DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 204026/S-005/S-006/S-008

SUPPLEMENT APPROVAL
FULFILLMENT OF POSTMARKETING REQUIREMENTS

Celgene Corporation
Attention: Emmanuel Gutierrez
Manager, Regulatory Affairs
400 Connell Drive, Suite 7000
Berkeley Heights, NJ 07922

Dear Mr. Gutierrez:

Please refer to your Supplemental New Drug Applications (sNDAs); S-005 dated April 30, 2014, received April 30, 2014; S-006 dated June 29, 2014, received June 30, 2014; and S-008 dated March 3, 2015, received March 3, 2015, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for POMALYST® (pomalidomide) capsules, 1, 2, 3, and 4 mg.

We acknowledge receipt of your amendments dated May 20; June 30; September 3 and 16; October 24; and November 6 , 2014; March 25; April 7, 9, 10, 14 and 20, 2015
The "Changes Being Effected" supplemental new drug application, S-005, provides for updates to the package insert regarding Tumor Lysis Syndrome and Pancytopenia.

The "Prior Approval" supplemental new drug application, S-006, provides for proposed modifications to the approved risk evaluation and mitigation strategy (REMS) for POMALYST® (pomalidomide), and revision of the approved indication. The revised indication, based upon results from CC-4047-MM-003, is "POMALYST, in combination with dexamethasone, is indicated for patients with multiple myeloma who have received at least two prior therapies including lenalidomide and a proteasome inhibitor and have demonstrated disease progression on or within 60 days of completion of the last therapy." Your June 30, 2014 submission under S-006 also contains the final report for PMR 2006-8, listed below. In addition, this final report addresses PMR 2006-1, listed below.

The "Changes Being Effected" supplemental new drug application, S-008, provides for the addition of angioedema information to the Dosage and Administration, Warning and Precautions, and Adverse Reactions sections of the package insert.

We also refer to your December 30, 2014 submission that provides for the final report of the QT prolongation trial required under PMR 2006-9.

We also refer to your May 14 and June 30, 2014 submissions containing the final report for trial CC-4047-MM-003 required under PMR 2006-8.

APPROVAL & LABELING

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, , 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.

SUBPART H FULFILLED

We approved this NDA under the regulations at 21 CFR 314 Subpart H for accelerated approval of new drugs for serious or life-threatening illnesses. Approval of Supplement S-006 fulfills your requirements made under 21 CFR 314.510.

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 indications 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.

FULFILLMENT OF POSTMARKETING REQUIREMENTS

We have received your submissions dated June 30, 2014 (for PMR 2006-1); May 14 and June 30, 2014 (for PMR 2006-8); and December 30, 2014 (for PMR 2006-9), containing the final reports for the following postmarketing requirements listed in the February 8, 2013 approval letter.

We also refer to our supplement approval letter, dated March 13, 2014, that describes fulfillment of PMR 2006-2 listed in the February 8, 2013 approval letter.

PMR 2006-1 Conduct a randomized controlled trial (CC-4047-MM-007) that isolates and demonstrates the efficacy and safety of Pomalyst (pomalidomide) in patients with previously treated multiple myeloma.

Final Protocol Submission:	12/2012 (completed)
Trial Completion:	4/2018
Final Report Submission:	1/2019

PMR 2006-8 Conduct a randomized controlled trial (MM-003) of the combination of pomalidomide and dexamethasone in patients with previously treated multiple myeloma, to determine the safety profile of pomalidomide and dexamethasone combination as compared to a treatment arm without pomalidomide.

The timetable you submitted on February 6, 2013, states that you will conduct this trial according to the following schedule:

Final Protocol Submission:	3/2011 (completed)
Trial Completion:	9/2012 (completed)
Final Report Submission:	6/2013

PMR 2006-9 Conduct a QT prolongation trial, per FDA guidance [E14 Clinical Evaluation of QT/QTc interval Prolongation and Proarrhythmic Potential for Non-

Antiarrhythmic Drugs], to assess the effect of Pomalyst (pomalidomide) on the QT interval.

