ANDA 214137

ANDA APPROVAL

Teva Pharmaceuticals USA, Inc.
Attention: Bernard Domnic
Director, Regulatory Affairs, US Generics

Dear Bernard Domnic:

This letter is in reference to your abbreviated new drug application (ANDA) received for review on December 30, 2019, submitted pursuant to section 505(j) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) for Estradiol Vaginal Inserts, 4 mcg and 10 mcg.

Reference is also made to the complete response letter issued by this office on October 29, 2020, 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 Vaginal Inserts, 4 mcg and 10 mcg to be bioequivalent and therapeutically equivalent to the reference listed drug (RLD), Imvexxy Vaginal Inserts, 4 mcg and 10 mcg, of Mayne Pharma LLC (Mayne) NDA 208564.

The RLD upon which you have based your ANDA, Mayne's Imvexxy Vaginal Inserts, 4 mcg and 10 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
9,180,091 (the '091 patent)	November 21, 2032
9,289,382 (the '382 patent)	November 21, 2032
10,258,630 (the '630 patent)	November 21, 2032
10,398,708 (the '708 patent)	November 21, 2032
10,471,072 (the '072 patent)	November 21, 2032

10,537,581 (the '581 patent)	November 21, 2032
10,568,891 (the '891 patent)	November 21, 2032
10,668,082 (the '082 patent)	November 21, 2032
10,806,697 (the '697 patent)	November 21, 2032
10,835,487 (the '487 patent)	November 21, 2032
10,888,516 (the '516 patent)	November 21, 2032
11,065,197 (the '197 patent)	November 21, 2032
11,116,717 (the '717 patent)	November 21, 2032
11,123,283 (the '283 patent)	November 21, 2032
11,241,445 (the '445 patent)	November 21, 2032
11,246,875 (the '875 patent)	November 21, 2032
11,266,661 (the '661 patent)	February 2, 2034
11,304,959 (the '959 patent)	November 21, 2032
11,351,182 (the '182 patent)	November 21, 2032
11,497,709 (the ‘709 patent)	November 21, 2032 (10 mcg strength only)

Your ANDA contains paragraph IV certifications to each of the patents 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 Vaginal Inserts, 4 mcg and 10 mcg, under this ANDA. You have notified the Agency that Teva Pharmaceuticals USA, Inc. (Teva) 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 Teva for infringement of the '091, '382, '630, '708, and '072, patents in the United States District Court for the District of New Jersey [TherapeuticsMD, Inc. v. Teva Pharmaceuticals USA, Inc. and Teva Pharmaceutical Industries Limited, Civil Action No. 20-03485]. Although this litigation remains ongoing, the 30-month period identified in section 505(j)(5)(B)(iii) of the FD&C Act, during which FDA was precluded from approving your ANDA, has expired.

With respect to 180-day generic drug exclusivity, we note Teva was a first ANDA applicant for Estradiol Vaginal Inserts, 4 mcg and 10 mcg, to submit a substantially complete ANDA with a paragraph IV certification. Therefore, with this approval, Teva

may be eligible for 180 days of generic drug exclusivity for Estradiol Vaginal Inserts, 4 mcg and 10 mcg. This exclusivity, which is provided for under 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 Teva failed to obtain tentative approval of this ANDA within 30 months after the date of 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 Teva's eligibility for 180-day generic drug exclusivity. We will do so only if a subsequent paragraph IV applicant becomes eligible for full approval (a) within 180 days after Teva begins commercial marketing of Estradiol Vaginal Inserts, 4 mcg and 10 mcg, or (b) at any time prior to the expiration of the '091, '382, '630, '708, and '072 patents if Teva has not begun commercial marketing. 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).

Please note that if FDA requires a Risk Evaluation and Mitigation Strategy (REMS) for a listed drug, an ANDA referencing that listed drug also will be required to have a REMS. See section 505-1(i) of the FD&C Act.

COMPENDIAL STANDARDS

A drug with a name recognized in the official United States Pharmacopeia or official National Formulary (USP-NF) generally must comply with the compendial standard for strength, quality, and purity, unless the difference in strength, quality, or purity is plainly stated on its label (see FD&C Act § 501(b), 21 USC 351(b)). FDA typically cannot share application-specific information contained in submitted regulatory filings with third parties, which includes USP-NF. To help ensure that a drug continues to comply with compendial standards, application holders may work directly with USP-NF to revise official USP monographs. More information on the USP-NF is available on USP's website as https://www.uspnf.com/.

REQUIREMENTS AND RECOMMENDATIONS POST APPROVAL

Under applicable statutes, regulations, and guidances, your ANDA may be subject to certain requirements and recommendations post approval, including requirements regarding changes to approved ANDAs, postmarketing reporting, promotional materials, and annual facility fees, among others.

For information on post-approval requirements and recommendations for ANDAs and a list of resources for ANDA holders, we refer you to https://www.fda.gov/drugs/abbreviated-new-drug-application-anda/requirements-and-resources-approved-andas.

Sincerely yours,

{See appended electronic signature page}

For Kendra S. Stewart, R.Ph., Pharm.D.
CAPT, United States Public Health Service
Director
Office of Regulatory Operations
Office of Generic Drugs
Center for Drug Evaluation and Research

Sarah Kurtz

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