



NDA 210656/S-002
NDA 210656/S-004

**SUPPLEMENT APPROVAL
FULFILLMENT OF POSTMARKETING
REQUIREMENTS/COMMITMENT**

Pfizer, Inc.
Attention: Carl DeJuliis, PharmD
Director, Pfizer Global Regulatory Affairs
445 Eastern Point Road
Groton, CT 06340

Dear Dr. DeJuliis:

Please refer to your supplemental new drug applications (sNDA) dated October 3, 2019, received October 3, 2019, and November 4, 2019, received November 4, 2019, and your amendments, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for DAURISMO™ (glasdegib) tablets.

These Prior Approval supplemental new drug applications provide for updates to Section 1 Indications and Usage, Section 2 Dosage and Administration, Section 7 Drug Interactions, Section 12.3 Pharmacokinetics, Medication Guide based on study results from study B1371017 entitled, "*A Phase 1, Open-Label, Single Dose, Parallel Group Study to Evaluate the Pharmacokinetics of Glasdegib in Subjects with Impaired Renal Function*" and the study B1371016 entitled, "*A Phase 1, Open-Label, Single Dose, Parallel Group Study to Evaluate the Plasma Pharmacokinetics of Glasdegib (PF-04449913) in Healthy Subjects with Normal Hepatic Function and in Subjects with Impaired Hepatic Function*".

APPROVAL & LABELING

We have completed our review of these applications. They are 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 Medication Guide), with the addition of any labeling

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

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 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.

FULFILLMENT OF POSTMARKETING REQUIREMENTS/COMMITMENT

We have received your submission dated November 4, 2019, containing the final reports for the following postmarketing requirements/commitment listed in the November 21, 2018, approval letter.

- 3519-1 Conduct a clinical pharmacokinetic trial to determine an appropriate dose of DAURISMO to minimize toxicity in patients with moderate and severe hepatic impairment. Design and conduct the trial in accordance with the FDA Guidance for Industry entitled, *Pharmacokinetics in Patients with Impaired Hepatic Function: Study Design, Data Analysis, and Impact on Dosing and Labeling*.

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>.

- 3519-2 Complete a clinical pharmacokinetic trial to determine an appropriate dose of DAURISMO to minimize toxicity in patients with severe renal impairment. Design and conduct the trial in accordance with the draft FDA Guidance for Industry entitled, Pharmacokinetics in Patients with Impaired Renal Function: Study Design, Data Analysis, and Impact on Dosing and Labeling.
- 3519-3 Use a physiologically-based pharmacokinetic (PBPK) modeling approach to determine an appropriate dose of DAURISMO when co-administered with moderate CYP3A inducers.

We have reviewed your submission and conclude that the above requirements/commitment were fulfilled.

This completes all of your postmarketing requirements and postmarketing commitments acknowledged in our November 21, 2018, letter.

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

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>.

[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

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, call Rachel McMullen, Senior Regulatory Project Manager, at 240-402-4574.

Sincerely,

{See appended electronic signature page}

R. Angelo de Claro, MD
Acting Division Director
Division of Hematologic Malignancies I
Office of Oncologic Diseases
Center for Drug Evaluation and Research

ENCLOSURES:

- Content of Labeling
 - Prescribing Information
 - Medication Guide

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>

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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