DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 21880/S-034

SUPPLEMENT APPROVAL
REMS MODIFICATION APPROVAL

Celgene Corporation
Attention: Katerina Tsironi, MBA
Associate Director, Regulatory Affairs
400 Connell Drive, Suite 7000
Connell Corporate Park
Berkeley Heights, NJ 07922

Dear Ms. Tsironi:

Please refer to your Supplemental New Drug Application (sNDA) dated December 5, 2012, received December 5, 2012, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Revlimid® (lenalidomide) capsules 2.5, 5, 10, 15, 20, and 25 mg.

We acknowledge receipt of your amendments dated February 15 and 22, 2013; March 15, 21, 26, 28, and 29, 2013; April 11 (2) 2013, May 9, 16, 29, and 31, 2013, and June 5, 2013 and your risk evaluation and mitigation strategy (REMS) assessment dated May 29, 2013.

This "Prior Approval" supplemental new drug application provides for a new indication for Revlimid® (lenalidomide) capsules in patients with Mantle Cell Lymphoma whose disease has relapsed or progressed after two prior therapies, one of which included bortezomib, and a proposed modification to the approved REMS to include this new indication. In addition, this supplement provides for a new dosage strength in the form of a 20 mg capsule.

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. In addition, we have found the REMS assessment to be adequate.

We remind you that your NDA is approved under the provisions of 21 CFR 314.520. Marketing of this drug product and related activities must adhere to the substance and procedures of the referenced regulations (21 CFR 314.550) until you are notified 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.

CARTON AND IMMEDIATE CONTAINER LABELS

Submit final printed carton and container labels that are identical to the enclosed carton and immediate container labels submitted on May 29, 2013 as soon as they are available, but no more than 30 days after they are printed.

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 COMMITMENTS SUBJECT TO REPORTING REQUIREMENTS UNDER SECTION 506B

We remind you of your postmarketing commitment:

PMC 2048-1 Continue to follow patients enrolled in trial CC-5013-MCL-001 for at least 4 years from the date that the last patient enrolled. Submit a report to the Agency describing the cumulative efficacy and safety data up to this 4 year time point.

The timetable you submitted on May 16, 2013, states that you will conduct this trial according to the following schedule:

Final Protocol Submission:	completed
Trial Completion:	03/2016
Final Report Submission:	12/2016

Submit clinical protocols to your IND 60100 for this product. Submit nonclinical and chemistry, manufacturing, and controls protocols and all postmarketing final reports to this NDA. In addition, under 21 CFR 314.81(b)(2)(vii) and 314.81(b)(2)(viii) you should include a status summary of each commitment in your annual report to this NDA. 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**."

RISK EVALUATION AND MITIGATION STRATEGY REQUIREMENTS

The REMS for Revlimid was originally approved on August 3, 2010, and a REMS modification was approved on May 9, 2012, and last modified on February 8, 2013. The REMS consists of 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 incorporating the new indication for Revlimid® (lenalidomide) capsules for the treatment of patients with mantle cell lymphoma whose disease has relapsed or progressed after two prior therapies, one of which included bortezomib, and to include a new 20 mg capsule.

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 May 31, 2013, 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 February 8, 2013 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 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 submissions 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 21880 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 21880 REMS ASSESSMENT

NEW SUPPLEMENT FOR NDA 21880
PROPOSED REMS MODIFICATION

NEW SUPPLEMENT (NEW INDICATION FOR USE)
FOR NDA 21880
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.

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 Carioti, Regulatory Project Manager, at (301) 796-2848.

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
Container Labeling
REMS

DOCKET ALARM

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Docket Alarm provides insights to develop a more informed litigation strategy and the peace of mind of knowing you're on top of things.

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Litigation and bankruptcy checks for companies and debtors.

E-DISCOVERY AND LEGAL VENDORS
Sync your system to PACER to automate legal marketing.