DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

BLA 125118/122

SUPPLEMENT BLA APPROVAL
July 29, 2011

Bristol-Myers Squibb Company
P.O. Box 4000 (Mail Stop: D32-07)
Princeton, New Jersey 08543-4000

Attention: Ashley Pereira, Pharm.D.
Director, Global Regulatory Sciences

Dear Dr. Pereira:

Please refer to your Supplemental Biologics License Application (sBLA), dated October 4, 2010, received October 4, 2010, submitted under section 351 of the Public Health Service Act for Orencia (abatacept).

We acknowledge receipt of your amendments dated December 2, and 14, 2010, and February 3, and 4, March 1, 10, 14, and 17, April 8, and 25, May 31, June 13, and 22, and July 7, 11, 14, 25, and 26 (2), 2011.

This "Prior Approval" efficacy supplement to your biologics license application proposes the subcutaneous use of abatacept for Rheumatoid Arthritis.

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.

We are waiving the requirements of 21 CFR 201.57(d)(8) regarding the length of Highlights of prescribing information. This waiver applies to all future supplements containing revised labeling unless we notify you otherwise.

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 text for the patient 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. For administrative purposes, please designate this submission "**Product Correspondence – Final SPL for approved BLA STN 125118/122**."

Also within 14 days, amend all pending supplemental applications 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.

The SPL will be accessible via publicly available labeling repositories.

CARTON AND IMMEDIATE CONTAINER LABELS

Submit final printed carton and container labels that are identical to the carton and immediate container labels submitted on July 25, 2011, as soon as they are available, but no more than 30 days after they are printed.

Please submit these labels electronically according to the guidance for industry titled "Providing Regulatory Submissions in Electronic Format – Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications (June 2008)." Alternatively, you may submit 12 paper copies, with 6 of the copies individually mounted on heavy-weight paper or similar material. For administrative purposes, designate this submission "**Product Correspondence – Final Printed Carton and Container Labels for approved BLA STN 125118/122**." Approval of this submission by FDA is not required before the labeling is used.

REQUIRED PEDIATRIC ASSESSMENTS

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients, new indications, new dosage forms, new dosing regimens, or new routes of administration are required to contain an assessment of the safety and effectiveness of the product for the claimed indication(s) in pediatric patients unless this requirement is waived, deferred, or inapplicable

We are waiving the pediatric study requirement for ages zero to 5 years because there is evidence strongly suggesting that the drug product would be ineffective and unsafe in this pediatric group. Given that the safety and efficacy of ORENCIA has not been established in pediatric patients below 6 years of age, ORENCIA is not recommended for use in this age group.

We are deferring submission of your pediatric study for ages 6 to 17 years for this application because this product is ready for approval for use in adults and the pediatric study have not been completed.

Your deferred pediatric study required by section 505B(a) of the Federal Food, Drug, and Cosmetic Act are required postmarketing study. The status of this postmarketing study must be

reported annually according to 21 CFR 601.28 and section 505B(a)(3)(B) of the Federal Food, Drug, and Cosmetic Act. This required study is listed below.

PMR#1: Conduct a PK/safety study of SC abatacept in polyaricular JIA patients ages 6 to 17 years of age.

Final Protocol Submission:	November 2012
Study Completion:	September 2017
Final Report Submission:	January 2018

Reports of this/these required pediatric postmarketing study(ies) must be submitted as a BLA or as a supplement to your approved BLA with the proposed labeling changes you believe are warranted based on the data derived from these studies. When submitting the reports, please clearly mark your submission "**SUBMISSION OF REQUIRED PEDIATRIC ASSESSMENTS**" in large font, bolded type at the beginning of the cover letter of the submission.

POSTMARKETING COMMITMENTS NOT SUBJECT TO THE REPORTING REQUIREMENTS UNDER SECTION 506B

We remind you of your postmarketing commitments:

PMC#1 Re-assess the bioburden action limits for the formulated drug product step (b) (4) based on the manufacturing scale data from 30 released drug product lots.

The timetable you submitted on July 7, 2011, states that you will conduct this study according to the following schedule:

Final Report Submission:	December 2014

PMC#2 Collect bioburden data at the drug product (b) (4) step and set appropriate bioburden limits for this step.

The timetable you submitted on July 7, 2011, states that you will conduct this study according to the following schedule:

Final Report Submission:	December 2014

PMC#3 Provide information and summary data on the product specific container closure integrity test (CCIT) method and provide an updated post-marketing stability protocol replacing the sterility test with CCIT.

