ANDA 214348

ANDA APPROVAL

eVenus Pharmaceutical Laboratories, Inc.
U.S. Agent for Jiangsu Hengrui Pharmaceuticals Co., Ltd
506 Carnegie Center, Suite 100
Princeton, NJ 08540
Attention: Junna Xin
Associate Director of RA

Dear Junna Xin:

This letter is in reference to your abbreviated new drug application (ANDA) received for review on August 20, 2021, submitted pursuant to section 505(j) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) for Bupivacaine Liposome Injectable Suspension, 1.3% [133 mg/10 mL (13.3 mg/mL)] and 1.3% [266 mg/20 mL (13.3 mg/mL)] Single-Dose Vials.

Reference is also made to the complete response letter issued by this office on February 12, 2024, 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 Bupivacaine Liposome Injectable Suspension, 1.3% [133 mg/10 mL (13.3 mg/mL)] and 1.3% [266 mg/20 mL (13.3 mg/mL)] Single-Dose Vials to be bioequivalent and therapeutically equivalent to the reference listed drug (RLD), Exparel Liposome Injectable Suspension, 1.3% [133 mg/10 mL (13.3 mg/mL)] and 1.3% [266 mg/20 mL (13.3 mg/mL)], of Pacira Pharmaceuticals, Inc. (Pacira).

Reference is also made to FDA's Competitive Generic Therapy Designation – Grant letter dated January 27, 2020.

The RLD upon which you have based your ANDA, Pacira's Exparel Liposome Injectable Suspension, 1.3% [133 mg/10 mL (13.3 mg/mL)] and 1.3% [266 mg/20 mL (13.3 mg/mL)], 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
11,033,495 (the '495 patent)	January 22, 2041
11,179,336 (the '336 patent)	January 22, 2041
11,278,494 (the '494 patent)	January 22, 2041
11,304,904 (the '904 patent)	January 22, 2041
11,311,486 (the '486 patent)	January 22, 2041
11,357,727 (the '727 patent)	January 22, 2041
11,426,348 (the '348 patent)	January 22, 2041
11,452,691 (the '691 patent)	January 22, 2041
11,819,574 (the '574 patent)	January 22, 2041
11,819,575 (the '575 patent)	January 22, 2041
11,918,565 (the '565 patent)	February 2, 2043
11,925,706 (the '706 patent)	January 22, 2041
11,931,459 (the '459 patent)	March 17, 2042

Your ANDA contains paragraph IV certifications to the '495, '336, '494, '904, '486, '727, '348, '691, '574, '575, and '706 patents[1] 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 Bupivacaine Liposome Injectable Suspension, 1.3% [133 mg/10 mL (13.3 mg/mL)] and 1.3% [266 mg/20 mL (13.3 mg/mL)] Single-Dose Vials, under this ANDA. You have notified the Agency that Jiangsu Hengrui Pharmaceuticals Co., Ltd (Jiangsu) complied with the requirements of section 505(j)(2)(B) of the FD&C Act. With respect to the 1.3% [266 mg/20 mL (13.3 mg/mL)] strength, litigation was initiated within the statutory 45-day period against Jiangsu for infringement of the '495 patent in the United States District Court for the District of New Jersey [Pacira Pharmaceuticals, Inc., and Pacira Biosciences, Inc. v. eVenus Pharmaceuticals Laboratories Inc., and Jiangsu Hengrui Pharmaceuticals Co. Ltd., a Chinese Pharmaceutical Co., Civil Action No. 21-19829]. With respect to the 1.3 % [133 mg/10 mL (13.3 mg/mL)] strength, litigation was initiated within the statutory 45-day period against Jiangsu for infringement of the '495 and '336 patents in the United States District Court for the District of New Jersey [Pacira Pharmaceuticals, Inc., and Pacira Biosciences, Inc. v. eVenus Pharmaceuticals Laboratories Inc., and Jiangsu

Hengrui Pharmaceuticals Co. Ltd., a Chinese Pharmaceutical, Civil Action No. 22-00718]. Although the litigation remains ongoing, the 30-month periods identified in section 505(j)(5)(B)(iii) of the FD&C Act, during which FDA was precluded from approving your ANDA, have expired.

With respect to the '565 and '459 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 conditions of use for which you are seeking approval under your ANDA.

With respect to 180-day generic drug exclusivity, we note that Jiangsu was a first ANDA applicant for Bupivacaine Liposome Injectable Suspension, 1.3% [133 mg/10 mL (13.3 mg/mL)] and 1.3% [266 mg/20 mL (13.3 mg/mL)] Single-Dose Vials, to submit a substantially complete ANDA with a paragraph IV certification. Therefore, with this approval, Jiangsu may be eligible for 180 days of generic drug exclusivity for Bupivacaine Liposome Injectable Suspension, 1.3% [133 mg/10 mL (13.3 mg/mL)] and 1.3% [266 mg/20 mL (13.3 mg/mL)] Single-Dose Vials. 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 Jiangsu failed to obtain tentative approval of its ANDA within 30 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 Jiangsu'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 Jiangsu begins commercial marketing of Bupivacaine Liposome Injectable Suspension, 1.3% [133 mg/10 mL (13.3 mg/mL)] and 1.3% [266 mg/20 mL (13.3 mg/mL)] Single-Dose Vials, or (b) at any time prior to the expiration of the '336 and '495 patents (with respect to both the 1.3% [133 mg/10 mL (13.3 mg/mL)] and 1.3% [266 mg/20 mL (13.3 mg/mL)] strengths) if Jiangsu 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).

We note that Jiangsu Hengrui Pharmaceuticals Co., Ltd (Jiangsu) was granted a Competitive Generic Therapy (CGT) designation for Bupivacaine Liposome Injectable Suspension, 1.3% [133 mg/10 mL (13.3 mg/mL)] and 1.3% [266 mg/20 mL (13.3 mg/mL)] Single-Dose Vials. However, as noted in the January 27, 2020, CGT Designation – Grant Letter, your drug products are not eligible for CGT exclusivity under section 505(j)(5)(B)(v) of the FD&C Act because there were unexpired patents or exclusivities listed in FDA's *Approved Drug Products with Therapeutic Equivalence Evaluations* (Orange Book) for the RLD at the time of submission of your ANDA.

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

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[1]With respect to the 1.3% [133 mg/10 mL (13.3 mg/mL)] strength, the Agency notes that the '494, '904, '486, '727, '348, '691, '574, '575, and '706 patents were submitted to the Agency after submission of your ANDA. With respect to the 1.3% [266 mg/20 mL (13.3 mg/mL)] strength, the Agency notes that the '336, '494, '904, '486, '727, '348, '691, '574, '575, and '706 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.

Catherine Poole

Digitally signed by Catherine Poole
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