NDA 204026/S-023

ACCELERATED APPROVAL

Celgene Corporation
Attention: Lisa Suttner
Director, Regulatory Affairs
86 Morris Avenue
Summit, NJ, 07901

Dear Ms. Suttner:

Please refer to your supplemental new drug application (sNDA) dated and received November 14, 2019, and your amendments, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for POMALYST (pomalidomide); capsules.

We acknowledge receipt of your risk evaluation and mitigation strategy (REMS) assessment dated November 14, 2019.

This "Prior Approval" supplemental new drug application provides for the addition of a new indication for the treatment of adult patients with AIDS-related Kaposi sarcoma (KS) after failure of highly active antiretroviral therapy (HAART) with associated changes and modifications to the Prescribing Information (PI) and proposed modifications to the approved REMS for POMALYST (pomalidomide).

APPROVAL & LABELING

We have completed our review of this application, as amended. It is approved under the provisions of accelerated approval regulations (21 CFR 314.500), effective on the date of this letter, for use as recommended in the enclosed agreed-upon labeling.

Marketing of this drug product and related activities must adhere to the substance and procedures of the referenced accelerated approval regulations.

WAIVER OF ½ PAGE LENGTH REQUIREMENT FOR HIGHLIGHTS

We are waiving the requirements of 21 CFR 201.57(d)(8) regarding the length of Highlights of Prescribing Information. This waiver applies to all future supplements containing revised labeling unless we notify you 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 FDA.gov.[1] Content of labeling must be identical to the enclosed labeling (text for the Prescribing Information 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 *SPL Standard for Content of Labeling Technical Qs and As*.[2]

The SPL will be accessible from publicly available labeling repositories.

Also within 14 days, amend all pending supplemental applications that include 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 Microsoft Word format, that includes the changes approved in this supplemental application, as well as annual reportable changes. To facilitate review of your submission(s), 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.

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 clinical trials with due diligence. If postmarketing clinical trials fail to verify clinical benefit or are not conducted with due diligence, we may, following a hearing in accordance with 21 CFR 314.530, withdraw this approval. We remind you of your postmarketing requirement specified in your submission dated May 5, 2020. This requirement, along with required completion dates, is listed below.

3855-1 Submit the final report from a clinical trial evaluating overall response rate, duration of response, and safety to verify and describe the clinical benefit of pomalidomide in patients with Kaposi sarcoma who are human

[1] http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm
[2] We update guidances periodically. For the most recent version of a guidance, check the FDA Guidance Documents Database https://www.fda.gov/RegulatoryInformation/Guidances/default.htm.

immunodeficiency virus (HIV) positive (after failure of highly active antiretroviral therapy) and HIV negative, that may inform product labeling.

Draft Protocol Submission:	09/2020
Final Protocol Submission:	03/2021
Trial Completion:	09/2026
Final Report Submission:	12/2027

Submit clinical protocols to your IND 113751 for this product. In addition, under 21 CFR 314.81(b)(2)(vii) and 314.81(b)(2)(viii) you should include a status summary of each requirement 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.

Submit final reports to this NDA as a supplemental application. For administrative purposes, all submissions relating to this post marketing requirement must be clearly designated "**Subpart H Postmarketing Requirement(s)**."

REQUIRED PEDIATRIC ASSESSMENTS

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients (which includes new salts and new fixed combinations), 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 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.

RISK EVALUATION AND MITIGATION STRATEGY (REMS) REQUIREMENTS

The REMS for Pomalyst (pomalidomide) was originally approved on February 8, 2013, and the most recent REMS modification was approved on June 27, 2017. 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 removing indication statements from REMS materials; modifying the REMS document to the new format to align with the recommendations in the October 2017 *Draft Guidance: Format and Content of a REMS Document* for Industry; and removing prescription forms from the REMS.

Your proposed modification, submitted on November 14, 2019 and appended to this letter, is approved.

