ANDA 215911

ANDA TENTATIVE APPROVAL

Lupin Inc.
400 Campus Drive
Somerset, NJ 08873
Attention: Kalpana Vanam
Sr. Vice President, Regulatory Affairs

Dear Kalpana Vanam:

This letter is in reference to your abbreviated new drug application (ANDA) received for review on April 12, 2021, submitted pursuant to section 505(j) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) for Calcium, Magnesium, Potassium, and Sodium Oxybates Oral Solution, 0.5 g/mL.

Reference is also made to the complete response letter issued by this office on April 12, 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 Calcium, Magnesium, Potassium, and Sodium Oxybates Oral Solution, 0.5 g/mL to be bioequivalent and therapeutically equivalent to the reference listed drug (RLD), Xywav Oral Solution, 0.5 g/mL of Jazz Pharmaceuticals Ireland Limited (Jazz Pharmaceuticals).

However, we are unable to grant final approval to your ANDA at this time because of the patent/exclusivity issues 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 reference listed drug (RLD) upon which you have based your ANDA, Jazz Pharmaceuticals' Xywav Oral Solution, 0.5 g/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
8,591,922 (the '922 patent)	January 11, 2033
8,772,306 (the '306 patent)	September 15, 2033*
8,901,173 (the '173 patent)	January 11, 2033
9,050,302 (the '302 patent)	September 15, 2033*
9,132,107 (the '107 patent)	January 11, 2033
9,486,426 (the '426 patent)	September 15, 2033*
10,195,168 (the '168 patent)	January 11, 2023
10,213,400 (the '400 patent)	September 15, 2033*
10,675,258 (the '258 patent)	January 11, 2023
10,864,181 (the '181 patent)	September 15, 2033*
11,253,494 (the '494 patent)	September 15, 2033*
11,426,373 (the '373 patent)	September 19, 2037
11,554,102 (the '102 patent)	January 11, 2033

*with pediatric exclusivity added

With respect to the '306 patent pertaining to the (b) (4) your ANDA contains a statement under section 505(j)(2)(A)(viii) of the FD&C Act that this is a method-of-use patent that does not claim any indication (b) (4)

With respect to 1) '922, '173, '302, '107, '426, '168, '400, '258, '181, '494, '373, and '102 patents and 2) the '306 patent (excluding those portions pertaining to (b) (4) 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 Calcium, Magnesium, Potassium, and Sodium Oxybates Oral Solution, 0.5 g/mL, under this ANDA. You have notified the Agency that Lupin Inc. (Lupin) 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 Lupin for infringement of the '922, '306, '173, '302, '107,

'426, '168, '400, '258, and '181 patents in the United States District Court for the District of New Jersey [Jazz Pharmaceuticals Ireland Limited v. Lupin Ltd., Lupin Inc., and Lupin Pharmaceuticals, Inc., Civil Action No. 21-14271].

Therefore, final approval cannot be granted until:

1. a. the expiration of the 30-month period provided for in section 505(j)(5)(B)(iii) of the FD&C Act,

   b. the date the court decides[2] that the '922, '306, '173, '302, '107, '426, '168, '400, '258, and '181 patents are invalid or not infringed (see sections 505(j)(5)(B)(iii)(I), (II), and (III) of the FD&C Act), or

   c. the '922, '306, '173, '302, '107, '426, '168, '400, '258, and '181 patents have expired, and

2. The Agency is assured there is no new information that would affect whether final approval should be granted.

The RLD upon which you have based your ANDA, Jazz Pharmaceuticals' Xywav, 0.5 g/mL, is subject to periods of exclusivity. As noted in the Orange Book, the ODE-361 exclusivity is scheduled to expire on July 21, 2027. Your ANDA contains a statement that you do not seek to market Calcium, Magnesium, Potassium, and Sodium Oxybates Oral Solution, 0.5 g/mL, prior to the expiration of this exclusivity. Therefore, final approval cannot be granted until the ODE-361 exclusivity has expired, currently July 21, 2027.

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)]. 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) 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 25, 2021.

(b) (4)

(b) (4)

Prior to the submission of your amendment, obtain an updated version of the REMS and appended materials to submit to your application, if applicable.

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 July 21, 2027, you should amend your ANDA accordingly.

For further information on the status of this ANDA or upon submitting an amendment to the ANDA, please contact Zera Kwende, Regulatory Project Manager, at (301) 796 - 3556.

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 '494, '373, and '102 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] This decision may be either a decision of the district court or the court of appeals, whichever court is the first to decide that the patent is invalid or not infringed.

John Ibrahim

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