BLA 761046/S-012

SUPPLEMENT APPROVAL
FULFILLMENT OF POSTMARKETING REQUIREMENT

Merck Sharp & Dohme Corp.
a subsidiary of Merck & Co., Inc.
Attention: Megan Wise, PhD
Director, Global Regulatory Affairs
351 North Sumneytown Pike
UG2D-68
North Wales, PA 19454-2505

Dear Dr. Wise:

Please refer to your supplemental biologics license application (sBLA) dated and received November 28, 2022, and your amendments, submitted under section 351(a) of the Public Health Service Act for Zinplava (bezlotoxumab) injection,1,000 mg/40 mL.

This Prior Approval sBLA provides for the expansion of the use of Zinplava injection to reduce recurrence of *Clostridioides difficile* infection (CDI) in patients who are receiving antibacterial drug treatment for CDI and are at a high risk for CDI recurrence to include pediatric patients 1 year to less than 18 years of age, based on the completion of post-marketing requirement (PMR) 3118-1, listed in the October 21, 2016, approval letter.

Additionally, this sBLA has been submitted in response to the Pediatric Written Request (PWR) dated April 13, 2020 and amended on April 29, 2022.

APPROVAL & LABELING

We have completed our review of this application, as amended, and 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, via the FDA automated drug registration and listing system (eLIST), the content of labeling [21 CFR 601.14(b)] in structured product labeling (SPL) format, as described at FDA.gov,[1] that is identical to the enclosed labeling (text for the Prescribing Information and Patient Package Insert) and include the labeling changes proposed in any pending "Changes Being Effected" (CBE) supplements.

[1] http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm

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 via publicly available labeling repositories.

Also within 14 days, amend all pending supplemental applications that include labeling changes for this BLA, including pending "Changes Being Effected" (CBE) supplements, for which FDA has not yet issued an action letter, with the content of labeling [21 CFR 601.12(f)] 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).

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 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(s) in pediatric patients unless this requirement is waived, deferred, or inapplicable.

We note that we waived the pediatric study requirement in patients less than 1 year of age in the approval letter dated October 21, 2016, because necessary studies are impossible or highly impracticable, as this disease does not occur commonly in this population.

We note that you have fulfilled the pediatric study requirement for ages 1 year to less than 18 years for this application.

FULFILLMENT OF POSTMARKETING REQUIREMENT (PMR)

We have received your submission dated November 28, 2022, containing the final report for the following postmarketing requirement listed in the October 21, 2016, approval letter.

3118-1: Conduct a randomized, double-blind, placebo-controlled trial of safety, efficacy and pharmacokinetics of ZINPLAVA (bezlotoxumab) in pediatric patients from 1 to less than 18 years of age receiving antibacterial therapy for *C. difficile* infection.

[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.

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

We remind you that there are postmarketing commitments listed in the October 21, 2016, 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.*[3]

As required under 21 CFR 601.12(f)(4), you must submit final promotional materials, and the Prescribing Information, at the time of initial dissemination or publication, accompanied by a Form FDA 2253. Form FDA 2253 is available at FDA.gov.[4] Information and Instructions for completing the form can be found at FDA.gov.[5]

REPORTING REQUIREMENTS

We remind you that you must comply with reporting requirements for an approved BLA (in 21 CFR 600.80 and in 21 CFR 600.81).

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

Sincerely,

{See appended electronic signature page}

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
  - Patient Package Insert

[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

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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.

/s/

PETER W KIM
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