NDA 202155/S-039
NDA 202155/S-040

SUPPLEMENT APPROVAL
FULFILLMENT OF POSTMARKETING REQUIREMENTS

Bristol-Myers Squibb Company
Attention: Dipika Tuteja Shringarpure, PhD, RAC
Senior Manager, Global Regulatory Strategy & Policy Division
P. O. Box 5326
Princeton, NJ 08543

Dear Dr. Shringarpure:

Please refer to your supplemental new drug applications (sNDAs) dated and received October 17, 2024, and your amendments, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Eliquis (apixaban) 2.5 mg and 5 mg tablets and 0.5 mg tablets for oral suspension.

These Prior Approval sNDAs provide for the addition of a new pediatric indication for the treatment of venous thromboembolism (VTE) and reduction in the risk of recurrent VTE in pediatric patients from birth and older after at least 5 days of initial anticoagulant treatment, and for the addition of 0.5 mg tablets for oral suspension.

APPROVAL & LABELING

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

The applications provide for pediatric labeling text pursuant to the Best Pharmaceuticals for Children Act (BPCA). This approval is in response to a written request.

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, Instructions for Use, and Medication Guide), with the addition of

[1] http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm

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).

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 202155/S-039 and NDA 202155/S-040**." Approval of this submission by FDA is not required before the labeling is used.

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.

We note that you have fulfilled the pediatric studies requirement for ages birth to <18 years for the applications.

[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.

FULFILLMENT OF POSTMARKETING REQUIREMENTS

We have received your submissions dated December 10, 2020, and October 17, 2024, containing the final reports for the following postmarketing requirements listed in the July 5, 2016, postapproval postmarketing requirement letter.

PMR 3103-1 Assess apixaban pharmacokinetics and pharmacodynamics in approximately 50 pediatric subjects aged 0 to less than 18 years, who are at risk for a venous or arterial thrombotic disorder, to determine dosing requirements for subsequent studies in children. Completion and submission of results of Study CV185118 and available data from CV185079 may be used to fulfill this requirement.

PMR 3103-2 Conduct a randomized, open-label, active-controlled, safety and descriptive efficacy study to assess apixaban treatment in 150 pediatric patients evaluable for efficacy and safety, aged 0 to less than 18 years, requiring anticoagulation for the treatment of a venous thromboembolic event (VTE). This trial will also evaluate apixaban pharmacokinetics, anti-Factor Xa activity, and imaging assessment of clot status at the end of treatment in pediatric patients requiring anticoagulation for the treatment of a VTE. Completion and submission of results of Study CV185325 may be used to fulfill this requirement.

We have reviewed your submissions and conclude that the above requirements were fulfilled.

This completes all of your postmarketing requirements acknowledged in our July 5, 2016, letter. You are not required to report on the status of closed (released or fulfilled) PMRs/PMC in your annual report required under 21 CFR 314.81(b)(2)(vii) of the FD&CA.

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.*[3]

[3] For the most recent version of a guidance, check the FDA guidance web page at https://www.fda.gov/media/128163/download.

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]

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).

REPORTING REQUIREMENTS

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

[4] http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM083570.pdf
[5] http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM375154.pdf

If you have any questions, contact Carleveva Thompson, Regulatory Project Manager, at 301-796-1403 or Carleveva.Thompson@fda.hhs.gov.

Sincerely,

{See appended electronic signature page}

Tanya Wroblewski, MD
Deputy Director
Division of Nonmalignant Hematology
Office of Cardiology, Hematology,
Endocrinology, and Nephrology
Center for Drug Evaluation and Research

ENCLOSURES:

- Content of Labeling
  - Prescribing Information
  - Medication Guide
  - Instructions for Use
- Carton and Container Labeling

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/

TANYA M WROBLEWSKI
04/17/2025 04:18:01 PM