

CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

209299Orig1s000

Trade Name: TAVALISSE tablets; 100 mg and 150 mg

Generic or Proper Name: fostamatinib disodium hexahydrate

Sponsor: Rigel Pharmaceuticals, Inc.

Approval Date: April 17, 2018

Indication: For the treatment of thrombocytopenia in adult patients with chronic immune thrombocytopenia (ITP) who have had an insufficient response to a previous treatment.

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APPROVAL LETTER



NDA 209299

NDA APPROVAL

Rigel Pharmaceuticals, Inc.
Attention: Yvonne Kim
Senior Director, Regulatory Affairs
1180 Veterans Blvd.
South San Francisco, CA 94080

Dear Ms. Kim:

Please refer to your New Drug Application (NDA) dated April 15, 2017, received April 17, 2017 and your amendments, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for TAVALISSE™ (fostamatinib disodium hexahydrate) tablets; 100 mg and 150 mg.

This new drug application provides for the use of TAVALISSE™ (fostamatinib disodium hexahydrate) tablets for the treatment of thrombocytopenia in adult patients with chronic immune thrombocytopenia (ITP) who have had an insufficient response to a previous treatment.

APPROVAL & LABELING

We have completed our review of this application, as amended. It is approved, effective on the date of this letter, for use as recommended in the enclosed agreed-upon labeling text.

CONTENT OF LABELING

As soon as possible, but no later than 14 days from the date of this letter, submit the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format using the FDA automated drug registration and listing system (eLIST), as described at <http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm>.

Content of labeling must be identical to the enclosed labeling (text for the prescribing information, text for the patient package insert). Information on submitting SPL files using eLIST may be found in the guidance for industry *SPL Standard for Content of Labeling Technical Qs and As*, available

at <http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf>.

The SPL will be accessible via publicly available labeling repositories.

CARTON AND IMMEDIATE CONTAINER LABELS

Submit final printed carton and immediate container labels that are identical to the carton and immediate container labels submitted on April 10, 2018, as soon as they are available, but no more than 30 days after they are printed. Please submit these labels electronically according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format — Certain Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications (May 2015, Revision 3)*. For administrative purposes, designate this submission “**Final Printed Carton and Container Labels for approved NDA 209299.**” Approval of this submission by FDA is not required before the labeling is used.

ADVISORY COMMITTEE

Your application for fostamatinib was not referred to an FDA advisory committee because the safety profile is acceptable for treatment of thrombocytopenia in adult patients with chronic immune thrombocytopenia (ITP) who have had an insufficient response to a previous treatment, and the clinical trial design is acceptable.

REQUIRED PEDIATRIC ASSESSMENTS

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients (which includes new salts and new fixed combinations), new indications, new dosage forms, new dosing regimens, or new routes of administration are required to contain an assessment of the safety and effectiveness of the product for the claimed indication in pediatric patients unless this requirement is waived, deferred, or inapplicable.

Because this drug product for this indication has an orphan drug designation, you are exempt from this requirement.

POSTMARKETING COMMITMENTS NOT SUBJECT TO THE REPORTING REQUIREMENTS UNDER SECTION 506B

We remind you of your postmarketing commitments:

PMC 3380-1: Develop a test method for [REDACTED] (b) (4) and hardness for the drug product and submit the validation data to the FDA. Include tests for [REDACTED] (b) (4) and hardness for drug product release and stability specifications with adequate justification. Submit a CBE-30 supplement to update the drug product specification.

