



BLA 103951/5337

**SUPPLEMENT APPROVAL
REMS MODIFICATION**

Amgen
Attention: Audrey Mancini, B.S
Senior Manager, Regulatory Affairs
One Amgen Center Drive
Mail Stop 17-2-C
Thousand Oaks, CA 91320-1799

Dear Ms. Mancini:

Please refer to your Supplemental Biologics License Application (sBLA), dated February 22, 2013, received February 25, 2013, submitted under section 351(a) of the Public Health Service Act for Aranesp[®] (darbepoetin alfa).

We acknowledge receipt of your amendment dated March 21, 2013.

This "Prior Approval" supplemental biologics application provides for a proposed modification to the approved risk evaluation and mitigation strategy (REMS) to eliminate the requirement of prescriber and hospital re-enrollment every three years in the ESA APPRISE Oncology Program.

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 REMS.

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.

Because none of these criteria apply to your application, you are exempt from this requirement.

RISK EVALUATION AND MITIGATION STRATEGY REQUIREMENTS

The REMS for Aranesp[®] (darbepoetin alfa) was originally approved on February 16, 2010, and a REMS modification was approved on June 24, 2011, and last modified on May 31, 2012. The REMS consists of a Medication Guide, communication plan, elements to assure safe use, implementation system, and a timetable for submission of assessments of the REMS. Your proposed modification to the REMS consists of removal of the requirement of prescriber and hospital re-enrollment every three years in the ESA APPRISE Oncology Program.

Your proposed modified REMS, submitted on March 21, 2013, and appended to this letter, is approved.

Also within 14 days, amend all pending supplemental applications that include modifications to the REMS for Aranesp[®] (darbepoetin alfa) for this BLA, including pending “Changes Being Effected” (CBE) supplements, for which FDA has not yet issued an action letter, in MS Word format that includes the changes approved in this supplemental application.

The timetable for submission of assessments of the REMS will remain the same as that approved on February 16, 2010.

There are no changes to the REMS assessment plan described in our February 16, 2010 letter.

The requirements for assessments of an approved REMS under section 505-1(g)(3) include with respect to each goal included in the strategy, an assessment of the extent to which the approved strategy, including each element of the strategy, is meeting the goal or whether 1 or more such goals or such elements should be modified.

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 the Food Drug and Cosmetic Act.

If the assessment instruments and methodology for your REMS assessments are not included in the REMS supporting document, or if you propose changes to the submitted assessment instruments or methodology, you should update the REMS supporting document to include specific assessment instrument and methodology information at least 90 days before the assessments will be conducted. Updates to the REMS supporting document may be included in a new document that references previous REMS supporting document submission(s) for unchanged portions. Alternatively, updates may be made by modifying the complete previous REMS supporting document, with all changes marked and highlighted. Prominently identify the submission containing the assessment instruments and methodology with the following wording in bold capital letters at the top of the first page of the submission:

**BLA 103951 REMS CORRESPONDENCE
(insert concise description of content in bold capital letters, e.g.,
UPDATE TO REMS SUPPORTING DOCUMENT - ASSESSMENT
METHODOLOGY**

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 103951 REMS ASSESSMENT

**NEW SUPPLEMENT FOR BLA 103951
PROPOSED REMS MODIFICATION**

**NEW SUPPLEMENT (NEW INDICATION FOR USE)
FOR BLA 103951
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
Office of Prescription Drug Promotion
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 Office of Prescription Drug Promotion (OPDP), 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 Ms. Diane Leaman, Safety Regulatory Project Manager, at (301) 796-1424.

Sincerely,

{See appended electronic signature page}

Robert C. Kane, M.D.
Deputy Director for Safety
Division of Hematology Products
Office of Hematology and Oncology Products
Center for Drug Evaluation and Research

ENCLOSURE:
REMS

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

/s/

ANN T FARRELL
03/27/2013
For Dr. Kane