DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

BLA 125288/S-70

SUPPLEMENT APPROVAL

Bristol-Myers Squibb Company
Attention: Dana Leeds, Ph.D.
US Regulatory Liaison,
P.O. Box 4000 (Mail Stop: D22-08)
Princeton, NJ 08543-4000

Dear Dr. Leeds:

Please refer to your Supplemental Biologics License Application (sBLA), dated and received August 4, 2016, and your amendments, submitted under section 351(a) of the Public Health Service Act for Nulojix (belatacept).

This Changes Being Effected supplemental biologics application provides for revisions to the ADVERSE REACTIONS/6.1 Clinical Studies Experience/Infusion Reactions subsection of the package insert and the addition of a new subsection, 6.2 Postmarketing Experience, with new information based on a case of anaphylaxis.

APPROVAL & LABELING

We have completed our review of this supplemental application, as amended. It is approved, effective on the date of this letter, for use as recommended in the enclosed, agreed-upon labeling text and with minor editorial revisions to italicize or not bold text.

LABELING REVISIONS

The revisions to the package insert are as follow: (additions are noted with double underline and deletions with ~~strikethrough~~)

In the **FULL PRESCRIBING INFORMATION** section, the following revisions have been made:

1. The **6.1 Clinical Studies Experience/***Infusion Reactions* subsection have been revised as follows:

   There ~~were~~ have been no reports of anaphylaxis or drug hypersensitivity in patients treated with NULOJIX in Studies 1 and 2 ~~through~~ up to three years of follow-up. However, milder ~~I~~infusion-related reactions within one hour of infusion were reported in 5% of patients treated with the recommended dose of NULOJIX, similar to the placebo

rate. ~~No serious events were reported through Year 3.~~ The most frequent reactions were hypotension and hypertension. A case of anaphylaxis was reported in the postmarketing experience. [*see Adverse Reactions (6.2*)].

2. A new subsection 6.2 has been added to the 6 ADVERSE REACTIONS section, titled **"Postmarketing Experience"** as follows:

6.2 Postmarketing Experience

Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

Immune System Disorder: Anaphylaxis

Spontaneous reports during the postmarketing experience included a case of anaphylaxis, which was observed in a kidney transplant patient whose belatacept therapy had been interrupted for two months during treatment of a systemic varicella infection. When belatacept therapy was resumed, within five minutes after the start of the belatacept infusion the patient developed a generalized rash, pruritus, hypotension, atrial fibrillation, respiratory distress and syncope, requiring medical treatment. Another belatacept infusion was attempted one month later, but was terminated when the patient experienced more pronounced symptoms of anaphylaxis and required medical treatment.

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 http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm, that is identical to the enclosed labeling (text for the prescribing information, Medication Guide) 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 titled "SPL Standard for Content of Labeling Technical Qs and As" at http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf.

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 MS Word format that includes the changes approved in this supplemental application.

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, MS., Safety Regulatory Project Manager, at 301-796-4024.

Sincerely,

{See appended electronic signature page}

Renata Albrecht, MD
Director
Division of Transplant and Ophthalmology Products
Office of Antimicrobial Products
Center for Drug Evaluation and Research

ENCLOSURE(S): Content of Labeling

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

RENATA ALBRECHT
02/02/2017