending on September 30, 2016. For all other applications, the 30-month period set forth in FD&C Act section 505(j)(5)(D)(i)(IV) applies.

the '251 and '793 patents if Watson has not begun commercial marketing. Please submit correspondence to this ANDA informing the agency of the date commercial marketing begins.

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 & 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.

Post-marketing 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,

William P.

Rickman -S

For Carol A. Holquist, RPh

Acting Deputy Director

Office of Regulatory Operations

Office of Generic Drugs

Center for Drug Evaluation and Research

Digitally signed by William P. Rickman -S
DN: c=US, o=U.S. Government, ou=HHS,
ou=FDA, ou=People,
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cn=William P. Rickman -S
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