ANDA 211607

ANDA APPROVAL

Apotex Corp.
U.S. Agent for Apotex Inc.
2400 North Commerce Parkway, Suite 400
Weston, FL 33326
Attention: Kiran Krishnan
Senior Vice President, Global Regulatory Affairs

Dear Kiran Krishnan:

This letter is in reference to your abbreviated new drug application (ANDA) received for review on January 31, 2018, submitted pursuant to section 505(j) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) for Tasimelteon Capsules, 20 mg.

Reference is also made to the tentative approval letter issued by this office on February 3, 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 Tasimelteon Capsules, 20 mg, to be bioequivalent and therapeutically equivalent to the reference listed drug (RLD), Hetlioz Capsules, 20 mg, of Vanda Pharmaceuticals Inc. (Vanda).

The RLD upon which you have based your ANDA, Vanda's Hetlioz Capsules, 20 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
9,060,995 (the '995 patent)	January 25, 2033
9,539,234 (the '243 patent)	January 25, 2033
9,549,913 (the '913 patent)	January 25, 2033
9,730,910 (the '910 patent)	May 17, 2034
9,855,241 (the '241 patent)	January 25, 2033

10,071,977 (the '977 patent)	February 12, 2035
10,149,829 (the '829 patent)	January 25, 2033
10,179,119 (the '119 patent)	August 29, 2035
10,376,487 (the '487 patent)	July 27, 2035
10,449,176 (the '176 patent)	January 25, 2033
10,610,510 (the '510 patent)	January 25, 2033
10,610,511 (the '511 patent)	October 10, 2034
10,829,465 (the '465 patent)	February 12, 2035
10,945,988 (the '988 patent)	January 25, 2033
10,980,770 (the '770 patent)	January 25, 2033
11,141,400 (the '400 patent)	October 10, 2034
11,266,622 (the '622 patent)	August 29, 2035
11,285,129 (the '129 patent)	January 25, 2033
RE46,604 (the '604 patent)	January 25, 2033

With respect to: 1) the '119 and ‘622 patent; 2) the portion(s) of the '234 patent pertaining to the use code U-3004: treatment of nighttime sleep disturbances in SmithMagenis Syndrome by avoiding the use of Tasimelteon in combination with a strong CYP1A2 inhibitor; 3) the portion(s) of the '910 patent pertaining to the use code U-3005: treatment of nighttime sleep disturbances in Smith-Magenis Syndrome by avoiding the use of Tasimelteon with rifampin; 4) the portion(s) of the '829 patent pertaining to the use code U-3006: treatment of nighttime sleep disturbances in Smith-Magenis Syndrome non-24 hour sleep-wake disorder by avoiding the use of Tasimelteon in combination with CYP1A2 strong inhibitors; 5) the portions of the '487 and '400 patents pertaining to the use code U-3007: treatment of nighttime sleep disturbances in Smith-Magenis Syndrome by avoiding the administration of Tasimelteon with food; 6) the portion(s) of the '770 patent pertaining to the use code U-3106: treatment of nighttime sleep disturbances in Smith-Magenis Syndrome by avoiding the administration of Tasimelteon to smokers or to patients being treated with a CYP1A2 inhibitor); and 7) the portion(s) of the '129 patent pertaining to use code U-3342: treatment of nighttime sleep disturbances in Smith-Magenis Syndrome by avoiding the administration of Tasimelteon beta-adrenergic receptor antagonists, your ANDA

contains a statements under section 505(j)(2)(A)(viii) of the FD&C Act that these are method-of-use patents that does/do not claim any indication or other conditions of use for which you are seeking approval under your ANDA.

