DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 202714/S-015

SUPPLEMENT APPROVAL
FULFILLMENT OF POSTMARKETING REQUIREMENTS

Onyx Pharmaceuticals, Inc., a wholly owned subsidiary of Amgen Inc.
Attention: Brian Stouch, RAC
Senior Manager, Regulatory Affairs
One Amgen Center Drive
Mail Stop 17-1-A
Thousand Oaks, CA 91320-1799

Dear Mr. Stouch:

Please refer to your Supplemental New Drug Application (sNDA) dated May 27, 2016, received May 27, 2016, and your amendments, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Kyprolis® (carfilzomib) for injection, 60 mg.

This Prior Approval supplemental new drug application (S-015) provides for updates to the Dosage and Administration (2.4), Use in Specific Populations (8.6 and 8.7), and Clinical Pharmacology (12.3) sections of the US Prescribing Information (USPI).

This supplement also provides for the fulfillment of postmarketing requirements (PMRs) 1908-6 and 1908-7.

APPROVAL & LABELING

We have completed our review of this supplemental application, as amended. It is approved, effective on the date of this letter, for use as recommended in the enclosed, agreed-upon labeling text.

WAIVER OF HIGHLIGHTS SECTION

Please note that we have previously granted a waiver of the requirements of 21 CFR 201.57(d)(8) regarding the length of Highlights of prescribing information.

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), 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 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 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).

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.

FULFILLMENT OF POSTMARKETING REQUIREMENTS

We have received your submission dated May 27, 2016, containing the final reports for the following postmarketing requirements listed in the July 20, 2012 approval letter.

PMR 1908-6 Conduct a clinical trial in patients with hepatic impairment to assess safety and PK characteristics of carfilzomib administered as a 30 minute infusion. The number of patients enrolled in the trial should be sufficient to detect PK differences that would warrant dosage adjustment recommendations in the labeling. The duration of the trial should be sufficient (several cycles) to reasonably characterize potential safety issues. The PK sampling scheme should be optimized to accurately estimate relevant PK parameters for the parent drug. A data analysis plan must be included in the protocol. Submit your protocol for Agency review and concurrence prior to initiation.

The timetable you submitted on July 17, 2012, states that you will conduct this trial according to the following schedule:

Final Protocol Submission:	March 2013
Trial Completion:	December 2015
Final Report Submission:	May 2016

PMR 1908-7 Conduct one or more clinical trials including Phase 3 Protocol 2011-003, supplemented as needed by an additional trial, to evaluate the PK, safety, and efficacy of carfilzomib in patients with varying degrees of renal impairment and those on chronic dialysis following the administration of carfilzomib when given as a 30 minute intravenous infusion at a sufficient dose level that will likely produce comparable exposure and clinical response to those patients without renal impairment who receive carfilzomib doses of 20/56 mg/m^2 using the 30 minute infusion as planned in your upcoming Phase 3 trial Protocol 2011-003. Collect PK samples following carfilzomib doses of 56 mg/m^2 or highest clinical dose in the protocol. Submit your protocol for Agency review and concurrence prior to initiation.

The timetable you submitted on July 17, 2012, states that you will conduct this trial according to the following schedule:

Final Protocol Submission:	March 2013
Trial Completion:	December 2015
Final Report Submission:	May 2016

We have reviewed your submission and conclude that the above requirements were fulfilled.

We remind you that there is a postmarketing requirement (PMR 3022-1) and a postmarketing commitment (PMC 3022-2) listed in the January 21, 2016 approval letter that are still open.

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:

OPDP Regulatory Project Manager
Food and Drug Administration
Center for Drug Evaluation and Research
Office of Prescription Drug Promotion (OPDP)
5901-B Ammendale Road
Beltsville, MD 20705-1266

Alternatively, you may submit a request for advisory comments electronically in eCTD format. For more information about submitting promotional materials in eCTD format, see the draft Guidance for Industry (available at: http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM443702.pdf).

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.

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 Laura Wall, Regulatory Project Manager, at (301) 796-2237.

Sincerely,

{See appended electronic signature page}

Ann T. Farrell, MD
Director
Division of Hematology Products
Office of Hematology and Oncology Products
Center for Drug Evaluation and Research

ENCLOSURE:
Content of Labeling

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

ANN T FARRELL
11/17/2016