DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 209115/S-003

SUPPLEMENT APPROVAL
FULFILLMENT OF POSTMARKETING REQUIREMENT
RELEASE FROM POSTMARKETING REQUIREMENT
NEW POSTMARKETING COMMITMENTS

Clovis Oncology, Inc.
Attention: Hanna Cho, PhD
Senior Manager, Regulatory Affairs
5500 Flatiron Parkway STE 100
Boulder, CO 80301

Dear Dr. Cho:

Please refer to your Supplemental New Drug Application (sNDA) dated October 6, 2017, received October 6, 2017, and your amendments, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Rubraca® (rucaparib) Tablets, 200 mg, 250 mg, and 300 mg.

This Prior Approval supplemental new drug application provides for a new indication for the maintenance treatment of adult patients with recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer who are in a complete or partial response to platinum-based chemotherapy. Furthermore, this supplemental application provides for regular approval for the treatment of patients with deleterious *BRCA* mutation-associated epithelial ovarian, fallopian tube, or primary peritoneal cancer who have been treated with two or more chemotherapies, which was granted accelerated approval under 21 CFR 314 Subpart H on December 19, 2016.

APPROVAL & LABELING

We have completed our review of this supplemental application. It is 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 and the patient 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).

CARTON AND IMMEDIATE CONTAINER LABELS

Submit final printed immediate container labels that are identical to the enclosed immediate container labels, 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 — Certain Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications (May 2015, Revision 3).* For administrative purposes, designate this submission "**Final Printed Container Labels for approved NDA 209115/S-003**." Approval of this submission by FDA is not required before the labeling is used.

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 this supplement fulfills your commitments made under 21 CFR 314.510.3141.

3141-1 Submit the progression-free survival (PFS) and overall survival (OS) analyses with datasets from clinical trial CO-338-014 entitled, "Phase 3 Study of Rucaparib as Switch Maintenance After Platinum in Relapsed High Grade Serous and Endometrioid Ovarian Cancer" (ARIEL3).

Final Protocol Submission (ARIEL3):	Submitted 9/9/2013
Interim Report Submission (PFS analysis):	3/2018
Trial Completion:	9/2020
Final Report Submission (OS analysis):	3/2021

RELEASE FROM POSTMARKETING REQUIREMENT

3141-2 Submit the progression-free survival (PFS) and overall survival (OS) analyses with datasets from clinical trial CO-338-043 entitled "A Phase 3 Multicenter, Randomized Study of Rucaparib Versus Chemotherapy in Patients With Relapsed, BRCA Mutant, High Grade Epithelial Ovarian, Fallopian Tube, or Primary Peritoneal Cancer," (ARIEL4).

Final Protocol Submission (ARIEL4)	Submitted 6/20/2016
Interim Report Submission (PFS analysis):	12/2022
Trial Completion:	6/2024
Final Report Submission (OS analysis):	12/2024

We have reviewed your submission and have determined that you are released from the above postmarketing requirement for the following reason:

ARIEL3 is a randomized, double-blind, placebo-controlled, multi-center trial to assess the efficacy of rucaparib maintenance monotherapy in relapsed high-grade serous ovarian cancer patients (including patients with primary peritoneal and/or fallopian tube cancer) or high-grade endometroid cancer who have responded to platinum-based chemotherapy. The results of progression free survival (PFS) reported and confirmed in the current supplemental application are statistically robust and clinically meaningful with a favorable benefit-risk analysis that supports the regular approval of rucaparib for the maintenance treatment of adult patients with recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer who are in a complete or partial response to platinum-based chemotherapy. Therefore, PMR 3141-2 is no longer needed.

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 ovarian cancer has an orphan drug designation, you are exempt from this requirement for the ovarian cancer indication.

We are waiving the pediatric study requirement for this application for the fallopian tube and primary peritoneal cancer indications because necessary studies are impossible or highly impracticable since these diseases/conditions do not occur in pediatric patients.

FULFILLMENT OF POSTMARKETING REQUIREMENT

We refer to your supplemental New Drug Application (sNDA) submitted under section 505(b) of the FDCA for Rubraca® (rucaparib) Tablets, 200 mg, 250 mg, and 300 mg.

We have received your submission dated October 6, 2017, containing the final report for the following postmarketing requirement listed in the December 19, 2016, approval letter.

3141-4 Complete the ongoing drug-drug interaction trial CO-338-044 and submit the final study report.

The timetable you submitted on November 28, 2016, states that you will conduct this trial according to the following schedule:

Final Report Submission: 4/2017

We have reviewed your submission and conclude that the above requirement was fulfilled.

We remind you that there are postmarketing requirements and postmarketing commitments listed in the December 19, 2016, approval letter that are still open.

POSTMARKETING COMMITMENTS SUBJECT TO REPORTING REQUIREMENTS UNDER SECTION 506B

We remind you of your postmarketing commitments:

3358-1 Submit to FDA the overall survival (OS) analyses with datasets from clinical trial CO-338-014 entitled, "Phase 3 Study of Rucaparib as Switch Maintenance After Platinum in Relapsed High Grade Serous and Endometrioid Ovarian Cancer" (ARIEL3).

The timetable you submitted on March 16, 2018, states that you will conduct this study according to the following schedule:

Trial Completion:	9/2020
Final Report Submission:	3/2021

3358-2 Submit to FDA the progression-free survival (PFS) and overall survival (OS) analyses with datasets from clinical trial CO-338-043 entitled "A Phase 3 Multicenter, Randomized Study of Rucaparib Versus Chemotherapy in Patients With Relapsed, BRCA Mutant, High Grade Epithelial Ovarian, Fallopian Tube, or Primary Peritoneal Cancer" (ARIEL4).

The timetable you submitted on March 16, 2018, states that you will conduct this study according to the following schedule:

Final Protocol Submission:	6/2016
Interim Report Submission (PFS) analysis:	12/2022
Trial Completion:	6/2024
Final Report Submission (OS analysis):	12/2024

Submit clinical protocols to your IND 106289 for this product. Submit nonclinical and chemistry, manufacturing, and controls protocols and all postmarketing final reports to this NDA. In addition, under 21 CFR 314.81(b)(2)(vii) and 314.81(b)(2)(viii), you should include a status summary of each commitment 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. All submissions, including supplements, relating to these postmarketing commitments should be prominently labeled **"Postmarketing Commitment Protocol," "Postmarketing Commitment Final Report," or "Postmarketing Commitment Correspondence."**

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, contact Amy Tilley, Regulatory Project Manager, at 301-796-3994 or amy.tilley@fda.hhs.gov.

Sincerely,

{See appended electronic signature page}

Julia Beaver, MD
Director
Division of Oncology Products 1
Office of Hematology and Oncology Products
Center for Drug Evaluation and Research

ENCLOSURES:
Content of Labeling
Container Labeling

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

/s/

JULIA A BEAVER
04/06/2018