

CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

213973Orig1s000

Trade Name: QINLOCK™ 50mg tablets, for oral use
Generic or Proper Name: (ripretinib)

Sponsor: Deciphera Pharmaceuticals, LLC

Approval Date: May 15, 2020

Indication: QINLOCK is indicated for the treatment of adult patients with advanced gastrointestinal stromal tumor (GIST) who have received prior treatment with 3 or more kinase inhibitors, including imatinib.

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APPLICATION NUMBER:

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APPROVAL LETTER

NDA 213973

NDA APPROVAL

Deciphera Pharmaceuticals, LLC
Attention: Shreya Mehta
Associate Director, Regulatory Affairs
200 Smith Street
Waltham, MA 02451

Dear Ms. Mehta:

Please refer to your new drug application (NDA) dated and received December 13, 2019, and your amendments, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA), for QINLOCK (ripretinib) tablet.

This new drug application provides for the use of QINLOCK (ripretinib) tablet for the treatment of adult patients with advanced gastrointestinal stromal tumor (GIST) who have received prior treatment with 3 or more kinase inhibitors, including imatinib.

APPROVAL & LABELING

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

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) 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 via publicly available labeling repositories.

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>.

CARTON AND CONTAINER LABELING

Submit final printed carton and container labeling that are identical to the enclosed carton and container labeling, as soon as they are available, but no more than 30 days after they are printed. Please submit these labeling electronically according to the guidance for industry *Providing Regulatory Submissions in Electronic Format — Certain Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications*. For administrative purposes, designate this submission “**Final Printed Carton and Container Labeling for approved NDA 213973.**” Approval of this submission by FDA is not required before the labeling is used.

DATING PERIOD

Based on the provided stability data, a 18-month expiration dating period is granted for the 50 mg QINLOCK (ripretinib) tablets when stored in the original container at 20 °C to 25°C (68 °F to 77°F); excursions permitted to 15 °C to 30°C (59 °F to 86°F) [see USP controlled room temperature].

ADVISORY COMMITTEE

Your application for QINLOCK was not referred to an FDA advisory committee because the drug is not the first in its class, the clinical trial design is acceptable, the application did not raise significant safety or efficacy issues in the intended population, and there were no controversial issues that would benefit from advisory committee discussion.

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 this indication has an orphan drug designation, you are exempt from this requirement.

POSTMARKETING REQUIREMENTS UNDER 505(o)

Section 505(o)(3) of the FDCA authorizes FDA to require holders of approved drug and biological product applications to conduct postmarketing studies and clinical trials for certain purposes, if FDA makes certain findings required by the statute.

We have determined that an analysis of spontaneous postmarketing adverse events reported under subsection 505(k)(1) of the FDCA will not be sufficient to assess the

potential for increasing/decreasing drug exposure and resultant serious drug risks and to determine an appropriate dose of ripretinib when used in patients with moderate or severe hepatic impairment or when used concomitantly with CYP2C8 substrates.

Furthermore, the active postmarket risk identification and analysis system as available under section 505(k)(3) of the FDCA will not be sufficient to assess these serious risks.

Finally, we have determined that only a clinical trial (rather than a nonclinical or observational study) will be sufficient to assess these risks.

Therefore, based on appropriate scientific data, FDA has determined that you are required to conduct the following trials:

3834-1 Conduct a clinical pharmacokinetic trial to assess the effect of varying degrees of hepatic impairment on the exposure of ripretinib and DP-5439. This trial should be designed and conducted in accordance with the FDA Guidance for Industry titled, "Pharmacokinetics in Patients with Impaired Hepatic Function: Study Design, Data Analysis, and Impact on Dosing and Labeling." The results from this trial should determine the magnitude of increase in the exposure of ripretinib and DP-5439, and an appropriate dosage recommendation of ripretinib for patients with moderate or severe hepatic impairment and may inform labeling.

The timetable you submitted on April 13, 2020 and April 28, 2020, states that you will conduct this trial according to the following schedule:

Final Protocol Submission:	07/2019 (completed)
Trial Completion:	07/2020
Final Report Submission:	05/2021

3834-2 Conduct a clinical pharmacokinetic trial to evaluate the effect of repeat doses of ripretinib on the single dose pharmacokinetics of a sensitive CYP2C8 substrate. This trial should be designed and conducted in accordance with the FDA Guidance for Industry titled, "Clinical Drug Interaction Studies – Study Design, Data Analysis, and Clinical Implications." The results from this trial should determine the magnitude of increase in the exposure of the CYP2C8 substrate and an appropriate

dosing recommendation of CYP2C8 substrates when they are administered concomitantly with ripretinib and may inform labeling.

The timetable you submitted on April 13, 2020 and April 28, 2020, states that you will conduct this trial according to the following schedule:

Draft Protocol Submission:	11/2019 (completed)
Final Protocol Submission:	03/2020 (completed)
Trial Completion:	08/2021
Final Report Submission:	03/2022

FDA considers the term *final* to mean that the applicant has submitted a protocol, the FDA review team has sent comments to the applicant, and the protocol has been revised as needed to meet the goal of the study or clinical trial.

