



NDA 021880/S-041

**SUPPLEMENT APPROVAL  
REMS MODIFICATION**

Celgene Corporation  
Attention: Maricel Fong, PharmD  
Senior Manager, Regulatory Affairs  
400 Connell Drive, Suite 7000  
Berkeley Heights, NJ 07922

Dear Dr. Fong:

Please refer to your Supplemental New Drug Application (sNDA) dated April 22, 2014, received April 22, 2014, 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, 20, and 25 mg.

We acknowledge receipt of your amendments dated May 19; June 11 and 20; July 15; August 21 and 26; September 2, 15, 23, and 29; October 13, 16, 20, 21, 24, and 28; November 5 and 11, 2014; January 30; and February 11, 2015; and your risk evaluation and mitigation strategy (REMS) assessment dated April 22, 2014.

This "Prior Approval" supplemental new drug application proposes to expand the indication for Revlimid<sup>®</sup> (lenalidomide) to include: Revlimid<sup>®</sup> (lenalidomide) in combination with dexamethasone is indicated for the treatment of patients with multiple myeloma. This supplement also proposes a modification to the approved Revlimid<sup>®</sup> (lenalidomide) REMS materials, which are a part of the REMS.

**APPROVAL & LABELING**

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.

**WAIVER OF HIGHLIGHTS SECTION**

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 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 package insert and 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 that includes labeling changes 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 this drug product for this indication has an orphan drug designation, you are exempt from this requirement.

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

The REMS for Revlimid<sup>®</sup> (lenalidomide) was originally approved on August 3, 2010 and REMS modifications were approved on May 9, 2012; February 8, 2013; June 5, 2013; November 15, 2013, and the REMS was last modified on September 12, 2014. The REMS consists of elements

to assure safe use, an implementation system, and a timetable for submission of assessments of the REMS.

Your proposed modification to the REMS includes incorporating the new proposed indication for Revlimid<sup>®</sup> (lenalidomide) in combination with dexamethasone for the treatment of multiple myeloma. The following REMS materials contain an indication statement and have been modified to include the new indication:

1. Prescriber Guide to the Revlimid REMS Program
2. Revlimid Risk Evaluation and Mitigation Strategy (REMS) Program Education and Safety Kit
3. Revlimid REMS website
4. Welcome Letter

We remind you that section 505-1(f)(8) of FDCA prohibits holders of an approved covered application with elements to assure safe use from using any element to block or delay approval of an application under section 505(b)(2) or (j). A violation of this provision in 505-1(f) could result in enforcement action.

Your proposed modified REMS, submitted on October 28, 2014, 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 November 15, 2013, letter.

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

**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/downloads/AboutFDA/ReportsManualsForms/Forms/UCM083570.pdf>. Information and Instructions for completing the form can be found at <http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM375154.pdf>. 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 Laura Wall, Regulatory Project Manager, at (301) 796-2237.

Sincerely,

*{See appended electronic signature page}*

Ann T. Farrell, MD

Director

Division of Hematology Products

Office of Hematology and Oncology Products

Center for Drug Evaluation and Research

### ENCLOSURES:

Content of Labeling

REMS

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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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ANN T FARRELL  
02/17/2015