



NDA 213004/S 007

## SUPPLEMENT APPROVAL

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

Dear Dr. Fathi:

Please refer to your supplemental new drug application (sNDA) dated and received December 10, 2021, 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.

We also refer to our letter dated November 22, 2021, notifying you, under Section 505(o)(4) of the FDCA, of new safety information that we believe should be included in the labeling for proton pump inhibitors (PPI). This information pertains to the risk of Severe Cutaneous Adverse Reactions (SCARs) such as drug reaction with eosinophilia and systemic symptoms (DRESS).

This Prior Approval supplement NDA provides for revisions to the labeling for Talicia, consistent with our November 22, 2021, letter.

Specifically, the **WARNINGS AND PRECAUTIONS (5)** section, **Severe Cutaneous Adverse Reactions (5.2)** subsection has been revised to state that DRESS has been reported with the components of TALICIA: rifabutin, amoxicillin, and omeprazole.

Additional revisions are also included in the following sections and subsections of the attached Prescribing Information (PI): **HIGHLIGHTS OF PRESCRIBING INFORMATION**, and **ADVERSE REACTIONS (6), Postmarketing Experience with Components of Talicia (6.3)** under the subheading **Omeprazole**.

Other requested changes not required under section 505(o)(4) of the FDCA have been made to the labeling to include DRESS for the **Amoxicillin** component of Talicia in the **WARNINGS AND PRECAUTIONS (5)** section, **Severe Cutaneous Adverse Reactions (5.2)** subsection and in the **ADVERSE REACTIONS (6)** section, **Postmarketing Experience with Components of Talicia (6.3)** subsection under *Skin and subcutaneous tissue disorders*.

Additionally, aseptic meningitis was added to the **ADVERSE REACTIONS (6)** section, **Post marketing Experience with Components of Talicia (6.3)** subsection under the Central Nervous System, Amoxicillin subheadings.

### **APPROVAL & LABELING**

We have completed our review of this application. 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.<sup>1</sup> 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 Effectuated” (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*.<sup>2</sup>

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

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<sup>1</sup> <http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm>

<sup>2</sup> 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>.

All promotional materials that include representations about your drug product must be promptly revised to be consistent with the labeling changes approved in this supplement, including any new safety information [21 CFR 314.70(a)(4)]. The revisions in your promotional materials should include prominent disclosure of the important new safety information that appears in the revised labeling. Within 7 days of receipt of this letter, submit your statement of intent to comply with 21 CFR 314.70(a)(4).

### **REPORTING REQUIREMENTS**

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

If you have any questions, call Jacquelyn Rosenberger, PharmD, RAC, Regulatory Project Manager, at (301) 796-9179.

Sincerely,

*{See appended electronic signature page}*

Dmitri Iarikov, MD, PhD  
Deputy Director  
Division of Anti-Infectives  
Office of Infectious Diseases  
Center for Drug Evaluation and Research

#### ENCLOSURE:

- Content of Labeling
  - Prescribing Information

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**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.**  
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/s/  
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DMITRI IARIKOV  
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