

NDA 209899/S-11  
 NDA 209899/S-12

**SUPPLEMENT APPROVAL AND  
 FULFILLMENT OF POSTMARKETING REQUIREMENT**

Bristol-Myers Squibb Company  
 Attention: Stacy Ly  
 Associate Director, Regulatory Affairs  
 PO Box 5326  
 Princeton, NJ 08543

Dear Stacy Ly:

Please refer to your supplemental new drug applications (sNDAs), and your amendments, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Zeposia (ozanimod) capsules, as follows:

| <b>NDA Number/<br/>Supplement<br/>Number</b> | <b>Submitted and<br/>received date</b> | <b>These Prior Approval sNDAs provide for:</b>  |
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| NDA 209899/S-11                              | November 9, 2023                       | Revisions to Section 5.6 (Warnings and Precautions; Increased Blood Pressure), Section 7 (Drug Interactions), Section 12.2 (Clinical Pharmacology; Pharmacodynamics), and Section 12.3 (Clinical Pharmacology; Pharmacokinetics) of the Prescribing Information to reflect the results of Study RPC-1063-CP-005 conducted to fulfill Postmarketing Requirement 3809-5. Corresponding revisions were made to the Medication Guide. |
| NDA 209899/S-12                              | March 4, 2024                          | Revisions to Section 5.4 (Warnings and Precautions; Liver Injury) and Section 17 (Patient Counseling Information), and addition of Section 6.2 (Adverse Reactions; Postmarketing Experience) of the Prescribing Information to reflect the risk of severe liver injury. Corresponding revisions were made to the Medication Guide.  |

## **APPROVAL & LABELING**

We have completed our review of these applications, as amended. They are approved, effective on the date of this letter, for use as recommended in the enclosed agreed-upon labeling.

## **WAIVER OF ½ PAGE LENGTH REQUIREMENT FOR HIGHLIGHTS**

We are waiving the requirements of 21 CFR 201.57(d)(8) regarding the length of Highlights of Prescribing Information. This waiver applies to all future supplements containing revised labeling unless we notify you otherwise.

## **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 and Medication Guide), 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 these supplemental applications, 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).

## **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

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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>.

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 none of these criteria apply to your applications, you are exempt from this requirement.

### **FULFILLMENT OF POSTMARKETING REQUIREMENT**

We have received your submission dated November 9, 2023, containing the final report for the following postmarketing requirement listed in the March 25, 2020, approval letter.

- 3809-5 A randomized, double-blind, placebo-controlled, active-controlled (phenelzine), multiple-dose, parallel-group trial to investigate the pressor effect of oral tyramine during Zeposia (ozanimod) treatment in healthy subjects.

We have reviewed your submission and conclude that the above requirement has been fulfilled.

We remind you that there are postmarketing requirements listed in the March 25, 2020, approval letter and the September 15, 2023, postapproval postmarketing requirement letter that are still open. We also remind you that there are postmarketing requirements and commitments listed in the May 27, 2021, supplement approval letter that are still open.

### **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>

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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>

All promotional materials that include representations about your drug product must be promptly revised to be consistent with the labeling changes approved in these supplements, 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).

### **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 Rania Younes, Senior Regulatory Project Manager, by email at [rania.younes@fda.hhs.gov](mailto:rania.younes@fda.hhs.gov) or by phone at (301) 837-7347.

Sincerely,

*{See appended electronic signature page}*

Paul R. Lee, MD, PhD, MA  
Director (Acting)  
Division of Neurology 2  
Office of Neuroscience  
Center for Drug Evaluation and Research

### **ENCLOSURES:**

- Content of Labeling
  - Prescribing Information
  - Medication Guide

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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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PAUL R LEE  
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