DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 021880/S-029/S-033

SUPPLEMENT APPROVAL
REMOVE REMS ELEMENT

Celgene Corporation
Marion Ceruzzi, PhD
Director of Regulatory Affairs
400 Connell Drive
Building 400, Suite 7000
Berkeley Heights, NJ 07922

Dear Dr. Ceruzzi:

Please refer to your Supplemental New Drug Applications (sNDA) dated December 29, 2011, received December 29, 2011, and November 7, 2012, received November 8, 2012, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Revlimid® (lenalidomide) Capsules 2.5, 5, 10, 15, and 25 mg.

We acknowledge receipt of your amendments dated January 12, 2012; February 1, 2012; August 6, 2012; November 21 and 27, 2012; December 6 and 19, 2012; February 6 and 7, 2013; and your risk evaluation and mitigation strategy (REMS) assessment dated August 3, 2012.

This "Prior Approval" sNDA S-029 provides for proposed modifications to the approved risk evaluation and mitigation strategy (REMS) that harmonizes the REMS programs for Revlimid® (lenalidomide) Capsules, Thalomid® (thalidomide) capsules, and Pomalyst (pomalidomide) capsules. Additionally, this sNDA proposes to eliminate the requirement for the approved Revlimid® (lenalidomide) Capsules Medication Guide as an element of the approved Revlimid® (lenalidomide) Capsules REMS.

The "Changes Being Effected" (CBE) sNDA, S-033, provides for the addition of new QTc information to the Pharmacodynamics Section 12.2 of the Revlimid® (lenalidomide) Capsules US Package Insert.

We have completed our review of these supplemental applications, as amended. They are 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 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 none of these criteria apply to your application, you are exempt from this requirement.

POSTMARKETING COMMITMENT SUBJECT TO REPORTING REQUIREMENTS UNDER SECTION 506B

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

RISK EVALUATION AND MITIGATION STRATEGY REQUIREMENTS

The REMS for Revlimid® (lenalidomide) Capsules was originally approved on August 3, 2010, and the most recent REMS modification was approved on May 9, 2012. The REMS consists of a Medication Guide, 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 eliminating the requirement for the Medication Guide as an element of the REMSand harmonizing the REMS programs for Revlimid® (lenalidomide) Capsules and Thalomid® (thalidomide).

We have determined that maintaining the Medication Guide as part of the approved labeling is adequate to address the serious and significant public health concern and meets the standard in 21 CFR 208.1. Therefore, it is no longer necessary to include the Medication Guide as an element of the approved REMS to ensure that the benefits of Revlimid® (lenalidomide) Capsules outweigh the risks. Therefore, we agree with your proposal, and a Medication Guide is no longer required as part of the REMS for Revlimid® (lenalidomide) Capsules.

Your proposed modified REMS, submitted on February 7, 2013, and appended to this letter, is approved.

The modified REMS consists of elements to assure safe use, implementation system, and a timetable for submission of assessments of the REMS. We remind you that the Medication Guide will continue to be part of the approved labeling for Revlimid® (lenalidomide) Capsules in accordance with 21 CFR 208.

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

The revised REMS assessment plan eliminates information regarding distribution and dispensing of the Medication Guide and the periodic surveys of prescribers and patients. The revised REMS assessment plan should include, but is not limited to, the following:

1. Pregnancies:

    a. Number of pregnancies reported during the current REMS assessment reporting period and during each previous REMS assessment reporting period;

    b. Outcome of each pregnancy;

    c. Follow-up of outstanding pregnancy reports from previous assessment reporting period;

    d. Root cause analysis of each reported pregnancy; and

    e. Discussion of any new information provided in the most recent Periodic Safety Update Report (PSUR) regarding pregnancy. In the electronic REMS assessment submission, include a hyperlink to the most recent PSUR that provides information on worldwide pregnancies.

2. Reporting on the restricted distribution program:

a. Number of pharmacies and physicians certified, and patients enrolled during the current REMS assessment reporting period and during each previous REMS assessment reporting period;

b. Patient demographics for the current REMS assessment reporting period and for previous REMS assessment reporting periods to include gender, age, diagnosis, females of reproductive potential (FRP); and

c. Number of female patients for whom pregnancy testing can be discontinued because menopause has been documented by follicle-stimulating hormone/luteinizing hormone (FSH/LH) levels during this REMS assessment reporting period and for previous REMS assessment reporting periods.

3. Documentation of safe use conditions

Based on information collected through patient enrollment and mandatory surveys that are used to document safe use conditions, provide information on:

a. Flagged prescriptions/documentations of safe use of particular interest include those that have the potential of allowing pregnant patients access to the drug, and those that result in a delay or interruption of treatment. Provide the following, relative to flagged prescriptions/documentation of safe use:

i. A list of identified flags, the reasons for the flags, and the actions taken to correct. Provide for the reporting period (by month); and summarize findings from each previous assessment report.

ii. Provide the number and proportion of flagged prescriptions intended for an FRP due to lack of documentation of a negative pregnancy test, positive pregnancy test, and/or a delay in obtaining a pregnancy test.

iii. Provide the number and proportion of flags that caused a delay in treatment initiation or a gap in therapy for patients. Provide the time to resolution of flags (mean, minimum, maximum) and include a graph of time to resolution versus numbers of prescriptions (or number of mandatory surveys conducted to document safe use conditions) for the reporting period and for each previous reporting period

We remind you that each REMS assessment report must be submitted with the title of the report stating that this is a REMS assessment report, and each report must address all items in the REMS assessment plan outlined in this approval 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 one 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 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 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}

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

ENCLOSURE(S):
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
02/08/2013