



NDA 207997/S-4

**ACKNOWLEDGMENT --
PRIOR APPROVAL SUPPLEMENT/SUPPLEMENT APPROVAL**

Novartis Pharmaceuticals
Attention: Sweta Shah, PharmD
Senior Global Program Regulatory Manager
Regulatory Affairs, Oncology
One Health Plaza
East Hanover, New Jersey 07936-1080

Dear Dr. Shah:

We have received your supplemental new drug application (sNDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA or the Act) for the following:

NDA NUMBER: 207997
SUPPLEMENT NUMBER: 4
PRODUCT NAME: Rydapt (midostaurin) capsule
DATE OF SUBMISSION: February 20, 2020
DATE OF RECEIPT: February 20, 2020

We refer to our letter dated April 15, 2019, requesting that you submit draft labeling for your U.S. Prescribing Information (USPI) proposing changes to the approved labeling to include a new Warnings and Precautions subsection regarding wound healing complications.

We also refer to your July 11, 2019 response wherein, you stated a “comprehensive review of data from all available sources did not reveal any new or changing safety signal related to the use of midostaurin and wound healing complication” and that you believe no change in the USPI is warranted at this point.

We further refer to our November 22, 2020, supplement request to remove reference of vascular endothelial growth factor receptor 2 (VEGFR2) from subsection 12.1 Mechanism of Action of the USPI because midostaurin is a relatively weak VEGFR2 inhibitor and as per 21 CFR 201.57(c)(13)(i)(A) “this subsection must summarize what is known about the established mechanism(s) or the drug’s action” .

This Prior Approval supplemental new drug application provides for the removal of VEGFR2 from subsection 12.1 Mechanism of Action and minor editorial changes to the label for midostaurin.

APPROVAL & LABELING

We have completed our review of this application. It is approved, effective on the date of this letter, for use as recommended in the enclosed agreed-upon labeling with minor editorial revisions listed below and reflected in the enclosed labeling.

Date at the end of the Highlights of Prescribing Information updated to “Revised: 3/2020”.

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 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 *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).

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

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>.

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 none of these criteria apply to your application, you are exempt from this requirement.

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 Prescribing Information 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 *Providing Regulatory Submissions in Electronic and Non-Electronic Format-Promotional Labeling and Advertising Materials for Human Prescription Drugs*.³

You must submit final promotional materials and Prescribing Information, 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 FDA.gov.⁴ Information and Instructions for completing the form can be found at FDA.gov.⁵ For more information about submission of promotional materials to the Office of Prescription Drug Promotion (OPDP), see FDA.gov.⁶

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>.

⁴ <http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM083570.pdf>

⁵ <http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM375154.pdf>

⁶ <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, you may contact Felicia Diggs, Safety Regulatory Health Project Manager at (240) 402-4932 or via email at Felicia.diggs@fda.hhs.gov.

Sincerely,

{See appended electronic signature page}

Meredith K. Chuk, MD
Supervisory Associate Director for Safety (acting)
Office of Oncologic Diseases
Center for Drug Evaluation and Research

ENCLOSURES:

- Content of Labeling
 - Prescribing Information
 - Patient Package Insert

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/

MEREDITH K CHUK
03/04/2020 11:08:22 AM