The timetable you submitted on February 6, 2013, states that you will conduct this trial according to the following schedule:

Final Protocol Submission:	8/2013
Trial Completion:	5/2014
Final Report Submission:	2/2015

We have reviewed your submissions. The results from trial CC-4047-MM-003 submitted to this supplement, along with the fulfillment of PMR 2006-2, have addressed the efficacy and safety of POMALYST® (pomalidomide) for the patient population specified in PMR 2006-1. Therefore, trial CC-4047-MM-007 is no longer needed to address this requirement because it has been fulfilled by submission of other data.

We conclude that the above requirements were fulfilled.

We remind you that there are postmarketing requirements and a postmarketing commitment listed in the February 8, 2013 approval letter that are still open.

RISK EVALUATION AND MITIGATION STRATEGY REQUIREMENTS (REMS)

The REMS for POMALYST® (pomalidomide) was originally approved on February 8, 2013, and 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 consists of the revised indication statement and information about arterial thromboembolism in the appended REMS materials.

Your proposed modified REMS, submitted on April 7, 2015, and appended to this letter, is approved.

The timetable for submission of assessment of the REMS will remain the same as that approved on February 8, 2013.

There are no changes to the REMS assessment plan described in our November 15, 2013 letter.

We remind you that in addition to the REMS assessments submitted according to the timetable in the approved REMS, you must include an adequate rationale to support a proposed REMS modification for the addition, modification, or removal of any of goal or element of the REMS, as described in section 505-1(g)(4) of the FDCA.

We also remind you that 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). This assessment

will be considered the adequate rationale to support any proposed REMS modification and should include:

a) An evaluation of how the benefit-risk profile will or will not change with the new indication;
b) A determination of the implications of a change in the benefit-risk profile for the current REMS;
c) *If the new indication for use introduces unexpected risks*: A description of those risks and an evaluation of whether those risks can be appropriately managed with the currently approved REMS.
d) *If a REMS assessment was submitted in the 18 months prior to submission of the supplemental application for a new indication for use*: A statement about whether the REMS was meeting its goals at the time of that the last assessment and if any modifications of the REMS have been proposed since that assessment.
e) *If a REMS assessment has not been submitted in the 18 months prior to submission of the supplemental application for a new indication for use:* Provision of as many of the currently listed assessment plan items as is feasible.
f) *If you propose a REMS modification based on a change in the benefit-risk profile or because of the new indication of use*: Provision of the reason(s) why the proposed REMS modification is necessary, the potential effect on the serious risk(s) for which the REMS was required, on patient access to the drug, and/or on the burden on the health care delivery system; and other appropriate evidence or data to support the proposed change. Additionally, include any changes to the assessment plan necessary to assess the proposed modified REMS. *If you are not proposing a REMS modification*, provide a rationale for why the REMS does not need to be modified

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 204026 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.

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.

Prominently identify any 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 204026 REMS ASSESSMENT

NEW SUPPLEMENT FOR NDA 204026
CHANGES BEING EFFECTED IN 30 DAYS
< other supplement identification **>**
PROPOSED MINOR REMS MODIFICATION

or

NEW SUPPLEMENT FOR NDA 204026
PRIOR APPROVAL SUPPLEMENT
< other supplement identification **>**
PROPOSED MAJOR REMS MODIFICATION

or

NEW SUPPLEMENT FOR NDA 204026
PRIOR APPROVAL SUPPLEMENT
PROPOSED REMS MODIFICATIONS DUE TO SAFETY LABEL CHANGES SUBMITTED IN SUPPLEMENT XXX

NEW SUPPLEMENT (NEW INDICATION FOR USE)
FOR NDA 204026 REMS ASSESSMENT
< other supplement identification **>**
PROPOSED REMS MODIFICATION (if included)

If you choose to submit a REMS revision, prominently identify the submission containing the REMS revisions with the following wording in bold capital letters at the top of the first page of the submission:

REMS REVISIONS FOR NDA 204026

To facilitate review of your submission, we request that you submit your proposed modified REMS and other REMS-related materials in Microsoft Word format. If certain documents, such as enrollment forms, are only in PDF format, they may be submitted as such, but the preference is to include as many as possible in Word format.

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 Tinya Sensie, Regulatory Project Manager, at (240) 402-4230.

Sincerely,

{See appended electronic signature page}

Edvardas Kaminskas, MD
Deputy Director
Division of Hematology Products
Office of Hematology and Oncology Products
Center for Drug Evaluation and Research

ENCLOSURES:
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/

EDVARDAS KAMINSKAS
04/23/2015