



ANDA 216511

ANDA TENTATIVE APPROVAL

Lupin Pharmaceuticals, Inc.
U.S. Agent for Lupin Limited
111 South Calvert Street,
Harborplace Tower, 21st Floor
Baltimore, MD 21202
Attention: Debashis Mohanty
Associate Director - Regulatory Affairs

Dear Debashis Mohanty:

This letter is in reference to your abbreviated new drug application (ANDA) received for review on August 16, 2021, submitted pursuant to section 505(j) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) for Darunavir, Cobicistat, Emtricitabine, and Tenofovir Alafenamide Tablets, 800 mg/150 mg/200 mg/10 mg.

Reference is also made to the complete response letter issued by this office on March 27, 2024, 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 Darunavir, Cobicistat, Emtricitabine, and Tenofovir Alafenamide Tablets, 800 mg/150 mg/200 mg/10 mg to be bioequivalent and therapeutically equivalent to the reference listed drug (RLD), Symtuza Tablets, 800 mg/150 mg/200 mg/10 mg, of Janssen Products LP (Janssen), NDA 210455.

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, Janssen's Symtuza Tablets, 800 mg/150 mg/200 mg/10 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>U.S. Patent Number</u>	<u>Expiration Date</u>
7,390,791 (the '791 patent)	April 17, 2025
7,700,645 (the '645 patent)	December 26, 2026
8,148,374 (the '374 patent)	September 3, 2029
8,754,065 (the '065 patent)	August 15, 2032
9,296,769 (the '769 patent)	August 15, 2032
10,039,718 (the '718 patent)	October 6, 2032
10,786,518 (the '518 patent)	July 19, 2038

With respect to the '791, '645, and '374 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 Lupin Limited (Lupin) will not market Darunavir, Cobicistat, Emtricitabine, and Tenofovir Alafenamide Tablets, 800 mg/150 mg/200 mg/10 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 '374 patent has expired, currently September 3, 2029.

With respect to 1) the '518 patent and 2) the '065 and '769 patents (insofar as it pertains to certain portions of the use code

(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.

Your ANDA contains paragraph IV certifications to 1) the '718 patent and 2) the '065 and '769 patents (excluding certain portions of the use code (b) (4) (b) (4)

(b) (4) 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 Darunavir, Cobicistat, Emtricitabine, and Tenofovir Alafenamide Tablets, 800 mg/150 mg/200 mg/10 mg, under this ANDA. You have notified the Agency that 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 '065 and '769 patents in the United States District Court for the District of Delaware [Gilead Sciences, Inc., v. Lupin Limited, Civil Action No. 21-01615]. You have also notified the Agency that this case was dismissed. You have further notified the Agency that litigation was initiated within the statutory 45-day period against Lupin for infringement of the '718 patent in the United States District Court for the District of Delaware [Gilead Sciences, Inc., Gilead Sciences Ireland UC, Janssen Products, L.P., and Janssen Sciences Ireland Unlimited Company v. Lupin Limited and Lupin Pharmaceuticals, Inc., et al., Civil Action No. 21-01621]. Although the litigation remains ongoing, the 30-month 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. You have further notified the Agency that, following Lupin sending an additional notice under 505(j)(2)(B) of the FD&C Act, litigation was initiated within the statutory 45-day period against Lupin for infringement of the '718 patent in the United States District Court for the District of Delaware [Gilead Sciences, Inc., Gilead Sciences Ireland UC, Janssen Products, L.P., and Janssen Sciences Ireland Unlimited Company v. Lupin Limited and Lupin Pharmaceuticals, Inc., et al., Civil Action No. 23-00508].

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 decides¹ that the '718 patent is invalid or not infringed (see sections 505(j)(5)(B)(iii)(I), (II), and (III) of the FD&C Act), or
 - c. the '718, '791, '645 and '374 patents have expired, and
2. The Agency is assured there is no new information that would affect whether final approval should be granted.

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.

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.

For further information on the status of this ANDA or upon submitting an amendment to the ANDA, please contact Diane Smith, PharmD, RPh, Regulatory Project Manager, at (301) 796 - 3652.

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 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.



Sarah
Kurtz

Digitally signed by Sarah Kurtz

Date: 1/28/2025 12:33:24PM

GUID: 54078879000a1b9e15dd31ed6f0343ca