



NDA 213004/S-014

## SUPPLEMENT APPROVAL

RedHill Biopharma Ltd.  
c/o Pharmaceutical Consulting  
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 on January 31, 2024, and your amendment, 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.

We also refer to our letter dated January 17, 2024, notifying you, under Section 505(o)(4) of the FDCA, of new safety information that we have determined should be included in the labeling for Talicia. This information pertains to the risk of amoxicillin-related linear IgA bullous dermatosis (LABD) and drug induced enterocolitis syndrome (DIES).

This supplemental new drug application provides for revisions to the labeling for Talicia.

The agreed upon changes to the language included in our January 17, 2024, letter are as follows (additions are noted by double underline and deletion are noted by ~~strikethrough~~).

### HIGHLIGHTS OF PRESCRIBING INFORMATION

#### WARNINGS AND PRECAUTIONS

Drug-induced enterocolitis syndrome (DIES) has been reported with use of amoxicillin, a component of TALICIA <sup>(b) (4)</sup>. If this occurs, discontinue TALICIA and institute appropriate therapy. (5.3)

## **FULL PRESCRIBING INFORMATION**

### **5 WARNINGS AND PRECAUTIONS**

#### **5.3 Drug-Induced Enterocolitis Syndrome (DIES)**

Drug-induced enterocolitis syndrome (DIES) has been reported with use of amoxicillin, a component of TALICIA <sup>(b) (4)</sup> [see *Adverse Reactions (6.3)*], with most cases occurring in pediatric patients  $\leq 18$  years of age.

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.<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 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*.<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>.

## **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*.<sup>3</sup>

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.<sup>4</sup> Information and Instructions for completing the form can be found at FDA.gov.<sup>5</sup>

[NOTE: The use of the term “new safety-related information” below includes new safety information (NSI) as described in section 505-1(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) (21 U.S.C. 355-1(b)) and other safety-related information unrelated to section 505(o)(4) of the FDCA.]

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-related information [21 CFR 314.70(a)(4)]. The revisions in your promotional materials should include prominent disclosure of the important new safety-related 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).

## **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).

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<sup>3</sup> For the most recent version of a guidance, check the FDA guidance web page at <https://www.fda.gov/media/128163/download>.

<sup>4</sup> <http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM083570.pdf>

<sup>5</sup> <http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM375154.pdf>

## **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, please contact Jennifer Grant, MSHS, Regulatory Project Manager at (301) 796-0480.

Sincerely,

*{See appended electronic signature page}*

Mukil Natarajan, MD  
Deputy Director for Safety  
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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MUKILAN NATARAJAN  
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