The timetable for submission of assessments remains the same as that approved September 14, 2015.

The revised REMS assessment plan must include, but is not limited to, the following:

Health Outcomes and/or Surrogates of Health Outcomes

1. Pregnancies: (per reporting period and cumulatively)

    a. Number of pregnancies reported
    b. Outcome of each pregnancy
    c. Follow-up of outstanding pregnancy reports
    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

Program Implementation and Operations

2. Reporting on the restricted distribution program: (per current and previous two reporting periods and cumulatively; where applicable)

    a. The number of pharmacies and physicians certified, and patients enrolled
    b. Patient demographics for the current REMS assessment reporting period 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

3. Data on the use of the mobile device application to conduct REMS functions (per current and previous two reporting periods and cumulatively)

    a. Number of downloads of the mobile application
    b. Uses of the mobile application, and the functions conducted via the mobile application.
    c. Number of prescribers using the mobile application for REMS functions, the number of instances of using the mobile application, and the functions conducted via the mobile application

4. REMS Pharmacy Compliance (per current reporting period and previous two reporting periods and for 5c. and 5d. cumulatively beginning June 4, 2018)

   a. Provide a copy of the Non-Compliance plan to include the following:
      i. Criteria for non-compliance
      ii. Actions taken to address non-compliance for each event identified
      iii. Criteria for de-certification
   b. Provide a copy of the audit plan
   c. Report of audit findings
      i. The number of audits expected, and the number of audits conducted
      ii. The number and type of deficiencies noted
         1) Number that successfully completed a corrective and preventative (CAPA) plan within 30 days of receipt of CAPA
         2) Describe actions taken for any that did not complete the CAPA within 30 days of receipt of CAPA
         3) Include a unique ID for each pharmacy that had deviations to track deviations over time
      iii. Documentation of completion of training for relevant staff
      iv. The existence of documented processes and procedure for complying with the REMS
   d. Non-compliance events: for each event provide the following
      i. Source of the report
      ii. Description of the event
      iii. Cause of the event
      iv. Corrective actions taken
      v. Events:
         1) Number of Pomalyst prescriptions dispensed that were written by non-certified prescribers
         2) Number of Pomalyst prescriptions dispensed by non-certified pharmacies
         3) Number of Pomalyst prescriptions dispensed to de-enrolled or non-enrolled patients
         4) Number of times a Pomalyst prescription was dispensed because a certified pharmacy bypassed REMS authorization processes

5) Number of shipments sent to non-certified pharmacies, sources of the reports, and actions taken to prevent future occurrences

6) Number of pharmacies who were de-certified for non-compliance and reasons for de-certification

Safe Use Behaviors

5. Documentation of safe use conditions (per current and previous two reporting periods and cumulatively, where applicable)

   Based on information collected from the mandatory surveys (used to document safe use conditions) provide information that could represent potential fetal exposure or that might result in a delay or interruption in treatment.

   Provide the following in a tabular format:

   a. The total number of authorization numbers issued and the number of authorization numbers flagged.

   b. The number and proportion of flagged authorization numbers intended for an FRP due to questions in the mandatory surveys related to pregnancy testing

   c. The number and proportion of flags that caused a delay in treatment initiation or a gap in therapy for patients due to REMS processes as the proportion of flagged authorization numbers compared to total authorization numbers. Include the time to resolution of flags in days (mean, minimum, maximum) for the reporting period and for each previous reporting period. Include the number of patients with a delay in treatment or a gap in therapy due to REMS processes.

