DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

BLA 125288/S-059

**SUPPLEMENT APPROVAL**

Bristol-Myers Squibb
Attention: Ashley Pereira, Pharm.D
Director, Global Regulatory Sciences, U.S. Liaison
PO Box 4000
Princeton, NJ 08543

Dear Dr. Pereira:

Please refer to your Supplemental Biologics License Application (sBLA), dated and received March 10, 2014, submitted under section 351(a) of the Public Health Service Act for Nulojix (belatacept).

This "Changes Being Effected" sBLA proposes revisions to the **DOSAGE AND ADMINISTRATION** and **HOW SUPPLIED/STORAGE AND HANDLING** sections of the package insert.

## APPROVAL & LABELING

We have completed our review of this supplemental application. It is approved, effective on the date of this letter, for use as recommended in the enclosed, agreed-upon labeling text which is identical to the labeling text submitted on March 10, 2014.

## 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. In the **2 DOSAGE and ADMINISTRATION/2.2 Preparation and Administration Instructions/Preparation for Administration** subsection, item number 7 has been revised as follows:

   7. Prior to intravenous infusion, the required volume of the reconstituted NULOJIX solution must be further diluted with a suitable infusion fluid (NS or D5W). NULOJIX ~~should be~~ reconstituted with:
      - SWFI should be further diluted with either NS or D5W
      - NS should be further diluted with NS
      - D5W should be further diluted with D5W

2. In the **2 DOSAGE and ADMINISTRATION/2.2 Preparation and Administration Instructions/Preparation for Administration** subsection, item number 8 has been revised as follows:

   8. From the appropriate size infusion ~~container~~bag or bottle, withdraw a volume of infusion fluid that is equal to the volume of the reconstituted NULOJIX solution required to provide the prescribed dose. With the same *silicone-free disposable syringe* used for reconstitution, withdraw the required amount of belatacept solution from the vial, inject it into the infusion ~~container~~bag or bottle, and gently rotate the infusion ~~container~~bag or bottle to ensure mixing.

      The final belatacept concentration in the infusion ~~container~~bag or bottle should range from 2 mg/mL to 10 mg/mL. Typically, an infusion volume of 100 mL will be appropriate for most patients and doses, but total infusion volumes ranging from 50 mL to 250 mL may be used. Any unused solution remaining in the vials must be discarded.

3. In the **16 HOW SUPPLIED/STORAGE AND HANDLING/16.1 Storage** subsection, the second paragraph has been revised as follows:

   The reconstituted solution should be transferred from the vial to the infusion bag or bottle immediately. The NULOJIX infusion must be completed within 24 hours of constitution of the NULOJIX lyophilized powder. If not used immediately, the infusion solution may be stored under refrigeration conditions: 2°-8°C (36°-46°F) and protected from light for up to 24 hours (a maximum of 4 hours of the total 24 hours can be at room temperature: 20°-25°C [68°-77°F] and room light) [see *Dosage and Administration (2.2)*].

## 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 package insert) 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 includes 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, 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: Content of labeling (package insert, medication guide)

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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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RENATA ALBRECHT
04/14/2014