With respect to the: 1) the '995, '913, '241, '977, '176, '465, '988, and '604 patents; 2) the '234 patent (excluding those portions pertaining to the use code U-3004); 3) the '910 patent (excluding those portions pertaining to the use code U-3005; 4) the '829 patent (excluding those portions pertaining to the use code U-3006); 5) the '487 and '400 patents (excluding those portions pertaining to the use code U-3007); 6) the '770 patent (excluding those portions pertaining to the use code U-3106); and 7) the '129 patent (excluding those portions pertaining to use code U-3342),[1] 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 Tasimelteon Capsules, 20 mg, under this ANDA. You have notified the Agency that Apotex Inc. (Apotex) 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 Apotex for infringement of the '995, '234, '913, '910, '241, and '604 patents in the United States District Court for the District of Delaware [Vanda Pharmaceuticals Inc. v. Apotex Inc., and Apotex Corp., Civil Action No. 18-00689]. Although this litigation remains ongoing, the 7.5-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 the '510 and '511 patents, the Agency has determined that information on these patents was submitted to the Agency by the new drug application (NDA) holder (a) after the date of the submission of your ANDA, and (b) more than 30 days after the patent was required to be submitted under 21 CFR 314.53. Therefore, under 21 CFR 314.94(a)(12)(vi), no person with an appropriate patent certification at the time of the submission of the patent was required to submit an amended patent certification to address the '510 and '511 patents. You elected not to submit an amended patent certification with respect to these patents.

With respect to 180-day generic drug exclusivity, we note that Apotex was one of the first ANDA applicants for Tasimelteon Capsules, 20 mg, to submit a substantially complete ANDA with a paragraph IV certification. Therefore, with this approval, Apotex is eligible for 180 days of shared generic drug exclusivity for Tasimelteon Capsules, 20 mg. FDA notes that after issuance of this approval letter, eligibility for 180-day exclusivity is subject to future events that may result in forfeiture of exclusivity under section 505(j)(5)(D) of the FD&C Act. This exclusivity, which is provided for under section 505(j)(5)(B)(iv) of the FD&C Act, will begin to run from the date of the commercial marketing by any first applicant, as identified in section 505(j)(5)(B)(iv). 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).

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 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.

REPORTING REQUIREMENTS

Postmarketing reporting requirements for this ANDA are set forth in 21 CFR 314.80-81 and 314.98 and at section 506I of the FD&C Act. The Agency should be advised of any change in the marketing status of this drug or if this drug will not be available for sale after approval. In particular, under section 506I(b) of the FD&C Act, you are required to notify the Agency in writing within 180 days from the date of this letter if this drug will not be available for sale within 180 days from the date of approval. As part of such written notification, you must include (1) the identity of the drug by established name and proprietary name (if any); (2) the ANDA number; (3) the strength of the drug; (4) the date on which the drug will be available for sale, if known; and (5) the reason for not marketing the drug after approval.

PROMOTIONAL MATERIALS

You may request advisory comments on proposed introductory advertising and promotional labeling materials prior to publication or dissemination. Please note that these submissions are voluntary. To do so, submit, in triplicate, a cover letter requesting advisory comments, the proposed materials in draft or mock-up form with annotated references, and the package insert (PI), Medication Guide, and patient PI (as applicable) to:

OPDP Regulatory Project Manager
Food and Drug Administration
Center for Drug Evaluation and Research
Office of Prescription Drug Promotion
5901-B Ammendale Road
Beltsville, MD 20705

Alternatively, you may submit a request for advisory comments electronically in eCTD format. For more information about submitting promotional materials in eCTD format, see the draft Guidance for Industry (available at: https://www.fda.gov/media/128163/download).

You must also submit final promotional materials and package insert(s), accompanied by a Form FDA 2253, at the time of initial dissemination or publication [21 CFR 314.81(b)(3)(i)]. Form FDA 2253 is available at https://www.fda.gov/media/73013/download. Information and Instructions for completing the form can be found at https://www.fda.gov/media/132152/download. For

more information about submission of promotional materials to the Office of Prescription Drug Promotion (OPDP), see https://www.fda.gov/about-fda/center-drug-evaluation-and-research-cder/opdp-ectd.

ANNUAL FACILITY FEES

The Generic Drug User Fee Amendments of 2012 (GDUFA) (Public Law 112-144, Title III) established certain provisions[2] 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 or active pharmaceutical ingredients 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.

CONTENT OF LABELING

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 https://www.fda.gov/media/71211/download. The SPL will be accessible via publicly available labeling repositories.

We remind you that you must continually monitor available labeling resources such as DRUGS@FDA for changes to your reference listed drug's labels and labeling and make any necessary revisions to your labels and labeling. More information on post-approval

labeling changes may be found in the guidance for industry titled “Changes to an Approved NDA or ANDA” at https://www.fda.gov/media/71846/download.

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] The Agency notes that the '977, '829, '119, '487, '176, '465, '988, '770, '510, '511, '400, '622, and '129 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.

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

John Ibrahim

Digitally signed by John Ibrahim
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