

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

761275Orig1s000

OTHER ACTION LETTERS



BLA 761275

COMPLETE RESPONSE

Fresenius Kabi USA, LLC
Three Corporate Drive
Lake Zurich, Illinois 60047

Attention: Brittany Duke, PhD
Associate Director, Regulatory Affairs

Dear Dr. Duke:

Please refer to your biologics license application (BLA) dated May 30, 2022, received May 31, 2022, and your amendments, submitted under section 351(k) of the Public Health Service Act for MSB11456, single-dose prefilled syringe and single-dose prefilled autoinjector (162 mg/0.9 mL), and single-dose vials (80 mg/4 mL, 200 mg/10 mL, and 400 mg/20 mL).

We have completed our review of this application, as amended, and have determined that we cannot approve this application in its present form. We have described our reasons for this action below and, where possible, our recommendations to address these issues.

FACILITIES

Following inspections of Fresenius Kabi Austria GmbH, Graz, Austria (FEI: 3003708554) and (b) (4) listed in this application, FDA conveyed deficiencies to the representative of the facility. Satisfactory resolution of these deficiencies is required before this application may be approved.

PRESCRIBING INFORMATION

We reserve comment on the proposed labeling until the application is otherwise adequate. We encourage you to review the labeling review resources on the Prescription Drug Labeling Resources¹ and Pregnancy and Lactation Labeling Final Rule² websites, including regulations and related guidance documents and the Selected Requirements for Prescribing Information (SRPI) – a checklist of important format items

¹ <https://www.fda.gov/drugs/laws-acts-and-rules/prescription-drug-labeling-resources>

² <https://www.fda.gov/drugs/labeling-information-drug-products/pregnancy-and-lactation-labeling-drugs-final-rule>

from labeling regulations and guidances. In addition, we encourage you to review the FDA guidance for industry *Labeling for Biosimilar Products*.

CARTON AND CONTAINER LABELING

We reserve comment on the proposed labeling until the application is otherwise adequate.

PROPRIETARY NAME

Please refer to correspondence dated, November 30, 2022, which addresses the proposed proprietary name, Tyenne. This name was found acceptable pending approval of the application in the current review cycle. Please resubmit the proposed proprietary name when you respond to the application deficiencies.

SAFETY UPDATE

When you respond to the above deficiencies, include a safety update. The safety update should include data from all nonclinical and clinical studies of the product under consideration regardless of indication, dosage form, or dose level.

- (1) Describe in detail any significant changes or findings in the safety profile and their relevance, if any, to whether there may be clinically meaningful differences between the proposed biosimilar product and the U.S.-licensed reference product.
- (2) When assembling the sections describing discontinuations due to adverse events, serious adverse events, and common adverse events, incorporate new safety data as follows:
 - Present new safety data from the clinical studies for the proposed indication using the same format as the original BLA submission.
 - Present tabulations of the new safety data combined with the original BLA data.
 - Include tables that compare frequencies of adverse events in the original BLA with the retabulated frequencies described in the bullet above.
- (3) Present a retabulation of the reasons for premature study discontinuation by incorporating the drop-outs from the newly completed studies. Describe any new trends or patterns identified.

- (4) Provide case report forms and narrative summaries for each subject who died during a clinical study or who did not complete a study because of an adverse event. In addition, provide narrative summaries for serious adverse events.
- (5) Describe any information that suggests a substantial change in the incidence of common, but less serious, adverse events between the new data and the original BLA data.
- (6) Provide updated exposure information for the clinical studies (e.g., number of subjects, person time).
- (7) Provide a summary of worldwide experience on the safety of this product, including adverse events known to be associated with the use of the product and immunogenicity. Include an updated estimate of use for this product marketed in other countries.
- (8) Provide English translations of current approved foreign labeling not previously submitted.

ADDITIONAL COMMENTS

We have the following comments/recommendations that are not approvability issues:

1. Revise the method for container closure integrity testing of MSB11456 drug product in vial to include a positive control that reflects a breach defect $\leq 20 \mu\text{m}$ and update the application accordingly.
2. The acceptance criteria for oxidized variants by RP-UPLC, degree of coloration, and device performance attributes for the prefilled syringe (b) (4) and autoinjector in the drug substance and/or drug product specifications are based on a limited number of MSB11456 batches, thus re-evaluation of the acceptance criteria for these attributes is needed after data from sufficient MSB11456 drug substance and/or drug product batches are available. Submit a rationale for the number of batches needed and a statistical plan that will be used to evaluate the results for each assessment.

OTHER

Within one year after the date of this letter, you are required to resubmit or take other actions available under 21 CFR 601.3(b). If you do not take one of these actions, we may consider your lack of response a request to withdraw the application under 21 CFR 601.3(c). You may also request an extension of time in which to resubmit the application.

A resubmission must fully address all the deficiencies listed in this letter and should be clearly marked with "**RESUBMISSION**" in large font, bolded type at the beginning of the cover letter of the submission. The cover letter should clearly state that you consider this resubmission a complete response to the deficiencies outlined in this letter. A partial response to this letter will not be processed as a resubmission and will not start a new review cycle.

You may request a meeting or teleconference with us to discuss what steps you need to take before the application may be approved. If you wish to have such a meeting, submit your meeting request as described in the draft Guidance for Industry, *Formal Meetings Between the FDA and Sponsors or Applicants of BsUFA Products*.

The product may not be legally marketed until you have been notified in writing that this application is approved.

If you have any questions, call Susie Choi, Regulatory Project Manager, at 240-402-2925.

Sincerely,

{See appended electronic signature page}

Rachel Glaser, MD
Associate Director for Therapeutic Review
Division of Rheumatology and Transplant Medicine
Office of Immunology and Inflammation
Office of New Drugs
Center for Drug Evaluation and Research

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/

RACHEL GLASER
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