NDA 017377/S-084

SUPPLEMENT APPROVAL

Sun Pharmaceutical Industries, Inc.
Attention: Nitesh Patel,
Senior Manager, Regulatory Affairs
2 Independence Way
Princeton, NJ 08540

Dear Nitesh Patel,

Please refer to your supplemental new drug application (sNDA) dated and received on March 22, 2024, and your amendment, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Bactrim and Bactrim DS Tablets.

We also refer to our letter dated March 11, 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 sulfamethoxazole and trimethoprim products. This information pertains to the risk of acute respiratory failure.

This supplemental new drug application provides for revisions to the labeling for Bactrim and Bactrim DS Tablets.

The agreed upon changes to the language included in our March 11, 2024, letter are as follows: (additions are noted by double underline and deletion are noted by ~~strikethrough~~).

Information for Patients

Hypersensitivity and Other Serious (b) (4) *Reactions:* Advise patients to stop taking BACTRIM immediately if they experience any clinical signs such as rash, pharyngitis, fever, arthralgia, cough, chest pain, dyspnea, pallor, purpura or jaundice and to contact their healthcare provider as soon as possible (see **WARNINGS** and **ADVERSE REACTIONS**).

OTHER REQUESTED CHANGES TO LABELING

WARNINGS

Hypersensitivity and Other Serious or Fatal Reactions

(b) (4)

Fatalities and serious adverse reactions including severe cutaneous adverse reactions (SCARs) including Stevens-Johnson syndrome, toxic epidermal necrolysis, drug reaction with eosinophilia and systemic symptoms (DRESS), acute febrile neutrophilic dermatosis (AFND), acute generalized erythematous pustulosis (AGEP); fulminant hepatic necrosis; agranulocytosis, aplastic anemia and other blood dyscrasias; acute and delayed lung injury; anaphylaxis and circulatory shock have occurred with the administration of sulfamethoxazole and trimethoprim products, including BACTRIM (see **ADVERSE REACTIONS**).

Management of Hypersensitivity and Other Serious Reactions

BACTRIM should be discontinued at the first appearance of skin rash or any sign of a serious adverse reaction. A skin rash may be followed by a more severe reaction, such as Stevens-Johnson syndrome, toxic epidermal necrolysis, DRESS, AFND, AGEP, hepatic necrosis, or serious blood disorders (see **PRECAUTIONS and ADVERSE REACTIONS**). Clinical signs, such as rash, pharyngitis, fever, arthralgia, cough, chest pain, dyspnea, pallor, purpura or jaundice may be early indications of serious reactions.

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

[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.

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).

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]

[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

[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

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).

If you have any questions, call J. Christopher Davi, MS, Senior Regulatory Project Manager, at (301) 796-0702.

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

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/

MUKILAN NATARAJAN
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