



ANDA 201046

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

Dear Madam:

This is in reference to your abbreviated new drug application (ANDA) received on May 17, 2010, and submitted pursuant to section 505(j) of the Federal Food, Drug, and Cosmetic Act (the Act), for Ranolazine Extended-release Tablets, 500 mg and 1000 mg.

Reference is made to the tentative approval letter issued by this office on April 25, 2013. We acknowledge receipt of your amendment dated May 3, 2013, and of your correspondence dated July 18, 2013 addressing patent issues associated with this ANDA.

We have completed the review of this ANDA and have concluded that adequate information has been presented to demonstrate that the drug is safe and effective for use as recommended in the submitted labeling. Accordingly the ANDA is approved, effective on the date of this letter. The Division of Bioequivalence has determined your Ranolazine Extended-release Tablets, 500 mg and 1000 mg, to be bioequivalent and, therefore, therapeutically equivalent to the reference listed drug (RLD), Ranexa Extended-release Tablets, 500 mg and 1000 mg, respectively, of Gilead Sciences, Inc. (Gilead). Your dissolution testing should be incorporated into the stability and quality control program using the same method proposed in your ANDA.

The "interim" dissolution specifications are as follows:

Apparatus: USP Type II (Paddle) with Sinkers  
Speed of Rotation: 50 rpm

Medium: 0.1N HCl  
 Volume: 900 mL

Sampling Times (hours) 0.5, 1, 2, 4, 6, 8, 10, 12, 16, 20, 24

Specifications for the 500 mg Tablet:

<u>Time (Hours)</u>	<u>Percent Dissolved</u>
1	(b) (4)
4	(b) (4)
12	(b) (4)
24	NLT (b) (4)

Specifications for the 1000 mg Tablet:

<u>Time (Hours)</u>	<u>Percent Dissolved</u>
1	(b) (4)
4	(b) (4)
12	(b) (4)
24	NLT (b) (4)

These "interim" dissolution test(s) and tolerances should be finalized by submitting dissolution data from the first three production size batches. These data should be submitted as a "Supplement - Changes Being Effected" if there are no revisions to be made to the "interim" specifications, or if the final specifications are tighter than the "interim" specifications. In all other instances, the information should be submitted in the form of a Prior Approval Supplement.

The RLD upon which you have based your ANDA, Gilead's Ranexa Extended-release Tablets, is subject to periods of patent protection. The following patents and their expiration dates are currently listed in the agency's publication titled Approved Drug Products with Therapeutic Equivalence Evaluations (the "Orange Book") for this drug product:

<u>U.S. Patent Number</u>	<u>Expiration Date</u>
6,303,607 (the '607 patent)	May 27, 2019
6,369,062 (the '062 patent)	May 27, 2019
6,479,496 (the '496 patent)	May 27, 2019
6,503,911 (the '911 patent)	May 27, 2019
6,525,057 (the '057 patent)	May 27, 2019

6,562,826 (the '826 patent)	May 27, 2019
6,617,328 (the '328 patent)	May 27, 2019
6,620,814 (the '814 patent)	May 27, 2019
6,852,724 (the '724 patent)	May 27, 2019
6,864,258 (the '258 patent)	May 27, 2019

Your ANDA contains paragraph IV certifications under section 505(j)(2)(A)(vii)(IV) of the Act stating that each of these patents is invalid, unenforceable, or will not be infringed by your manufacture, use, or sale of Ranolazine Extended-Release Tablets, 500 mg and 1000 mg, under this ANDA. You have notified the agency that Lupin Limited (Lupin) complied with the requirements of section 505(j)(2)(B) of the Act, and that litigation for infringement of the '607, '496, '911, '057, '826, '328, '814, '724, '258 patents was brought against Lupin within the statutory 45-day period in the United States District Court for the District of New Jersey [Roche Palo Alto LLC, Gilead Palo Alto, Inc., and Gilead Sciences, Inc., v. Lupin Pharmaceuticals, Inc., and Lupin Ltd, Civil Action No. 2:10-cv-03561-WJM-MF]. Although this litigation remains ongoing, the expiration of the 7½-year period provided for in section 505(j)(5)(B)(iii) of the Act, during which time FDA was precluded from approving your ANDA, has expired.

With respect to 180-day generic drug exclusivity, we note that Lupin was the first ANDA applicant to submit a substantially complete ANDA with a paragraph IV certification to the one or more of the patents listed for Ranolazine Extended-release Tablets, 500 mg and 1000 mg. Therefore, with this approval, Lupin is eligible for 180 days of generic drug exclusivity for Ranolazine Extended-release Tablets, 500 mg and 1000 mg. This exclusivity, which is provided for under section 505(j)(5)(B)(iv) of the Act, will begin to run from the commercial marketing identified in section 505(j)(5)(B)(iv). Please submit correspondence to this ANDA informing the agency of the date the exclusivity begins to run.

Under section 506A of the 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 & 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 Act.

Postmarketing reporting requirements for this ANDA are set forth in 21 CFR 314.80-81 and 314.98. The Office of Generic Drugs should be advised of any change in the marketing status of this drug.

Promotional materials may be submitted to FDA for comment prior to publication or dissemination. Please note that these submissions are voluntary. If you desire comments on proposed launch promotional materials with respect to compliance with applicable regulatory requirements, we recommend you submit, in draft or mock-up form, two copies of both the promotional materials and package insert directly to:

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

We call your attention to 21 CFR 314.81(b)(3) which requires that all promotional materials be submitted to the Office of Prescription Drug Promotion with a completed Form FDA 2253 at the time of their initial use.

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

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(1)] 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

<http://www.fda.gov/downloads/DrugsGuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf>. The SPL will be accessible via publicly available labeling repositories.

Sincerely yours,

*{See appended electronic signature page}*

Kathleen Uhl, M.D.  
Acting Director  
Office of Generic Drugs  
Center for Drug Evaluation and Research

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**This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.**  
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/s/  
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ROBERT L WEST

07/29/2013

Deputy Director, Office of Generic Drugs, for  
Kathleen Uhl, M.D.