Knowledge, Attitude, Behavior

6. Inform prescribers, patients, and pharmacists on the serious risks and safe-use conditions for Pomalyst/pomalidomide (per current reporting period and previous two reporting periods beginning June 4, 2018).

   a. Ensure that Pomalyst will only be dispensed to patients enrolled in the Pomalyst REMS Program with evidence or other documentation of safe-use conditions

      i. Number and proportion of total number of unflagged patient survey questions answered relating to knowledge compared to the total number of patient survey questions relating to knowledge reported per patient risk category

b. Ensure healthcare providers counsel patients on the benefits and risks of Pomalyst therapy, including risks described in the boxed warnings

   i. Number and proportion of total number of unflagged prescriber surveys compared to the total number of prescriber surveys reported per risk category

c. Educate pharmacies on the risks and safe-use conditions of Pomalyst

   i. Total number of pharmacy quizzes administered

   ii. Number of pharmacists with a passing rate/Total number of certified pharmacists on the last day of the reporting period

7. 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.

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 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) of the FDCA. This assessment 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 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, submit an adequate rationale to support the modification, including*: 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 REMS modifications*, 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 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

or

NEW SUPPLEMENT FOR NDA 204026/S-000
CHANGES BEING EFFECTED IN 30 DAYS
PROPOSED MINOR REMS MODIFICATION

or

NEW SUPPLEMENT FOR NDA 204029/S-000
PRIOR APPROVAL SUPPLEMENT
PROPOSED MAJOR REMS MODIFICATION

or

NEW SUPPLEMENT FOR NDA 204026/S-000
PRIOR APPROVAL SUPPLEMENT
PROPOSED REMS MODIFICATIONS DUE TO SAFETY LABELING CHANGES SUBMITTED IN SUPPLEMENT XXX

or

NEW SUPPLEMENT (NEW INDICATION FOR USE)
FOR NDA 204026/S-000
REMS ASSESSMENT
PROPOSED REMS MODIFICATION (if included)

Should 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, or website screenshots are only in PDF format, they may be submitted as such, but Word format is preferred.

SUBMISSION OF REMS DOCUMENT IN SPL FORMAT

FDA can accept the REMS document in Structured Product Labeling (SPL) format. If you intend to submit the REMS document in SPL format, as soon as possible, but no later than 14 days from the date of this letter, submit the REMS document in SPL format using the FDA automated drug registration and listing system (eLIST).

For more information on submitting REMS in SPL format, please email FDAREMSwebsite@fda.hhs.gov.

PROMOTIONAL MATERIALS

Under 21 CFR 314.550, you are required to submit, during the application pre-approval review period, all promotional materials, including promotional labeling and advertisements, that you intend to use in the first 120 days following marketing approval (i.e., your launch campaign). If you have not already met this requirement, you must immediately contact the Office of Prescription Drug Promotion (OPDP) at (301) 796-1200. Please ask to speak to a regulatory project manager or the appropriate reviewer to discuss this issue.

As further required by 21 CFR 314.550, submit all promotional materials that you intend to use after the 120 days following marketing approval (i.e., your post-launch materials) at least 30 days before the intended time of initial dissemination of labeling or initial publication of the advertisement. We ask that each submission include a detailed cover letter together with three copies each of the promotional materials, annotated references, and approved Prescribing Information, Medication Guide, and Patient Package Insert (as applicable).

For information about submitting promotional materials, see the final guidance for industry *Providing Regulatory Submissions in Electronic and Non-Electronic Format-Promotional Labeling and Advertising Materials for Human Prescription Drugs*.[3]

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, contact Haroon Vohra Pharm.D., Regulatory Health Project Manager, at 240-402-4471.

Sincerely,

{See appended electronic signature page}

Steven Lemery, M.D., M.H.S.
Director (Acting)
Division of Oncology 3
Office of Oncologic Diseases
Center for Drug Evaluation and Research

[3] For the most recent version of a guidance, check the FDA guidance web page at https://www.fda.gov/media/128163/download.

ENCLOSURES:

- Content of Labeling
  - Prescribing Information
  - Medication Guide
- REMS

This is a representation of an electronic record that was signed electronically. Following this are manifestations of any and all electronic signatures for this electronic record.

/s/

STEVEN J LEMERY
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