U.S. FOOD & DRUG ADMINISTRATION

ANDA 208455

ANDA TENTATIVE APPROVAL

Sun Pharmaceutical Industries, Inc.
U.S. Agent for Sun Pharmaceutical Industries Limited
2 Independence Way
Princeton, NJ 08540
Attention: Ronak Patel

Dear Sir:

This letter is in reference to your abbreviated new drug application (ANDA) received for review on May 4, 2015, submitted pursuant to section 505(j) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) for Linagliptin Tablets, 5 mg.

Reference is also made to the complete response letter issued by this office on October 30, 2018, 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. We have determined your Linagliptin Tablets, 5 mg, to be bioequivalent and therapeutically equivalent to the reference listed drug (RLD), Tradjenta Tablets, 5 mg, of Boehringer Ingelheim Pharmaceuticals, Inc. (Boehringer Ingelheim).

However, we are unable to grant final approval to your ANDA at this time because of the patent issue noted below. Therefore, the ANDA is **tentatively approved**.[1] This determination is based upon information available to the Agency at this time (e.g., information in your ANDA and the status of current good manufacturing practices (cGMPs) of the facilities used in the manufacturing and testing of the drug product). This determination is subject to change on the basis of new information that may come to our attention. This letter does not address issues related to the 180-day exclusivity provisions under section 505(j)(5)(B)(iv) of the FD&C Act.

The RLD upon which you have based your ANDA, Boehringer Ingelheim's Tradjenta Tablets, 5 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
7,407,955 (the '955 patent)	May 2, 2025
8,119,648 (the '648 patent)	August 12, 2023
8,178,541 (the '541 patent)	August 12, 2023
8,673,927 (the '927 patent)	May 4, 2027
8,846,695 (the '695 patent)	June 4, 2030
8,883,805 (the '805 patent)	November 26, 2025
8,853,156 (the '156 patent)	March 5, 2031
9,173,859 (the '859 patent)	May 4, 2027
9,486,526 (the '526 patent)	August 5, 2029
10,034,877 (the '877 patent)	August 5, 2029

With respect to the '927, '695, and '859 (those portions pertaining to U-1503: Method of treating type 2 diabetes mellitus by administering linagliptin in combination with metformin) 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 the '156, '805, '859 (those portions pertaining to U-1768: Method of treating type 2 diabetes mellitus by administering linagliptin), '526, and '877 patents[2], your ANDA contains paragraph IV certifications 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 Linagliptin Tablets, 5 mg, under this ANDA. You have notified the Agency that Sun Pharmaceutical Industries Limited (Sun) 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 Sun for infringement of the '156 patent in the United States District Court for the District of New Jersey [Boehringer Ingelheim Pharmaceuticals Inc., Boehringer Ingelheim International GmbH, Boehringer Ingelheim Corporation, and Boehringer Ingelheim Pharma GmbH & Co. KG, v. Sun Pharmaceutical Industries Limited and Sun Pharma Global FZE, et al., Civil Action No. 15-05982 (consolidated)]. You have also notified the Agency that this case was dismissed.

With respect to the '955, '648, and '541 patents, your ANDA contains paragraph III certifications to each of the patents under section 505(j)(2)(A)(vii)(III) of the FD&C Act stating that Sun will not market Linagliptin Tablets, 5 mg, prior to the expiration of the patents. Therefore, final approval of your ANDA may not be granted pursuant to section 505(j)(5)(B)(ii) of the FD&C Act until the '955 patent has expired, currently May 2, 2025.

Please note that if FDA requires a Risk Evaluation and 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.

RESUBMISSION

To request final approval, please submit an amendment titled “FINAL APPROVAL REQUESTED” with enough time to permit FDA review prior to the date you believe that your ANDA will be eligible for final approval. A request for final approval that contains no new data, information, or other changes to the ANDA generally requires a period of 3 months for Agency review. Accordingly, such a request for final approval should be submitted no later than 3 months prior to the date on which you seek approval. A request for final approval that contains substantive changes to this ANDA or changes in the status of the manufacturing and testing facilities’ compliance with cGMPs will be classified and reviewed according to OGD policy in effect at the time of receipt. Applicants should review available Agency guidance for industry related to amendments under the generic drug user fee program to determine the duration of Agency review needed to review the changes submitted. As part of this consideration, applicants should monitor any changes to the RLD that occur after tentative approval, including changes in labeling, patent or exclusivity information, or marketing status. The submission of multiple amendments prior to final approval may also result in a delay in the issuance of the final approval letter.

