BLA 125288/S-101

SUPPLEMENT APPROVAL

Bristol Myers Squibb Company
PO Box 5326
Princeton, NJ 08543-5326

Attention: Kurt Zhu, Ph.D.
US Regulatory Lead, Global Regulatory and Safety Sciences

Dear Dr. Zhu:

Please refer to your supplemental biologics license application (sBLA), dated and received May 7, 2021, and your amendments, submitted under section 351(a) of the Public Health Service Act for Nulojix (belatacept).

We also refer to our letter dated April 9, 2021, notifying you, under Section 505(o)(4) of the Federal Food, Drug, and Cosmetic Act (FDCA), of new safety information that we believe should be included in the labeling for Nulojix (belatacept). This information pertains to the risk of rejection with conversion from a CNI based maintenance regimen.

This supplemental biologics license application provides for revisions to the labeling for Nulojix. The agreed upon changes to the language included in our April 9, 2021 safety labeling change notification letter are as follows (additions are noted by double underline and deletion are noted by ~~strikethrough~~).

> **5.10 Risk of Rejection with Conversion From a CNI Based Maintenance Regimen**
> Conversion of patients receiving a CNI based maintenance regimen to a NULOJIX based maintenance regimen increases the risk of acute rejection. In two randomized controlled studies, kidney transplant recipients at least six months post-transplant, and stable on a CNI based regimen who were converted to a belatacept based regimen experienced higher rejection rates mostly during the first ~~7 months~~ year post-conversion than patients maintained on their CNI based regimens. Conversion of stable kidney transplant recipients from a CNI based maintenance therapy to a belatacept based maintenance therapy is not recommended unless the patient is CNI intolerant.

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.

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 include the labeling changes proposed in any pending "Changes Being Effected" (CBE) supplements.

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).

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]

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

[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.

[3] For the most recent version of a guidance, check the FDA guidance web page athttps://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

All promotional materials for your drug product that include representations about your drug product must be promptly revised to make it consistent with the labeling changes approved in this supplement, including any new safety information [21 CFR 601.12(a)(4)]. The revisions to your promotional materials should include prominent disclosure of the important new safety information that appears in the revised labeling. Within 7 days of receipt of this letter, submit your statement of intent to comply with 21 CFR 601.12(a)(4).

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 Ms. June Germain, Safety Regulatory Project Manager, at 301-796-4024.

Sincerely,

{See appended electronic signature page}

Ozlem Belen, MD, MPH
Deputy Director
Division of Rheumatology and Transplant Medicine
Office of Immunology and Inflammation
Center for Drug Evaluation and Research

ENCLOSURE: Content of Labeling

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/

OZLEM A BELEN
07/28/2021 04:19:40 PM