

**CENTER FOR DRUG EVALUATION AND  
RESEARCH**

*APPLICATION NUMBER:*

**761073Orig1s000**

**OTHER ACTION LETTERS**



BLA 761073

## COMPLETE RESPONSE

Amgen Inc.  
Attention: Jennifer Khiem  
Manager, Global Biosimilars Regulatory Affairs  
One Amgen Center Drive  
Thousand Oaks, CA 91320-1799

Dear Ms. Khiem:

Please refer to your Biologics License Application (BLA) dated July 28, 2017, received July 28, 2017, and your amendments, submitted under section 351(k) of the Public Health Service Act for Kanjinti (ABP 980).

We have completed our review of this application, 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.

### **FACILITY INSPECTIONS**

During a recent inspection of the [REDACTED] (b) (4) manufacturing facility for this application, our field investigator 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 [PLR Requirements for Prescribing Information](#) and [Pregnancy and Lactation Labeling Final Rule](#) websites, including regulations and related guidance documents and the Selected Requirements for Prescribing Information (SRPI) – a checklist of important format items from labeling regulations and guidances. In addition, we encourage you to review the draft FDA Guidance for Industry, “Labeling for Biosimilar Products,” March 2016 at: <https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM493439.pdf>.

If you revise labeling, use the SRPI checklist to ensure that the prescribing information conforms with format items in regulations and guidances. Your response must include updated content of labeling [21 CFR 601.14(b)] in structured product labeling (SPL) format as described at: <http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm>.

## **CARTON AND CONTAINER LABELING**

Submit draft carton and container labeling based on our proposed revisions dated March 6, 2018.

## **PROPRIETARY NAME**

Please refer to correspondence dated, September 25, 2017, which addresses the proposed proprietary name, Kanjinti. 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 patient 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. Implement a FcγRIIIa binding test on drug substance release specification and submit a proposal for the FcγRIIIa binding drug substance release acceptance criterion.
2. Conduct additional characterization to further understand the impact of drug product manufacturing and stability conditions on Fc functions. Submit results of the data evaluation and update the proposed overall control strategy for Fc effector functions.
3. Section 3.2.P.3.5 of the BLA did not include (b) (4) sterilization validation information for (b) (4). Provide the validation information for (b) (4) in section 3.2.P.3.5 of the resubmission.
4. Media fill simulations to support the ABP 980 (b) (4) did not include the (b) (4). Perform media fill simulations that include the (b) (4) and submit the media fill data in section 3.2.P.3.5 of the resubmission.
5. The (b) (4) validation data provided in the BLA did not include (b) (4) and submit the summary validation data to section 3.2.P.3.5 of the resubmission.
6. The ABP 980 drug product manufacturing process does not include (b) (4). Implement the necessary equipment modifications to designate the (b) (4).

### **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 FDA Guidance for Industry, "Formal Meetings Between the FDA and Biosimilar Biological Product Sponsors or Applicants," November 2015 at: <https://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM345649>.

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

If you have any questions, contact Amy Tilley, Regulatory Project Manager, at 301-796-3994 or [amy.tilley@fda.hhs.gov](mailto:amy.tilley@fda.hhs.gov).

Sincerely,

*{See appended electronic signature page}*

Laleh Amiri-Kordestani, MD  
Acting Supervisory Associate Director  
Division of Oncology Products 1  
Office of Hematology and Oncology Products  
Center for Drug Evaluation and Research

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**This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.**  
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/s/  
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LALEH AMIRI KORDESTANI  
05/25/2018