



NDA 021880/S-031

**SUPPLEMENT APPROVAL**

Celgene Corporation  
86 Morris Avenue  
Summit, New Jersey 07901

Attention: Marion Ceruzzi, PhD  
Director, Regulatory Affairs

Dear Dr. Ceruzzi:

Please refer to your Supplemental New Drug Application (sNDA) dated March 28, 2012, received March 29, 2012, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Revlimid<sup>®</sup> (lenalidomide) capsules 2.5, 5, 10, 15, and 25 mg.

We acknowledge receipt of your amendments dated April 4, April 9, and May 1, 2012 and your risk evaluation and mitigation strategy (REMS) assessment dated August 3, 2011.

This "Prior Approval" supplemental new drug application provides for updates to the Medication Guide to ensure consistency with the US Package Insert approved in Supplement 28. The proposed updates include the addition of the 2.5 mg dose, the risk of second primary malignancies, notification for the presence of lactose in Revlimid, and warning of the presence of Revlimid in human semen. Your approved Medication Guide will remain part of the REMS. In addition, this supplement provides for updates to the Revlimid<sup>®</sup> Patient-Physician Agreement form for adult male and male child regarding the statement that Revlimid<sup>®</sup> is present in human semen. These forms were updated and remain part of the 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 the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format using the FDA automated drug registration and listing system (eLIST), as described at <http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm>. Content of labeling must be identical to the enclosed labeling (text for the Medication Guide), with the addition of any labeling changes in pending "Changes Being Effected" (CBE) supplements, as well as annual reportable changes not included in the enclosed labeling.

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/DrugsGuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf>.

The SPL will be accessible from publicly available labeling repositories.

Also within 14 days, amend all pending supplemental applications for this NDA, including CBE supplements for which FDA has not yet issued an action letter, with the content of labeling [21 CFR 314.50(l)(1)(i)] in MS Word format, that includes the changes approved in this supplemental application, as well as annual reportable changes and annotate each change. To facilitate review of your submission, provide a highlighted or marked-up copy that shows all changes, as well as a clean Microsoft Word version. The marked-up copy should provide appropriate annotations, including supplement number(s) and annual report date(s).

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

#### **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.

#### **POSTMARKETING REQUIREMENTS AND COMMITMENTS SUBJECT TO REPORTING REQUIREMENTS UNDER SECTION 506B**

We remind you that there is a postmarketing requirement and a postmarketing commitment subject to reporting requirements under section 506B listed in the June 29, 2006 approval letter that are still open.

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

The REMS for Revlimid<sup>®</sup> (lenalidomide) capsules was originally approved on August 3, 2010. 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 modifications to the REMS consist of a revised Medication Guide to include information about the risk of second primary malignancies, the addition of the 2.5 mg dosage form, warning that Revlimid<sup>®</sup> (lenalidomide) capsules is present in human semen, and notification of the presence of lactose in Revlimid<sup>®</sup> (lenalidomide) capsules.

Your modified REMS, submitted on May 1, 2012, and appended to this letter, is approved.

The timetable for submission of assessments of the REMS will remain the same as that approved on August 3, 2010.

There are no changes to the REMS assessment plan described in our August 3, 2010 letter.

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.

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:

**NDA 021880 REMS CORRESPONDENCE  
(insert concise description of content in bold capital letters, e.g.,  
UPDATE TO REMS SUPPORTING DOCUMENT - ASSESSMENT  
METHODOLOGY)**

An authorized generic drug under this NDA must have an approved REMS prior to marketing. Should you decide to market, sell, or distribute an authorized generic drug under this NDA, contact us to discuss what will be required in the authorized generic drug REMS submission.

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:

**NDA 021880 REMS ASSESSMENT**

**NEW SUPPLEMENT FOR NDA 021880  
PROPOSED REMS MODIFICATION  
REMS ASSESSMENT**

**NEW SUPPLEMENT (NEW INDICATION FOR USE)  
FOR NDA 021880  
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 the following, in triplicate, (1) a cover letter requesting advisory comments, (2) the proposed materials in draft or mock-up form with annotated references, and (3) the package insert(s) to:

Food and Drug Administration  
Center for Drug Evaluation and Research  
Office of Prescription Drug Promotion (OPDP)  
5901-B Ammendale Road  
Beltsville, MD 20705-1266

You must submit final promotional materials and package insert(s), accompanied by a Form FDA 2253, at the time of initial dissemination or publication [21 CFR 314.81(b)(3)(i)]. Form FDA 2253 is available at <http://www.fda.gov/opacom/morechoices/fdaforms/cder.html>; instructions are provided on 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>.

All promotional materials that include representations about your drug product must be promptly revised to be consistent with the labeling changes approved in this supplement, including any new safety information [21 CFR 314.70(a)(4)]. The revisions in 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 314.70(a)(4) to the address above or by fax to 301-847-8444.

## **REPORTING REQUIREMENTS**

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

If you have any questions, call Theresa Ferrara, Regulatory Project Manager, at (301) 796-2848.

Sincerely,

*{See appended electronic signature page}*

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

ENCLOSURE:  
Content of Labeling  
REMS

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

/s/  
-----

ROBERT C KANE  
05/09/2012