



NDA 209115/S-004

ACCELERATED APPROVAL

Clovis Oncology, Inc.
Attention: Amanda Cannon
Associate Director, Regulatory Affairs
5500 Flatiron Parkway, Suite 100
Boulder, CO 80301

Dear Ms. Cannon:

Please refer to your supplemental new drug application (sNDA) dated November 15, 2019, received November 15, 2019, and your amendments, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Rubraca (rucaparib), 200 mg, 250 mg, and 300 mg tablets.

This "Prior Approval" supplemental new drug application provides for a new indication for Rubraca (rucaparib) for the treatment of adult patients with a deleterious *BRCA* mutation (germline and/or somatic)-associated metastatic castration-resistant prostate cancer who have been treated with androgen receptor-directed therapy and a taxane-based chemotherapy.

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.

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, 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.

¹ <http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm>

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).

ACCELERATED APPROVAL REQUIREMENTS

Products approved under the accelerated approval regulations, 21 CFR 314.510, require further adequate and well-controlled clinical trials to verify and describe clinical benefit. You are required to conduct such clinical trial 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 submissions dated April 9 and 14, 2020. This requirement, along with required completion dates, is listed below.

- 3833-1 Submit the progression-free survival and overall survival analyses and datasets demonstrating clinical benefit of rucaparib from a phase 3 randomized trial in patients with metastatic castrate-resistant prostate cancer associated with homologous recombination deficiency who have been treated with androgen receptor directed therapy. The results may inform product labeling.

Final Protocol Submission:	10/2016 (completed)
Interim Report Submission (PFS analysis):	12/2024
Trial Completion:	06/2025
Final Report Submission (OS analysis):	10/2025

Submit clinical protocols to your IND 129840 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.

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>.

Submit final reports to this NDA as a supplemental application. For administrative purposes, all submissions relating to this postmarketing 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.

We are waiving the pediatric study requirement for this application because necessary studies are impossible or highly impracticable to conduct in the pediatric population.

POSTMARKETING COMMITMENTS SUBJECT TO REPORTING REQUIREMENTS UNDER SECTION 506B

We remind you of your postmarketing commitments:

- 3833-2 Submit the final report of analytical and clinical validation studies that use cell-free/circulating tumor DNA (cf/ctDNA) isolated from plasma specimens from the TRITON2 clinical trial that is adequate to support labeling of an in vitro diagnostic device that demonstrates the device is essential to the safe and effective use of rucaparib for prostate cancer patients with BRCA1 and BRCA2 gene alterations. The analytical validation should consist of precision, limit of detection, and accuracy studies using samples, consistent with the clinical trial patient population, to support prostate cancer indication. The clinical validation should be supported by a clinical bridging study comparing intended CDx test(s) and the clinical trial enrollment assays.

The timetable you submitted on May 12, 2020, states that you will conduct this study according to the following schedule:

PMA Submission: 12/2019 (completed)
Final Report Submission: 12/2021

- 3833-3 Submit the final report from analytically and clinically validated tumor tissue test, which may be used in conjunction with the plasma-based test, to maximize the identification of BRCA1 and BRCA2 gene mutations in patients with prostate cancer who may benefit from rucaparib. The analytical validation should consist of precision, limit of detection, and accuracy studies using samples, consistent with the clinical trial patient population, to support prostate cancer indication. The clinical validation

should be supported by a clinical bridging study comparing intended CDx test(s) and the clinical trial enrollment assays. The results of the validation study may inform product labeling.

The timetable you submitted on May 12, 2020, states that you will conduct this study according to the following schedule:

PMA Submission: 12/2024
Final Report Submission: 06/2025

Submit clinical protocols to your IND 129840 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

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 (PI)/Medication Guide/Patient Package Insert (as applicable).

Send each submission directly to:

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

Alternatively, you may submit promotional materials for accelerated approval products electronically in eCTD format. For more information about submitting promotional materials in eCTD format, see the draft 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 Jessica Kim, Regulatory Project Manager, at 240-402-0883 or Jessica.Kim1@fda.hhs.gov.

Sincerely,

{See appended electronic signature page}

Amna Ibrahim, MD
Deputy Director
Division of Oncology 1
Office of Oncologic Diseases
Center for Drug Evaluation and Research

ENCLOSURE(S):

- Content of Labeling
 - Prescribing Information
 - Patient Package Insert

³ When final, this guidance will represent the FDA's current thinking on this topic. For the most recent version of a guidance, check the FDA guidance web page at <https://www.fda.gov/RegulatoryInformation/Guidances/default.htm>.

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/

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