



DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration  
Silver Spring MD 20993

BLA 125057/128

**SUPPLEMENT BLA APPROVAL**

March 14, 2011

Abbott Laboratories  
200 Abbott Park Road  
Dept. PA76  
BLDG. AP30-1NE  
Abbott Park, IL 60064

Attention: Bryan Peterson, Ph.D.  
Associate Director, Global Pharmaceutical Regulatory Affairs

Dear Mr. Peterson:

Please refer to your Supplemental Biologics License Application (sBLA 125057/128) dated December 21, 2007, received December 21, 2007, under section 351 of the Public Health Service Act for HUMIRA (adalimumab).

We acknowledge receipt of your amendments dated March 21, May 16, October 28, 2008, and February 6, April 1, December 8, 2009, and July 2, and November 29, 2010, and January 28, February 28, and March 4, and 9, 2011. We also acknowledge your risk evaluation and mitigation strategy (REMS) assessment dated February 28, 2011.

This "Prior Approval" labeling supplement to your biologics license application provides for addition of the following information to the Full Prescribing Information: hepatosplenic T-cell lymphoma (HSTCL) to the Boxed Warnings and Warnings and Precautions sections; serious infection with the concomitant use with abatacept or anakinra to the Warnings and Precautions section; and diverticulitis, appendicitis, pancreatitis, and Stevens Johnson syndrome to the Postmarketing Experience subsection of the Adverse Reactions section. This supplement also provides for revisions to the Medication Guide and the patients instructions for use for the Humira Pen and the Humira Pre-Filled Syringe, as well as new postmarketing safety information to incorporate changes approved by FDA in other supplements, and a proposed modification to the approved REMS.

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.

## **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, text for the patient package insert, 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>. For administrative purposes, please designate this submission “**Product Correspondence – Final SPL for approved BLA STN 125057/128.**”

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.

We request that the labeling approved today be available on your website within 10 days of receipt of this letter.

## **RISK EVALUATION AND MITIGATION STRATEGY REQUIREMENTS**

The REMS for HUMIRA (adalimumab) was originally approved on April 8, 2010. The REMS consists of a Medication Guide, a communication plan, and a timetable for submission of assessments of the REMS. Your proposed modification to the REMS consists of a revised Medication Guide that updates the safety information associated with the use of Humira (adalimumab).

Your proposed modified REMS submitted on March 9, 2011, and appended to this letter, is approved.

The timetable for submission of assessments of the REMS will remain the same as that approved on April 8, 2010.

There are no changes to the REMS assessment plan described in our April 8, 2010 letter.

We remind you that assessments of an approved REMS must include, under section 505-1(g)(3)(B) and (C), information on the status of any postapproval study or clinical trial required under section 505(o) or otherwise undertaken to investigate a safety issue. With respect to any such postapproval study, you must include the status of such study, including whether any difficulties completing the study have been encountered. With respect to any such postapproval

clinical trial, you must include the status of such clinical trial, including whether enrollment has begun, the number of participants enrolled, the expected completion date, whether any difficulties completing the clinical trial have been encountered, and registration information with respect to requirements under subsections (i) and (j) of section 402 of the Public Health Service Act. You can satisfy these requirements in your REMS assessments by referring to relevant information included in the most recent annual report required under section 506B and 21 CFR 601.70 and including any material or significant updates to the status information since the annual report was prepared. Failure to comply with the REMS assessments provisions in section 505-1(g) could result in enforcement action.

In addition to the assessments submitted according to the timetable included in the approved REMS, you must submit a REMS assessment and may propose a modification to the approved REMS when you submit a supplemental application for a new indication for use as described in section 505-1(g)(2)(A) of FDCA.

Prominently identify the submission containing the REMS assessments or proposed modifications of the REMS with the following wording in bold capital letters at the top of the first page of the submission as appropriate:

**BLA 125057 REMS ASSESSMENT**

**NEW SUPPLEMENT FOR BLA 125057  
PROPOSED REMS MODIFICATION  
REMS ASSESSMENT**

**NEW SUPPLEMENT (NEW INDICATION FOR USE)  
FOR BLA 125057  
REMS ASSESSMENT  
PROPOSED REMS MODIFICATION (if included)**

If you do not submit electronically, please send 5 copies of REMS-related submissions.

**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>.

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 package labeling. Within 7 days of receipt of this letter, submit your statement of intent to comply with 21 CFR 601.12(a)(4) to the address above or by fax to 301-847-8444.

### **LETTERS TO HEALTH CARE PROFESSIONALS**

If you decide to issue a letter communicating important safety-related information about this drug product (i.e., a “Dear Health Care Professional” letter), we request that you submit, at least 24 hours prior to issuing the letter, an electronic copy of the letter to this BLA to the following address:

MedWatch Program  
Office of Special Health Issues  
Food and Drug Administration  
10903 New Hampshire Ave  
Building 32, Mail Stop 5353  
Silver Spring, MD 20993

### **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 Sadaf Nabavian, Regulatory Project Manager, at (301) 796-2777.

Sincerely,

Sally Seymour, M.D.  
Deputy Director for Safety  
Division of Pulmonary, Allergy, and Rheumatology  
Products  
Office of Drug Evaluation II  
Center for Drug Evaluation and Research

ENCLOSURE(S):  
Content of Labeling, REMS