ANDA 205016

ANDA TENTATIVE APPROVAL

Ascend Laboratories, LLC
U.S. Agent for Alkem Laboratories Limited
339 Jefferson Road
Parsippany, NJ 07054
Attention: Hindy Schiff
Authorized U.S. Agent

Dear Hindy Schiff:

This letter is in reference to your abbreviated new drug application (ANDA) received for review on November 20, 2012, submitted pursuant to section 505(j) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) for Tapentadol Extended-Release Tablets, 50 mg, 100 mg, 150 mg, 200 mg and 250 mg.

Reference is also made to the complete response letter issued by this office on October 21, 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. We have determined your Tapentadol Extended-Release Tablets, 50 mg, 100 mg, 150 mg, 200 mg and 250 mg to be bioequivalent and therapeutically equivalent to the reference listed drug (RLD), Nucynta ER Tablets, 50 mg, 100 mg, 150 mg, 200 mg and 250 mg, of Collegium Pharmaceuticals, Inc. (Collegium).

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**. 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, Collegium's Nucynta ER Tablets, 50 mg, 100 mg, 150 mg, 200 mg and 250 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
7,994,364 (the '364 patent)	June 27, 2025
8,075,872 (the '872 patent)	November 20, 2023
8,114,383 (the '383 patent)	October 10, 2024
8,309,060 (the '060 patent)	November 20, 2023
8,420,056 (the '056 patent)	November 20, 2023
8,536,130 (the '130 patent)	September 22, 2028
11,344,512 (the '512 patent)	April 21, 2028

With respect to: 1) the '872, '383 and '056 patents; 2) the '364 and '060 patents (b) (4) (b) (4) and 3) the '512 patent (b) (4) (b) (4) (b) (4), your ANDA contains paragraph III certifications under section 505(j)(2)(A)(vii)(III) of the FD&C Act stating that Alkem Laboratories Limited (Alkem) will not market Tapentadol Extended-Release Tablets, 50 mg, 100 mg, 150 mg, 200 mg, and 250 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 '512 patent has expired, currently April 21, 2028.

With respect to: 1) '130 patent; 2) the '364 and '060 patents (b) (4) (b) (4) (b) (4); and 3) the '512 patent (b) (4) (b) (4) (b) (4), 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.

RISK EVALUATION AND MITIGATION STRATEGY REQUIREMENTS

Section 505-1 of the FD&C Act authorizes FDA to require the submission of a risk evaluation and mitigation strategy (REMS), if FDA determines that such a strategy is

necessary to ensure that the benefits of the drug outweigh the risks [section 505-1(a) of the FD&C Act]. In accordance with section 505-1(i) of the FD&C Act, a drug that is the subject of an ANDA under section 505(j) of the FD&C Act is subject to certain elements of the REMS required for the applicable listed drug.

The details of the REMS requirements were outlined in our REMS notification letter dated June 26, 2019.

Your final proposed REMS, known as the Opioid Analgesic shared system REMS, referenced in Drug Master File (DMF) (b) (4), can be approved with your application.

The REMS consists of a Medication Guide, and elements to assure safe use (ETASU).

REQUIREMENTS AND RECOMMENDATIONS POST APPROVAL

Under applicable statutes, regulations, and guidances, if your ANDA receives final approval, it 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.

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 April 21, 2028, you should amend you ANDA accordingly

For further information on the status of this ANDA or upon submitting an amendment to the ANDA, please contact Kimberly McCullough, Regulatory Project Manager, at (240) 402 - 9021.

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

Catherine Poole

Digitally signed by Catherine Poole
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