

NDA 212327/S-006

**SUPPLEMENT APPROVAL  
FULFILLMENT OF POSTMARKETING  
REQUIREMENT**

Bristol-Myers Squibb Company  
Attention: Isabella Smalera-Birns, MS  
Associate Director, Global Regulatory Strategy and Policy  
Route 206 and Province Line Road  
Princeton, NJ 08543

Dear Isabella Smalera-Birns:

Please refer to your supplemental new drug application (sNDA) dated January 31, 2024, received January 31, 2024, and your amendments, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Inrebic (fedratinib) capsules.

This Prior Approval sNDA provides updates to the Prescribing Information and Medication Guide based on results from Study FEDR-MF-002<sup>1</sup> (regarding the use of thiamine) and Study FEDR-CP-001<sup>2</sup> (regarding the use of Inrebic in patients with hepatic impairment, conducted to fulfill PMR 3664-2).

**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.<sup>3</sup> Content of labeling must be identical to the enclosed labeling (text for the Prescribing Information and Medication Guide), with the addition of any labeling changes in pending “Changes Being Effectuated” (CBE) supplements, as well as annual

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<sup>1</sup> Randomized Phase 3 Study evaluating the efficacy and the safety of fedratinib compared to best available therapy (BAT) in myelofibrosis patients previously treated with ruxolitinib

<sup>2</sup> A Phase 1, Open-Label, Single-Dose Study to Assess the Pharmacokinetics, Safety, and Tolerability of Fedratinib in Subjects with Moderate and Severe Hepatic Impairment Compared with Healthy Subjects

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*.<sup>4</sup>

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(I)(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 supplemental application, you are exempt from this requirement.

### **FULFILLMENT OF POSTMARKETING REQUIREMENT**

We have received your submission dated September 27, 2023, containing the final report for the following postmarketing requirement listed in the August 16, 2019 letter.

- 3664-2 Conduct a clinical pharmacokinetic trial to determine an appropriate dose of fedratinib to minimize toxicity in subjects with 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*.

We have reviewed your submission and conclude that the above requirement was fulfilled.

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<sup>4</sup> 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>.

We remind you that there is a postmarketing requirement listed in the August 16, 2019, approval letter that is still open.

### **PROMOTIONAL MATERIALS**

You may request advisory comments on proposed introductory advertising and promotional labeling. For information about submitting promotional materials, see the final guidance for industry *Providing Regulatory Submissions in Electronic and Non-Electronic Format-Promotional Labeling and Advertising Materials for Human Prescription Drugs*.<sup>5</sup>

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.<sup>6</sup> Information and Instructions for completing the form can be found at FDA.gov.<sup>7</sup>

All promotional materials that include representations about your drug product must be promptly revised to be consistent with the labeling changes approved in this supplement, including any new safety-related information [21 CFR 314.70(a)(4)]. The revisions in your promotional materials should include prominent disclosure of the important new safety-related information that appears in the revised labeling. Within 7 days of receipt of this letter, submit your statement of intent to comply with 21 CFR 314.70(a)(4).

### **PATENT LISTING REQUIREMENTS**

Pursuant to 21 CFR 314.53(d)(2) and 314.70(f), certain changes to an approved NDA submitted in a supplement require you to submit patent information for listing in the Orange Book upon approval of the supplement. You must submit the patent information required by 21 CFR 314.53(d)(2)(i)(A) through (C) and 314.53(d)(2)(ii)(A) and (C), as applicable, to FDA on Form FDA 3542 within 30 days after the date of approval of the supplement for the patent information to be timely filed (see 21 CFR 314.53(c)(2)(ii)). You also must ensure that any changes to your approved NDA that require the submission of a request to remove patent information from the Orange Book are submitted to FDA at the time of approval of the supplement pursuant to 21 CFR 314.53(d)(2)(ii)(B) and 314.53(f)(2)(iv).

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<sup>5</sup> For the most recent version of a guidance, check the FDA guidance web page at <https://www.fda.gov/media/128163/download>.

<sup>6</sup> <http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM083570.pdf>

<sup>7</sup> <http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM375154.pdf>

## **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 Melissa Button, Regulatory Project Manager, at 240-402-1995 or email at [melissa.button@fda.hhs.gov](mailto:melissa.button@fda.hhs.gov).

Sincerely,

*{See appended electronic signature page}*

Ann Farrell, MD  
Director  
Division of Nonmalignant Hematology  
Office of Cardiology, Hematology,  
Endocrinology, and Nephrology  
Office of New Drugs  
Center for Drug Evaluation and Research

### ENCLOSURES:

- Content of Labeling
  - Prescribing Information
  - Medication Guide

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**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.**  
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/s/  
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