

**CENTER FOR DRUG EVALUATION AND  
RESEARCH**

*APPLICATION NUMBER:*

**211225Orig1s000**

**SUMMARY REVIEW**

## Division Director Summary Review

<b>Date</b>	March 18, 2019
<b>From</b>	Patricia Keegan, M.D.
<b>Subject</b>	Division Director Summary Review
<b>NDA #</b>	NDA 211225
<b>Applicant</b>	Novartis Pharmaceuticals Corp.
<b>Date of Submission</b>	May 18, 2018
<b>PDUFA Goal Date</b>	March 18, 2019
<b>Proprietary Name</b>	Zykadia
<b>Established or Proper Name</b>	ceritinib
<b>Dosage Form(s)</b>	Tablets, for oral administration
<b>Applicant Proposed Indication(s)/Population(s)</b>	None (this dosage form can be used interchangeably for the capsule dosage form for the indications approved under NDA 205755)
<b>Action:</b>	Approval

<b>Material Reviewed/Consulted</b>	<b>Names of discipline reviewers</b>
OND Action Package, including:	
Regulatory Health Project Manager	Norma Griffin & Lydia Springs
Clinical Review	Barbara Sceपुरa (primary reviewer) Erin Larkins (Team Leader)
OPQ Review	Gaetan Ladoceur (drug substance & DMF review) Amit Mitra (drug product review) Quamrul Majumder (process, microbiology, & facility review) Zhoutun Zhao (biopharmaceutics review) Nina Ni (Application Team Lead)
Clinical Pharmacology Review	Xiling Jiang (primary reviewer) Hong Zhao (Team Leader)
OSIS/DGDBE	Melkamu Getie-Kebtie (primary reviewer) Stanley Au (Team Leader) Seongeun Cho (Director, DGDBE)
OSE/DMEPA	Collen Little (proprietary name review) Chi-Ming (Alice) Tu (Team Leader)
OSE/DRISK	
DOP2 ADL	Stacy Shord

OND=Office of New Drugs

OPQ=Office of Pharmaceutical Quality

OPDP=Office of Prescription Drug Promotion

OSIS/DGDBE=Office of Study Integrity and Surveillance/ Division of Generic Drug Bioequivalence Evaluation

DMEPA=Division of Medication Error Prevention and Analysis

DOP2 ADL=Division of Oncology Products 2/Associate Director for Labeling

## **1. Executive Summary**

This New Drug Application (NDA) seeks approval for a new dosage form (tablets for oral administration) for ceritinib. The proposed dosage form would be used interchangeably with the approved dosage form (capsules for oral administration), approved under NDA 205755 on April 29, 2014. The strength of the new dosage form is that same as the approved dosage form, which is approved for a single strength, 150 mg. The CMC information established the quality of the new dosage form as acceptable, with adequate controls, and the clinical pharmacology studies have verified that the two dosage forms are bioequivalent.

## **2. Product Quality**

The application relied on the drug substance information submitted to NDA 205755 and contained new information for drug product manufacturing processed, release testing, biopharmaceutics testing, and stability data for three drug product batches. The drug product was determined to be manufactured in a sterile and adequately controlled manner, with sufficient data to support a 24-month expiry dating period. There were no inspections of drug substance or drug product manufacturing facilities as all facilities were deemed acceptable based on the existing and acceptable profile established during prior drug product and drug substance facilities inspections. The quality reviewer recommended granting of the request for categorical exclusion from environmental assessment.

## **3. Nonclinical Pharmacology/Toxicology**

No new nonclinical pharmacology/toxicology data were submitted to this NDA and none were required to support this new dosage form of ceritinib. All excipients in the new drug product dosage form were compendial.

## **4. Clinical Pharmacology**

Novartis provided the results of the two bioavailability/bioequivalence studies which demonstrated that the proposed tablet dosage form is bioequivalent (BE) to the approved 150 mg capsule dosage form and a food effects study demonstrating more modest food effects for the tablet dosage form than with the capsule dosage form. The laboratory responsible for the BE studies was inspected by OSIS, who determined that based on the inspectional findings, these data were reliable.

## **5. Clinical Microbiology**

Not applicable.

## **6. Clinical/Statistical-Efficacy**

No new efficacy data were submitted in this NDA and none were required for approval, based on the demonstration of bioequivalence between the proposed ceritinib dosage form and the approved ceritinib capsule dosage form.

## **7. Safety**

New safety data were limited to adverse events observed in the three bioequivalence studies. No additional safety data were required for approval, based on the demonstration of bioequivalence between the proposed ceritinib dosage form and the approved ceritinib capsule dosage form.

## **8. Advisory Committee Meeting**

Not applicable as this is not an NME and the review identified no controversial issues.

## **9. Pediatrics**

Ceritinib was granted orphan drug exclusivity for treatment of patients with non-small cell lung cancer (NSCLC) that is anaplastic lymphoma kinase(ALK)-positive on September 27, 2013. Thus, this application is exempt from the requirements of the Pediatric Research Equity Act.

## **10. Other Relevant Regulatory Issues**

None.

## **11. Labeling**

The review team reached agreement with Novartis on the physician package insert, carton and container labeling. The existing product labeling for Zykadia was modified to include the information regarding the new dosage form in Sections 2 (Dosage and Administration), 3 (Dosage Forms), 11 (Description), and 12 (Clinical Pharmacology). Product labeling was also edited for brevity and clarity for dosing information and description of clinical pharmacology (fasted or fed conditions and dosage).

## **12. Postmarketing**

I concur with the recommendations of the review team that no postmarketing studies or commitments are needed to address outstanding quality or clinical pharmacology issues.

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/s/  
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