DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 204026

**ACCELERATED APPROVAL**

Celgene Corporation
Attention: Paul McInulty
Director, Regulatory Affairs
400 Connell Drive, Suite 7000
Berkeley Heights, NJ 07922

Dear Mr. McInulty:

Please refer to your New Drug Application (NDA) dated April 10, 2012, received April 10, 2012, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Pomalyst (pomalidomide) capsules.

We acknowledge receipt of your amendments dated April 12; May 11 and 31; July 3, 10, and 20; August 3, 7 (2), 13, 24, and 30; September 7 (2), 18, and 19; October 10, 22, and 29; November 5 and 26; December 4, 7, 14, 17 and 21, 2012; January 4, 7, 10, 14, 22, 24, 28, and 31; February 4, 6 (2), and 7, 2013.

This new drug application provides for the use of Pomalyst (pomalidomide) capsules in the treatment of patients with multiple myeloma who have received at least two prior therapies including lenalidomide and bortezomib and have demonstrated disease progression on or within 60 days of completion of the last therapy.

We have completed our review of this application, as amended. It is approved under the provisions of accelerated approval regulations (21 CFR 314.510), effective on the date of this letter, for use as recommended in the enclosed agreed-upon labeling text. Marketing of this drug product and related activities must adhere to the substance and procedures of the referenced accelerated approval regulations.

## 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). 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/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf.

The SPL will be accessible via publicly available labeling repositories.

## CARTON AND IMMEDIATE CONTAINER LABELS

Submit final printed carton and container labels that are identical to the carton and immediate container labels submitted on January 31, 2013, as soon as they are available, but no more than 30 days after they are printed. Please submit these labels electronically according to the guidance for industry titled "Providing Regulatory Submissions in Electronic Format – Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications (June 2008)." Alternatively, you may submit 12 paper copies, with 6 of the copies individually mounted on heavy-weight paper or similar material. For administrative purposes, designate this submission "**Final Printed Carton and Container Labels for approved NDA 204026**." Approval of this submission by FDA is not required before the labeling is used.

Marketing the product with FPL that is not identical to the approved labeling text may render the product misbranded and an unapproved new drug.

## ADVISORY COMMITTEE

Your application for Pomalyst (pomalidomide) capsules was not referred to an FDA advisory committee because this drug is not the first in its class and the safety profile is similar to that of other drugs or biologics approved for this indication.

## ACCELERATED APPROVAL REQUIREMENTS

Products approved under the accelerated approval regulations, 21 CFR 314.510, require further adequate and well-controlled studies/clinical trials to verify and describe clinical benefit. You are required to conduct such studies/clinical trials with due diligence. If postmarketing studies/clinical trials fail to verify clinical benefit or are not conducted with due diligence, we may, following an opportunity for a hearing in accordance with 21 CFR 314.530, withdraw this

approval. We remind you of your postmarketing requirements specified in your submission dated February 6, 2013. These requirements, along with required completion dates, are listed below.

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 2006-2 Conduct a clinical trial, per FDA guidance [Drug Interaction Studies—Study Design, Data Analysis, Implications for Dosing, and Labeling Recommendations], to determine the effect of CYP3A induction, which may decrease drug exposure, on the PK of Pomalyst (pomalidomide).

Final Report Submission: 9/2013

Submit final reports to this NDA as a supplemental application. For administrative purposes, all submissions relating to these postmarketing requirements must be clearly designated "**Subpart H Postmarketing Requirement**."

## 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.

## POSTMARKETING REQUIREMENTS UNDER 505(o)

Section 505(o)(3) of the FDCA authorizes FDA to require holders of approved drug and biological product applications to conduct postmarketing studies and clinical trials for certain purposes, if FDA makes certain findings required by the statute.

We have determined that an analysis of spontaneous postmarketing adverse events reported under subsection 505(k)(1) of the FDCA will not be sufficient to assess the known serious risk of venous thromboembolic events (VTE). Furthermore, the new pharmacovigilance system that FDA is required to establish under section 505(k)(3) of the FDCA will not be sufficient to assess this serious risk.