The timetable you submitted on March 29, 2018, states that you will conduct this study according to the following schedule:

Study Completion:	06/2018
Final Report Submission:	08/2018

PMC 3380 -2: Conduct and submit a risk assessment for the presence of elemental impurities as described in the ICH guidance *Q3D Elemental Impurities* (<https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM371025.pdf>). Your risk assessment should identify known and potential sources of elemental impurities that may be present in the drug product, and evaluate the presence of each particular elemental impurity likely to be present in the drug product by determining the observed or predicted level of the impurity and comparing it with the permitted daily exposure (PDE) established in ICH Q3D. If the risk assessment or testing results fail to show that an elemental impurity level is consistently less than the control threshold (defined as being 30 percent of the established PDE in the drug product), you should propose additional controls (e.g., component, in-process, or drug product controls) to ensure that the elemental impurity level does not exceed the PDE in the drug product. For additional information, also see: <https://www.fda.gov/Drugs/DevelopmentApprovalProcess/Manufacturing/ucm590075.htm>
Submit a CBE-30 supplement with the data and/or update the drug product specification.

The timetable you submitted on March 29, 2018, states that you will conduct this study according to the following schedule:

Study Completion:	06/2018
Final Report Submission:	08/2018

Submit clinical protocols to your IND 074939 for this product. Submit nonclinical and chemistry, manufacturing, and controls protocols and all postmarketing final reports to this NDA. In addition, under 21 CFR 314.81(b)(2)(vii) and 314.81(b)(2)(viii) you should include a status summary of each commitment in your annual report to this NDA. The status summary should include expected summary completion and final report submission dates, any changes in plans since the last annual report, and, for clinical studies/trials, number of patients entered into each study/trial. All submissions, including supplements, relating to these postmarketing commitments should be prominently labeled **“Postmarketing Commitment Protocol,” “Postmarketing Commitment Final Report,”** or **“Postmarketing Commitment Correspondence.”**

PROMOTIONAL MATERIALS

You may request advisory comments on proposed introductory advertising and promotional labeling. To do so, submit, in triplicate, a cover letter requesting advisory comments, the proposed materials in draft or mock-up form with annotated references, and the prescribing information, Medication Guide, and patient PI (as applicable) to:

OPDP Regulatory Project Manager
Food and Drug Administration
Center for Drug Evaluation and Research
Office of Prescription Drug Promotion
5901-B Ammendale Road
Beltsville, MD 20705-1266

Alternatively, you may submit a request for advisory comments electronically in eCTD format. For more information about submitting promotional materials in eCTD format, see the draft Guidance for Industry (available at: <http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM443702.pdf>).

As required under 21 CFR 314.81(b)(3)(i), you must submit final promotional materials, and the prescribing information, at the time of initial dissemination or publication, accompanied by a Form FDA 2253. Form FDA 2253 is available at <http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM083570.pdf>. Information and Instructions for completing the form can be found at <http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM375154.pdf>. For more information about submission of promotional materials to the Office of Prescription Drug Promotion (OPDP), see <http://www.fda.gov/AboutFDA/CentersOffices/CDER/ucm090142.htm>.

REPORTING REQUIREMENTS

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

MEDWATCH-TO-MANUFACTURER PROGRAM

The MedWatch-to-Manufacturer Program provides manufacturers with copies of serious adverse event reports that are received directly by the FDA. New molecular entities and important new biologics qualify for inclusion for three years after approval. Your firm is eligible to receive copies of reports for this product. To participate in the program, please see the enrollment instructions and program description details at <http://www.fda.gov/Safety/MedWatch/HowToReport/ucm166910.htm>.

POST APPROVAL FEEDBACK MEETING

New molecular entities and new biologics qualify for a post approval feedback meeting. Such meetings are used to discuss the quality of the application and to evaluate the communication process during drug development and marketing application review. The purpose is to learn from successful aspects of the review process and to identify areas that could benefit from improvement. If you would like to have such a meeting with us, call the Regulatory Project Manager for this application.

If you have any questions, call Rachel McMullen, Regulatory Project Manager, at (240) 402-4574.

Sincerely,

{See appended electronic signature page}

Richard Pazdur, MD
Director (acting)
Office of Hematology and Oncology Products
Center for Drug Evaluation and Research

Enclosure:
Content of Labeling

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

ANN T FARRELL
04/17/2018
signing on behalf of Dr. Pazdur