Submit clinical protocols to your IND 125279 with a cross-reference letter to this NDA. Submit nonclinical and chemistry, manufacturing, and controls protocols and all final reports to your NDA. Prominently identify the submission with the following wording in bold capital letters at the top of the first page of the submission, as appropriate:

Required Postmarketing Protocol Under 505(o), Required Postmarketing Final Report Under 505(o), Required Postmarketing Correspondence Under 505(o).

Section 505(o)(3)(E)(ii) of the FDCA requires you to report periodically on the status of any study or clinical trial required under this section. This section also requires you to periodically report to FDA on the status of any study or clinical trial otherwise undertaken to investigate a safety issue. Section 506B of the FDCA, as well as 21 CFR 314.81(b)(2)(vii) requires you to report annually on the status of any postmarketing commitments or required studies or clinical trials.

FDA will consider the submission of your annual report under section 506B and 21 CFR 314.81(b)(2)(vii) to satisfy the periodic reporting requirement under section 505(o)(3)(E)(ii) provided that you include the elements listed in 505(o) and 21 CFR 314.81(b)(2)(vii). We remind you that to comply with 505(o), your annual report must also include a report on the status of any study or clinical trial otherwise undertaken to investigate a safety issue. Failure to submit an annual report for studies or clinical trials required under 505(o) on the date required will be considered a violation of FDCA section 505(o)(3)(E)(ii) and could result in enforcement action.

POSTMARKETING COMMITMENTS SUBJECT TO REPORTING REQUIREMENTS UNDER SECTION 506B

We remind you of your postmarketing commitments:

3834-3	Conduct a clinical pharmacokinetic trial to evaluate the effect of repeat doses of a strong CYP3A inducer on the single dose pharmacokinetics of
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Silver Spring, MD 20993
www.fda.gov

ripretinib and DP-5439. This trial should be designed and conducted in accordance with the FDA Guidance for Industry titled, "Clinical Drug Interaction Studies – Study Design, Data Analysis, and Clinical Implications." This trial should determine the magnitude of decreased exposure of ripretinib and DP-5439 and an appropriate dosage recommendation for ripretinib when it is administered concomitantly with strong CYP3A inducers. The results from this study may inform product labeling.

The timetable you submitted on April 13, 2020 states that you will conduct this study according to the following schedule:

Draft Protocol Submission:	12/2019 (completed)
Final Protocol Submission:	02/2020 (completed)
Trial Completion:	04/2020
Final Report Submission:	01/2021

3834-4 Conduct a physiologically-based pharmacokinetic modeling/simulation study to assess the effect of repeat doses of a moderate CYP3A inducer on the single dose pharmacokinetics of ripretinib and DP-5439. This study should be designed and conducted in accordance with the FDA Guidance for Industry titled, "Physiologically Based Pharmacokinetic Analyses — Format and Content Guidance for Industry." This study should estimate the magnitude of decrease in the exposure of ripretinib and DP-5439 and determine an appropriate dosage recommendation for ripretinib when it is administered concomitantly with moderate CYP3A inducers. The results from this study may inform product labeling.

The timetable you submitted on April 13, 2020 states that you will conduct this study according to the following schedule:

Final Report Submission: 01/2021

A final submitted protocol is one that the FDA has reviewed and commented upon, and you have revised as needed to meet the goal of the study or clinical trial.

Submit clinical protocols to your IND 125279. 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, in triplicate, a cover letter requesting advisory comments, the proposed materials in draft or mock-up form with annotated references, and the Prescribing Information, Medication Guide, and Patient Package Insert (as applicable) to:

OPDP Regulatory Project Manager
Food and Drug Administration
Center for Drug Evaluation and Research
Office of Prescription Drug Promotion
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

As required under 21 CFR 314.81(b)(3)(i), you must submit final promotional materials, and the Prescribing Information, at the time of initial dissemination or publication, accompanied by a Form FDA 2253. 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

REPORTING REQUIREMENTS

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

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>

MEDWATCH-TO-MANUFACTURER PROGRAM

The MedWatch-to-Manufacturer Program provides manufacturers with copies of serious adverse event reports that are received directly by the FDA. New molecular entities and important new biologics qualify for inclusion for three years after approval. Your firm is eligible to receive copies of reports for this product. To participate in the program, please see the enrollment instructions and program description details at FDA.gov.⁷

POST APPROVAL FEEDBACK MEETING

New molecular entities and new biological products qualify for a post approval feedback meeting. Such meetings are used to discuss the quality of the application and to evaluate the communication process during drug development and marketing application review. The purpose is to learn from successful aspects of the review process and to identify areas that could benefit from improvement. If you would like to have such a meeting with us, call the Regulatory Project Manager for this application.

If you have any questions, contact Leah Her, Senior Regulatory Health Project Manager, at (240) 402-6611 or leah.her@fda.hhs.gov.

Sincerely,

{See appended electronic signature page}

Marc Theoret, M.D.
Deputy Director (Acting)
Office of Oncologic Diseases
Center for Drug Evaluation and Research

ENCLOSURE(S):

- Content of Labeling
 - o Prescribing Information
 - o Patient Package Insert
- Carton and Container Labeling

⁷ <http://www.fda.gov/Safety/MedWatch/HowToReport/ucm166910.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/

MARC R THEORET
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