NDA 213004/S-010

SUPPLEMENT APPROVAL

RedHill Biopharma Ltd.
Attention: Reza Fathi, PhD
Senior Vice President, Research & Development
260 Forest Avenue
Oradell, NJ 07649

Dear Dr. Fathi:

Please refer to your supplemental new drug application (sNDA) dated and received November 30, 2022, and your amendments, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Talicia (omeprazole magnesium, amoxicillin, rifabutin) delayed-release capsules, 10 mg/250 mg/12.5 mg.

This Prior Approval sNDA provides for the following:

- Revisions to the **HIGHLIGHTS OF PRESCRIBING INFORMATION**, **TABLE OF CONTENTS**, and **FULL PRESCRIBING INFORMATION**. Specifically,
  - In the **HIGHLIGHTS OF PRESCRIBING INFORMATION**, the **RECENT MAJOR CHANGES**, and **DOSAGE AND ADMINISTRATION** sections were updated to reflect the change in dosing regimen to "three times daily (at least 4 hours apart, e.g., morning, mid-day, and evening)".
  - Under the **TABLE OF CONTENTS**:
    - Subsections **2.1 Recommended Dosage** and **2.2 Missed Doses** were added under Section **2 DOSAGE AND ADMINISTRATION**.
  - Under the **FULL PRESCRIBING INFORMATION,** the following were revised:
    - Under Section **2 DOSAGE AND ADMINISTRATION**, subsections **2.1 Recommended Dosage** and **2.2 Missed Doses** were added.
      - Under subsection **2.1 Recommended Dosage**, the dosing regimen was revised to "three times daily (at least 4 hours apart, e.g., morning, mid-day, and evening) with food".
      - Under subsection **2.2 Missed Doses**, the following was added: "If a dose is missed and the next dose is not within 4 hours, administer the missed dose as soon as possible" and "If a dose is missed and the next dose is within 4 hours, administer the missed dose as soon as possible and delay the next dose to ensure there are at least 4 hours between two doses".

- Under Section **17 PATIENT COUNSELING INFORMATION**, the instructions under "Important Administration Instructions for TALICIA" were revised to update (1) the dosing regimen to "three times daily (at least 4 hours apart, e.g., morning, mid-day, and evening)" and (2) the "*Missed Doses*" to advise patients "that if a dose is missed, and the next dose is not within 4 hours, administer as soon as possible. However, if a dose is missed and the next dose is within 4 hours, administer the missed dose as soon as possible and delay the next dose to ensure there are at least 4 hours between two doses."

- Updates to the prescribing information (PI), to include the recently approved safety labeling changes (SLC) dated July 18, 2023.
- Minor editorial revisions throughout the PI.

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.

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 FDA.gov.[1] Content of labeling must be identical to the enclosed labeling (text for the Prescribing Information), with the addition of any labeling changes in pending "Changes Being Effected" (CBE) supplements, as well as annual reportable changes not included in the enclosed labeling.

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*.[2]
The SPL will be accessible from publicly available labeling repositories.

Also within 14 days, amend all pending supplemental applications that include labeling changes for this NDA, including CBE supplements for which FDA has not yet issued an action letter, with the content of labeling [21 CFR 314.50(l)(1)(i)] in Microsoft Word format, that includes the changes approved in this supplemental application, as well as annual reportable changes. To facilitate review of your submission(s), provide a highlighted or marked-up copy that shows all changes, as well as a clean Microsoft

[1] http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm
[2] We update guidances periodically. For the most recent version of a guidance, check the FDA Guidance Documents Database https://www.fda.gov/RegulatoryInformation/Guidances/default.htm.

Word version. The marked-up copy should provide appropriate annotations, including supplement number(s) and annual report date(s).

PROMOTIONAL MATERIALS

You may request advisory comments on proposed introductory advertising and promotional labeling. For information about submitting promotional materials, see the final guidance for industry *Providing Regulatory Submissions in Electronic and Non-Electronic Format-Promotional Labeling and Advertising Materials for Human Prescription Drugs.*[3]

You must submit final promotional materials and Prescribing Information, accompanied by a Form FDA 2253, at the time of initial dissemination or publication [21 CFR 314.81(b)(3)(i)]. Form FDA 2253 is available at FDA.gov.[4] Information and Instructions for completing the form can be found at FDA.gov.[5]

PATENT LISTING REQUIREMENTS

Pursuant to 21 CFR 314.53(d)(2) and 314.70(f), certain changes to an approved NDA submitted in a supplement require you to submit patent information for listing in the Orange Book upon approval of the supplement. You must submit the patent information required by 21 CFR 314.53(d)(2)(i)(A) through (C) and 314.53(d)(2)(ii)(A) and (C), as applicable, to FDA on Form FDA 3542 within 30 days after the date of approval of the supplement for the patent information to be timely filed (see 21 CFR 314.53(c)(2)(ii)). You also must ensure that any changes to your approved NDA that require the submission of a request to remove patent information from the Orange Book are submitted to FDA at the time of approval of the supplement pursuant to 21 CFR 314.53(d)(2)(ii)(B) and 314.53(f)(2)(iv).

REPORTING REQUIREMENTS

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

[3] For the most recent version of a guidance, check the FDA guidance web page at https://www.fda.gov/media/128163/download.
[4] http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM083570.pdf
[5] http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM375154.pdf

If you have any questions, please contact Jennifer Grant, MSHS, Regulatory Project Manager, at jennifer.grant@fda.hhs.gov or (301) 796-0480.

Sincerely,

{See appended electronic signature page}

Peter Kim, MD, MS
Director
Division of Anti-Infectives
Office of Infectious Diseases
Center for Drug Evaluation and Research

ENCLOSURE(S):

- Content of Labeling
  - Prescribing Information

This is a representation of an electronic record that was signed electronically. Following this are manifestations of any and all electronic signatures for this electronic record.

/s/

PETER W KIM
09/08/2023 05:07:58 PM