The amendment requesting final approval should provide the legal/regulatory basis for your request for final approval and should include a copy of a court decision, settlement or licensing agreement, or other information described in 21 CFR 314.107, as appropriate. It should also identify changes, if any, in the conditions under which the ANDA was tentatively approved, e.g., updated information such as final-printed labeling, chemistry, manufacturing, and controls data as appropriate. This amendment should be submitted even if none of these changes were made, and it should be designated clearly in your cover letter as a “FINAL APPROVAL REQUESTED”

In addition to the amendment requested above, the Agency may request, at any time prior to the date of final approval, that you submit an additional amendment containing information as specified by the Agency. Failure to submit either or, if requested, both types of amendments described above may result in a delay in the issuance of the final approval letter.

This drug product may not be marketed without final Agency approval under section 505(j) of the FD&C Act. The introduction or delivery for introduction into interstate commerce of this drug product before the final approval date is prohibited under section 301 of the FD&C Act. Also, until the Agency issues the final approval letter, this drug product will not be deemed approved for marketing under section 505(j) of the FD&C Act, and will not be listed in the Orange Book. Should you believe that there are grounds for issuing the final approval letter prior to May 2, 2025, you should amend your ANDA accordingly.

ANNUAL FACILITY FEES

The Generic Drug User Fee Amendments of 2012 (GDUFA) (Public Law 112-144, Title III) established certain provisions[3] 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 1st 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.

In addition, we note that GDUFA requires that certain non-manufacturing sites and organizations listed in generic drug submissions comply with the self-identification requirement. The failure of any facility, site, or organization to comply with its obligation to self-identify and/or to pay fees when due may raise significant concerns about that site or organization and is a factor that may increase the likelihood of a site inspection prior to approval. FDA does not expect to give priority to completion of inspections that are required simply because facilities, sites, or organizations fail to comply with the law requiring self-identification or fee payment.

For further information on the status of this ANDA or upon submitting an amendment to the ANDA, please contact Megan Tychinski, Regulatory Project Manager, at (240) 402 - 2717.

Sincerely yours,

{See appended electronic signature page}

For CAPT Vincent Sansone, PharmD
Deputy Director
Office of Regulatory Operations
Office of Generic Drugs
Center for Drug Evaluation and Research

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[1] With this Tentative Approval letter, the Agency informs you that FDA is continuing to evaluate whether one or more supplements to NDA No. 201280, which is the RLD cited as the Basis of Submission for this ANDA, is eligible for three-year exclusivity under section 505(c)(3)(E)(iii), (c)(3)(E)(iv), (j)(5)(F)(iii), and (j)(5)(F)(iv) of the FD&C Act. Upon making its decision, the Agency will identify any period of exclusivity for which NDA No. 201280 is eligible in the *Approved Drug Products with Therapeutic Equivalence Evaluations*, also known as the Orange Book. Please note that any determination that a supplement to NDA No. 201280 qualifies for exclusivity may affect the date on which your ANDA is eligible for Final Approval. Please also note that if you seek to omit any exclusivity-protected indication or aspect of labeling under 21 CFR 314.94(a)(8)(iv), FDA will need to evaluate the acceptability of your proposed labeling. FDA recommends that you request Final Approval in a manner consistent with recommendations in the Guidance for Industry: *ANDA Submissions-Amendments and Request for Final Approval to Tentatively Approved ANDAs* taking into account when you believe all barriers to final approval will be extinguished.

[2] The Agency notes that the '859, '526, and '877 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.

[3] Some of these provisions were amended by the Generic Drug User Fee Amendments of 2017 (GDUFA II) (Public Law 115-52, Title III).

Sarah Kurtz

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