Therefore, based on appropriate scientific data, FDA has determined that you are required to conduct the following:

PMR 2006-3 Conduct an observational multi-site inception cohort study of Pomalyst (pomalidomide) users to address the questions detailed below:

1. To determine the failure rate for each of the different types of initial VTE prophylaxis for multiple myeloma patients treated with a Pomalyst (pomalidomide)-containing regimen.

2. To determine the failure rate for each type of VTE treatment for those patients with multiple myeloma and a VTE who continue to receive ongoing treatment with a Pomalyst (pomalidomide)-containing regimen.

3. To determine the failure rate for each type of post-VTE prophylaxis for those patients with multiple myeloma and a VTE who continue to receive ongoing treatment with a Pomalyst (pomalidomide)-containing regimen.

This observational study will enroll relapsed and refractory multiple myeloma patients identified through data sources currently part of the current THAL/REV TEE-01 clinical trial; two managed care databases, and a large claims database.

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

| | |
|---|---|
| Final Protocol Submission: | 6/2013 |
| Study Completion: | 3/2016 |
| Final Report Submission: | 1/2017 |

Finally, we have determined that only clinical trials (rather than nonclinical or observational studies) will be sufficient to:

- Identify an unexpected serious risk of more frequent and/or more severe adverse effects of Pomalyst (pomalidomide) due to increased drug exposure resulting from the effects of hepatic impairment;
- Identify an unexpected serious risk of more frequent and/or more severe adverse effects of Pomalyst (pomalidomide) due to increased drug exposure resulting from the effects of renal impairment;
- Identify an unexpected serious risk of more frequent and/or more severe adverse effects of Pomalyst (pomalidomide) due to increased drug exposure resulting from the effect of CYP3A inhibition;
- Identify an unexpected serious risk of more frequent and/or more severe adverse effects of Pomalyst (pomalidomide) due to increased drug exposure resulting from the effect of food on drug absorption;

- Identify an unexpected serious risk of more frequent and/or more severe adverse effects of Pomalyst (pomalidomide) when it is used in combination with dexamethasone.
- Identify an unexpected serious risk of QT prolongation with Pomalyst (pomalidomide) treatment;

Therefore, based on appropriate scientific data, FDA has determined that you are required to conduct the following:

PMR 2006-4 Conduct a clinical trial, per FDA guidance [Pharmacokinetics in Patients with Impaired Hepatic Function: Study Design, Data Analysis, and Impact on Dosing and Labeling], in patients with baseline hepatic impairment to determine the influence of hepatic impairment on the pharmacokinetics (PK) and safety of Pomalyst (pomalidomide).

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

| | |
|---|---|
| Final Protocol Submission: | 5/2013 |
| Trial Completion: | 5/2015 |
| Final Report Submission: | 2/2016 |

PMR 2006-5 Conduct a clinical trial, per FDA guidance [Pharmacokinetics in Patients with Impaired Renal Function--Study Design, Data Analysis, and Impact on Dosing and labeling, in patients with baseline renal impairment and those on chronic dialysis], to determine the influence of renal impairment on the PK and safety of Pomalyst (pomalidomide).

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

| | |
|---|---|
| Final Protocol Submission: | 5/2013 |
| Trial Completion: | 5/2015 |
| Final Report Submission: | 2/2016 |

PMR 2006-6 Conduct a clinical trial, per FDA guidance [Drug Interaction Studies—Study Design, Data Analysis, Implications for Dosing, and Labeling Recommendations], in order to determine the effect of CYP3A inhibition, which may increase drug exposure and thereby drug toxicity, on Pomalyst (pomalidomide) pharmacokinetics.

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

| | |
|---|---|
| Final Protocol Submission: | 9/2012 (completed) |
| Trial Completion: | 11/2012 (completed) |

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