BLA 125261 / S-166
BLA 761044 / S-014

SUPPLEMENT APPROVAL

Janssen Biotech, Inc.
Attention: Matthew Phillips, PhD, RAC
Associate Director, Global Regulatory Affairs
Welsh & McKean Roads, PO Box 776
Spring House, PA 19477

Dear Dr. Phillips:

Please refer to your supplemental biologics license applications (sBLAs), dated and received April 3, 2024, and your amendments, submitted under section 351(a) of the Public Health Service Act for Stelara (ustekinumab) injection.

These Prior Approval supplemental biologics applications provide for revisions to the Prescribing Information in the DRUG INTERACTIONS, *CYP450 Substrates* and CLINCIAL PHARMACOLOGY, *Pharmacokinetics* subsections based on results from a drug interaction study with CYP450 substrates in subjects with Crohn's disease conducted as a postmarketing commitment (PMC 3112-4).

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 with minor editorial revisions listed below and reflected in the enclosed labeling:

- Updated the revision date at the end of Highlights of the Prescribing Information to the approval month
- Corrected the revision date in the Medication Guide to the date of the last approved revision (03/2024)

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, Medication Guide and Instructions for Use) 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).

FULFILLMENT OF POSTMARKETING COMMITMENT

We have received your submission dated April 3, 2024, containing the final report for the following postmarketing commitment listed in our approval letter for BLA 761044.

3112-4 Conduct a clinical trial to assess whether STELARA (ustekinumab) alters the metabolism or pharmacokinetics of cytochrome P450 (CYP) substrates in Crohn's disease (CD) patients treated with ustekinumab (e.g., using a cocktail of relevant CYP probe drugs).

Final Protocol Submission: 03/2017
Trial Completion: 09/2019
Final Report Submission: 03/2020

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

We remind you that there are postmarketing requirement and postmarketing commitment listed in the September 23, 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-*

[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.

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]

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, contact Jay Fajiculay, PharmD, Senior Regulatory Health Project Manager, at (301) 796-9007 or email at jay.fajiculay@fda.hhs.gov.

Sincerely,

{See appended electronic signature page}

Joyce Korvick, MD
Deputy Director for Safety
Division of Gastroenterology
Office of Immunology and Inflammation
Center for Drug Evaluation and Research

ENCLOSURE(S):

- Content of Labeling
  - Prescribing Information
  - Medication Guide
  - Instructions for Use

[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/

JOYCE A KORVICK
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