The timetable you submitted on July 7, 2011, states that you will conduct this study according to the following schedule:

Final Report Submission: December 2012

PMC#4 Re-evaluate the acceptance criteria for drug product specifications based on manufacturing data from at least 30 released commercial lots and data from lots used in clinical trials.

The timetable you submitted on July 26, 2011, states that you will conduct this study according to the following schedule:

Final Report Submission: March 2015

PMC#5 Establish separate release and shelf-life limits and/or acceptance criteria for product attributes that are stability indicating and submit a PMC final report.

The timetable you submitted on July 26, 2011, states that you will conduct this study according to the following schedule:

Final Report Submission: March 2012

PMC#6 Develop and validate a quantitative IEF specification using a method such as CE-IEF and submit a PMC final report.

The timetable you submitted on July 26, 2011, states that you will conduct this study according to the following schedule:

Final Report Submission: July 2013

PMC#7 Develop and validate a quantitative B7 binding specification that includes measurements of Keq and/or kd using a method such SPR and submit a PMC final report.

The timetable you submitted on July 26, 2011, states that you will conduct this study according to the following schedule:

Final Report Submission: July 2013

PMC#8 Develop characterization methodology for micron and submicron subvisible particulates using stressed and/or accelerated drug product samples to assess whether a correlation may exist between subvisible particulates in the micron and submicron ranges and propose an appropriate control strategy for drug product based on the risks to product quality when stored under the approved conditions.

The timetable you submitted on July 26, 2011, states that you will conduct this study according to the following schedule:

Final Report Submission: March 2013

PMC#9 Perform real time and accelerated stability studies on two additional batches of drug product produced from drug substance manufactured (b) (4) in accordance with the time points specified in the approved post-approval stability protocol and submit a PMC final report.

The timetable you submitted on July 26, 2011, states that you will conduct this study according to the following schedule:

Final Report Submission: February 2015

PMC#10 Provide the results of the extractables analysis under the appropriate exaggerated conditions using the prefilled syringe components that come into contact with the drug (b) (4) .

Provide results of leachables analysis on one lot of the drug product in the assembled prefilled syringe unit using the Drug Product Vehicle with the Active Pharmaceutical Ingredient, as extraction medium. This data will include the real-time conditions 2°-8°C, as well as at the accelerated storage condition of 25°C/60% RH at multiple stability time-points throughout the shelf life of the product. Leachable analysis to employ validated methods of ICP-MS, LC-DAD and GC-FID. Provide a justification of the sample size used (i.e., number of lots and units within each lot).

The timetable you submitted on July 26, 2011, states that you will conduct this study according to the following schedule:

Final Report Submission: August 2012

Submit clinical protocols to your IND 9391 for this product. Submit nonclinical and chemistry, manufacturing, and controls protocols and all final reports to this BLA. In addition, under 21 CFR 601.70 you should include a status summary of each commitment in your annual progress report of postmarketing studies to this BLA. The status summary should include expected summary completion and final report submission dates, any changes in plans since the last annual report, and, for clinical studies/trials, number of patients entered into each study/trial. All submissions, including supplements, relating to these postmarketing commitments should be prominently labeled "**Postmarketing Commitment Protocol**," "**Postmarketing Commitment Final Report**," or "**Postmarketing Commitment Correspondence**."

PROMOTIONAL MATERIALS

You may request advisory comments on proposed introductory advertising and promotional labeling. To do so, submit, in triplicate, a cover letter requesting advisory comments, the proposed materials in draft or mock-up form with annotated references, and the package insert(s) to:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Drug Marketing, Advertising, and Communications
5901-B Ammendale Road
Beltsville, MD 20705-1266

As required under 21 CFR 601.12(f)(4), you must submit final promotional materials, and the package insert(s), at the time of initial dissemination or publication, accompanied by a Form FDA 2253. For instruction on completing the Form FDA 2253, see page 2 of the Form. For more information about submission of promotional materials to the Division of Drug Marketing, Advertising, and Communications (DDMAC), see http://www.fda.gov/AboutFDA/CentersOffices/CDER/ucm090142.htm.

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 Colette Jackson, Senior Regulatory Health Project Manager, at (301) 796-1230.

Sincerely,

/Badrul A. Chowdhury, M.D., Ph.D./
Badrul A. Chowdhury, M.D., Ph.D.
Director
Division of Pulmonary, Allergy, and Rheumatology Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

ENCLOSURE(S):
Content of Labeling
Carton and Container Labeling