



ANDA 213154

**ANDA APPROVAL**

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

Dear Debashis Mohanty:

This letter is in reference to your abbreviated new drug application (ANDA) received for review on February 8, 2019, submitted pursuant to section 505(j) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) for Bosentan Tablets for Oral Suspension, 32 mg.

Reference is also made to the tentative approval letter issued by this office on April 1, 2021, 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 Bosentan Tablets for Oral Suspension, 32 mg to be bioequivalent and therapeutically equivalent to the reference listed drug (RLD), Tracleer Tablets for Oral Suspension, 32 mg, of Actelion Pharmaceuticals US, Inc. (Actelion) NDA - 209279.

The RLD upon which you have based your ANDA, Actelion's Tracleer Tablets for Oral Suspension, 32 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>
7,959,945 (the '945 patent)	December 28, 2027
8,309,126 (the '126 patent)	May 15, 2026

Your ANDA contains paragraph IV certifications to each of the patents 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 Bosentan Tablets for Oral Suspension, 32 mg, under this ANDA. You have notified the Agency that Natco Pharma Limited (Natco) 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 Natco for infringement of the '126 patent in the United States District Court for the District of New Jersey [Actelion Pharmaceuticals Ltd. and Actelion Pharmaceuticals US, Inc. v. Natco Pharma Limited, Civil Action No. 19-12984]. You have also notified the Agency that this case was dismissed.

With respect to 180-day generic drug exclusivity, we note that Natco was the first ANDA applicant to submit a substantially complete ANDA with a paragraph IV certification for Bosentan Tablets for Oral Suspension, 32 mg. Therefore, with this approval, Natco is eligible for 180 days of generic drug exclusivity for Bosentan Tablets for Oral Suspension, 32 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, begins to run from the date of the commercial marketing 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).

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.

### **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 April 4, 2019.

Your final proposed REMS, received on January 17, 2025, is approved, and will be posted on the FDA REMS website: <http://www.fda.gov/remis>. Other products may be added in the future if additional NDAs or ANDAs are approved.

The Bosentan REMS consists of Elements to Assure Safe Use (ETASU) and an implementation system.

Your REMS must be fully operational before you introduce your drug into interstate commerce.

Under section 505-1(g)(2)(C) of the FD&C Act, FDA can require the submission of a REMS assessment if FDA determines an assessment is needed to evaluate whether the REMS should be modified to ensure the benefits of the drug outweigh the risks or to minimize the burden on the healthcare delivery system of complying with the REMS.

We remind you that you must include an adequate rationale to support a proposed REMS modification for the addition, modification, or removal of any goal or element of the REMS, as described in section 505-1(g)(4) of the FD&C Act.

We also remind you that section 505-1(f)(8) of the FD&C Act prohibits holders of an approved covered application from using any element to assure safe use to block or delay approval of an application under section 505(b)(2) or (j). A violation of this provision in 505-1(f) of the FD&C Act could result in enforcement action.

Prominently identify any submission containing a REMS assessment or proposed modifications of the REMS with the following wording in bold capital letters at the top of the first page of the submission as appropriate:

**ANDA 213154 REMS ASSESSMENT**

*or*

**NEW SUPPLEMENT FOR ANDA 213154/S-000  
CHANGES BEING EFFECTED IN 30 DAYS  
PROPOSED MINOR REMS MODIFICATION**

*or*

**NEW SUPPLEMENT FOR ANDA 213154/S-000  
PRIOR APPROVAL SUPPLEMENT  
PROPOSED MAJOR REMS MODIFICATION**

*or*

**NEW SUPPLEMENT FOR ANDA 213154/S-000  
PRIOR APPROVAL SUPPLEMENT  
PROPOSED REMS MODIFICATIONS DUE TO SAFETY LABELING  
CHANGES SUBMITTED IN SUPPLEMENT XXX**

Should you choose to submit a REMS revision, prominently identify the submission containing the REMS revisions with the following wording in bold capital letters at the top of the first page of the submission:

**REMS REVISION FOR ANDA 213154**

To facilitate review of your submission, we request that you submit your proposed modified REMS and other REMS-related materials in Microsoft Word format. If certain documents, such as enrollment forms, are only in PDF format, they may be submitted as such, but the preference is to include as many as possible in Word format.

**SUBMISSION OF REMS DOCUMENT IN SPL FORMAT**

As soon as possible, but no later than 14 days from the date of this letter, submit the REMS document in Structured Product Labeling (SPL) format using the FDA automated drug registration and listing system (eLIST). Do not submit the SPL to your application. Content of the REMS document must be identical to the approved REMS document. The SPL will be publicly available.

Information on submitting REMS in SPL format may be found in the guidance for industry *Providing Regulatory Submission in Electronic Format – Content of the Risk Evaluation and Mitigation Strategies Document Using Structured Product Labeling*.

For additional information on submitting REMS in SPL format, please email [REMSWebsite@fda.hhs.gov](mailto:REMSWebsite@fda.hhs.gov).

**COMPENDIAL STANDARDS**

A drug with a name recognized in the official United States Pharmacopeia or official National Formulary (USP-NF) generally must comply with the compendial standard for strength, quality, and purity, unless the difference in strength, quality, or purity is plainly stated on its label (see FD&C Act § 501(b), 21 USC 351(b)). FDA typically cannot share application-specific information contained in submitted regulatory filings with third parties, which includes USP-NF. To help ensure that a drug continues to comply with compendial standards, application holders may work directly with USP-NF to revise official USP monographs. More information on the USP-NF is available on USP's website as <https://www.uspnf.com/>.

**REQUIREMENTS AND RECOMMENDATIONS POST APPROVAL**

Under applicable statutes, regulations, and guidances, your ANDA 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>.

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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