CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

761180Orig1s000

OTHER ACTION LETTERS

U.S. FOOD & DRUG ADMINISTRATION

BLA 761180

COMPLETE RESPONSE

LEO Pharma A/S
c/o LEO Pharma Inc.
Attention: Encarnacion Suarez, PharmD
Senior Director, US Regulatory Affairs
7 Girlada Farms, 2nd Floor
Madison, NJ 07940

Dear Dr. Suarez:

Please refer to your biologics license application (BLA) dated and received April 27, 2020, submitted under section 351(a) of the Public Health Service Act for tralokinumab injection, 150 mg/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.

PRODUCT QUALITY

(1) You provided a response to an information request dated, December 14, 2020, which provided documentation of (b) (4) associated 510(k) references to address our request for data verifying the needle safety performance of your combination product at an appropriate reliability limit (95% confidence /99% reliability) and pre-conditioning (aging, drop testing and shipping). While the testing provided evidence for performance of the 510(k) cleared needle safety device component, the testing did not include testing of your final finished combination product or testing after the requested representative preconditioning (aging of the device, dropping of the device, and simulated shipping). You also provided additional information in your Late-Cycle background package dated January 22, 2021, where you asserted that (b) (4) a 510(k) FDA cleared medical device that is manufactured (b) (4)

a) This device has been cleared by the FDA to provide protection from accidental needle stick injury.
b) It has been commercially marketed worldwide since 2001 with numerous products.

c) A study evaluating the [redacted] (b) (4) device is summarized in the attached document from [redacted] (b) (4) demonstrating 512 successful device safety feature activation with 0 failures.

Needle safety performance needs to be tested on the final finished combination product because the prefilled syringe, design differences between your final finished combination product and currently marketed products, combination product manufacturing and preconditioning would impact the performance and reliability. Failure of the needle safety device to perform adequately may result in serious risks (accidental contaminated needle sticks). Provide testing demonstrating that your final finished combination product needle safety performance (needle safety activation and lockout) can meet a confidence and reliability of 95%/99% after aging of the device to the proposed shelf -life, drop testing and simulated shipping per ASTM 4169-16 *Standard Practice for Performance Testing of Shipping Containers and Systems* sequentially.

The recommended confidence and reliability information for sharps injury prevention devices can be found in FDA guidance: *Medical Devices with Sharps Injury Prevention Features* https://www.fda.gov/media/71142/download.

PRESCRIBING INFORMATION

(2) Your proposed Prescribing Information (PI) must conform to the content and format regulations found at 21 CFR 201.56(a) and (d) and 201.57. As you develop your proposed PI, we encourage you to review the labeling review resources on the PLR Requirements for Prescribing Information[1] and Pregnancy and Lactation Labeling Final Rule[2] websites, which include:

- The Final Rule (Physician Labeling Rule) on the content and format of the PI for human drug and biological products
- The Final Rule (Pregnancy and Lactation Labeling Rule) on the content and format of information in the PI on pregnancy, lactation, and females and males of reproductive potential
- Regulations and related guidance documents
- A sample tool illustrating the format for Highlights and Contents, and
- The Selected Requirements for Prescribing Information (SRPI) − a checklist of important format items from labeling regulations and guidances.
- FDA's established pharmacologic class (EPC) text phrases for inclusion in the

[1] http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/LawsActsandRules/ucm084159.htm
[2] http://www.fda.gov/Drugs/DevelopmentApprovalProcess/DevelopmentResources/Labeling/ucm093307.htm

Highlights Indications and Usage heading.

PROPRIETARY NAME

(3) Please refer to correspondence dated, July 2, 2020 which addresses the proposed proprietary name, (b) (4) 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 as described at 21 CFR 314.50(d)(5)(vi)(*b*). The safety update should include data from all nonclinical and clinical studies/trials of the drug under consideration regardless of indication, dosage form, or dose level.

(1) Describe in detail any significant changes or findings in the safety profile.

(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 studies/clinical trials for the proposed indication using the same format as in the original submission.
- Present tabulations of the new safety data combined with the original application data.
- Include tables that compare frequencies of adverse events in the original application with the retabulated frequencies described in the bullet above.
- For indications other than the proposed indication, provide separate tables for the frequencies of adverse events occurring in clinical trials.

(3) Present a retabulation of the reasons for premature trial discontinuation by incorporating the drop-outs from the newly completed trials. Describe any new trends or patterns identified.

(4) Provide case report forms and narrative summaries for each patient who died during a clinical trial or who did not complete a trial 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 application data.

(6) Provide updated exposure information for the clinical studies/trials (e.g., number of subjects, person time).

(7) Provide a summary of worldwide experience on the safety of this product. Include an updated estimate of use for product marketed in other countries.

(8) Provide English translations of current approved foreign labeling not previously submitted.

POSTMARKETING REQUIREMENTS UNDER 505(o)(3)

As described in our letter dated January 29, 2021, we have determined that, if this application is approved, you will be required to conduct postmarketing studies/trials of tralokinumab injection, 150 mg/ML to support dosing in subjects 6 months to less than (b) (4) years, (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.

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, call Strother D. Dixon, Regulatory Project Manager, at (301) 796-1015.

Sincerely,

{See appended electronic signature page}

Julie A. Beitz, MD
Director
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/

JULIE G BEITZ
04/23/2021 04:43:56 PM