DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 020785/S-050

SUPPLEMENT APPROVAL
REMS ASSESSMENT ACKNOWLEDGEMENT
REMS ASSESSMENT PLAN REVISION

Celgene Corporation
Attention: Marion Ceruzzi, PhD
Senior Director, Regulatory Affairs
400 Connell Drive, Suite 7000
Connell Corporate Park
Berkley Heights, NJ 07922

Dear Dr. Ceruzzi:

Please refer to your Supplemental New Drug Application (sNDA) dated May 17, 2013, received May 17, 2013, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Thalomid® (thalidomide) capsules 50, 100, 150, and 250 mg.

We acknowledge receipt of your amendments dated July 19, September 16, and October30, 2013, and your risk evaluation and mitigation strategy (REMS) assessment dated August 2, 2013. We have found the REMS assessment to be complete.

This "Prior Approval" supplemental new drug application (S-050) provides for proposed modifications to the REMS to continue the harmonization of the REMS for Thalomid® (thalidomide), Revlimid® (lenalidomide), and Pomalyst® (pomalidomide) capsules, that began with the February 8, 2013 approval of the REMS modifications for Revlimid® (lenalidomide) and Thalomid® (thalidomide) capsules, and the approval of the REMS for Pomalyst® (pomalidomide) capsules.

APPROVAL

We have completed our review of this supplemental application, as amended. It is approved, effective on the date of this letter. Your proposed modified REMS, submitted on October 30, 2013, and appended to this letter, is approved.

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 Thalomid® (thalidomide) capsules was originally approved on August 3, 2010. The REMS consists of elements to assure safe use, an implementation system, and a timetable for submission of assessments of the REMS. Your proposed modifications to the REMS consist of the following:

1. Harmonization of the REMS with Revlimid® (lenalidomide), and Pomalyst® (pomalidomide) capsules
2. Addition and implementation of a pharmacy portal to facilitate pharmacy activity within the REMS
3. Dispensing Thalomid® (thalidomide) through certified pharmacies
4. Harmonization of the training that pharmacists receive to dispense Thalomid® (thalidomide) capsules with the training pharmacists receive for Revlimid® (lenalidomide) and Pomalyst® (pomalidomide) capsules

In addition, the REMS assessment plan will now include implementation of a survey of contraceptive use in females of reproductive potential and a survey of knowledge for pharmacists.

Your proposed modified REMS, submitted on October 30, 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.

Our February 8, 2013REMS modification approval letter described the REMS assessment plan. The REMS assessment plan should be revised to include the results from the Pharmacist Risk Assessment Survey Protocol of pharmacist understanding of the serious risks and safe-use conditions, and the results from the Adult Female of Reproductive Potential (AFRP) Contraception Choice Survey Protocol regarding contraceptive use.

The revised REMS assessment plan now includes two additional components - the addition of results of pharmacist survey of knowledge regarding the serious risks and safe-use conditions and patient survey data including documentation of choice of contraception. The revised REMS assessment plan should include, but is not limited to, the following:

1. Pregnancies:
    a. Number of pregnancies reported during the REMS assessment reporting period and annually for each REMS 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

e. Link to most recent Periodic Safety Update Report (PSUR) or Periodic Benefit-Risk Evaluation Report (PBRER) that provides information on worldwide pregnancies. Discussion of any new information provided in the PSUR or PBRER regarding pregnancy

2. Reporting on the restricted distribution program:

   a. The 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)

   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 summary of identified flags, the reasons for the flags, and the actions taken to correct. Provide for the reporting period; and summarize findings from each previous assessment report.

         ii. 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. The number and proportion of flags that caused a delay in treatment initiation or a gap in therapy for patients. 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.

4. Results of pharmacist survey of knowledge regarding the serious risks and safe-use conditions.

5. Using patient survey data, documentation of choice of contraception (information from patients of method/use), and of changes to methods used (numbers of FRP using method at entry and ongoing): numbers/proportions using highly effective form of birth control; number/proportions using other less effective forms of birth control.

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 020785 REMS CORRESPONDENCE
(insert concise description of content in bold capital letters, e.g.,
UPDATE TO REMS SUPPORTING DOCUMENT - ASSESSMENT METHODOLOGY

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.

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 020785 REMS ASSESSMENT

NEW SUPPLEMENT FOR NDA 020785
PROPOSED REMS MODIFICATION

NEW SUPPLEMENT (NEW INDICATION FOR USE)
FOR NDA 020785
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 Amy Baird, Regulatory Project Manager, at (301) 796-4969.

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:
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
11/15/2013