ANDA 213605

ANDA APPROVAL

Freyr Inc.
U.S. Agent for Crystal Pharmaceutical (Suzhou) Co., Ltd.
150 College Road West, Suite 102
Princeton, NJ 08540
Attention: Chandrika Lucki
Manager

Dear Chandrika Lucki:

This letter is in reference to your abbreviated new drug application (ANDA) received for review on July 8, 2019, submitted pursuant to section 505(j) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) for Sacubitril and Valsartan Tablets, 24 mg/26 mg, 49 mg/51 mg, and 97 mg/103 mg.

Reference is also made to the complete response letter issued by this office on December 28, 2022, 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 Sacubitril and Valsartan Tablets, 24 mg/26 mg, 49 mg/51 mg, and 97 mg/103 mg to be bioequivalent and therapeutically equivalent to the reference listed drug (RLD), Entresto Tablets, 24 mg/26 mg, 49 mg/51 mg, and 97 mg/103 mg, of Novartis Pharmaceuticals Corporation (Novartis).

The RLD upon which you have based your ANDA, Novartis ’s Entresto Tablets, 24 mg/26 mg, 49 mg/51 mg and 97 mg/103 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.S. Patent Number	Expiration Date
8,101,659 (the '659 patent)	July 15, 2025*
8,877,938 (the '938 patent)	November 27, 2027*
9,388,134 (the '134 patent)	May 8, 2027*

9,517,226 (the '226 patent)	August 22, 2033
9,937,143 (the '143 patent)	August 22, 2033
11,058,667 (the '667 patent)	May 9, 2036
11,135,192 (the '192 patent)	August 22, 2033

* with pediatric exclusivity added

Your ANDA contains paragraph IV certifications to each of the 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 Sacubitril and Valsartan Tablets, 24 mg/26 mg, 49 mg/51 mg, and 97 mg/103 mg, under this ANDA. You have notified the Agency that Crystal Pharmaceutical (Suzhou) Co., Ltd. (Crystal) 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 Crystal for infringement of the '659, '938, and '134 patents in the United States District Court for the District of Delaware [Novartis Pharmaceuticals Corporation v. Alkem Laboratories Ltd., S&B Pharma, Inc., Aurobindo Pharma USA Inc., Aurobindo Pharma Ltd., Biocon Pharma Limited, Biocon Limited, Biocon Pharma, Inc., Crystal Pharmaceutical (Suzhou) Co., Ltd., Laurus Labs Limited, Laurus Generics Inc., Lupin Atlantis Holdings, S.A., Lupin Limited, Lupin Inc., Lupin Pharmaceuticals, Inc., Nanjing Noratech Pharmaceutical Co., Limited, Teva Pharmaceuticals USA, Inc., Teva Pharmaceutical Industries Ltd., Torrent Pharma Inc., Torrent Pharmaceuticals Ltd., Civil Action No. 19-01979]. Although this litigation remains ongoing, the 8 year 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 that Crystal was a first ANDA applicant for Sacubitril and Valsartan Tablets, 24 mg/26 mg, 49 mg/51 mg, and 97 mg/103 mg, to submit a substantially complete ANDA with a paragraph IV certification. Therefore, with this approval, Crystal may be eligible for 180 days of generic drug exclusivity for Sacubitril and Valsartan Tablets, 24 mg/26 mg, 49 mg/51 mg, and 97 mg/103 mg. 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 Crystal 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 Crystal'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 Crystal begins commercial marketing of Sacubitril and Valsartan Tablets, 24 mg/26 mg, 49 mg/51 mg, and 97 mg/103 mg, or (b) at any time prior to the expiration of the '659, '938, and '134 patents if Crystal 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.

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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

[1] The Agency notes that the '226, '143, '667, and '192 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.

John Ibrahim

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