NDA 022512/S-041

SUPPLEMENT APPROVAL/
FULFILLMENT OF POSTMARKETING REQUIREMENTS

Boehringer Ingelheim Pharmaceuticals, Inc.
Attention: Charles R. Mazzarella
Director, Regulatory Affairs
900 Ridgebury Road, PO Box 368
Ridgefield, CT 06877

Dear Mr. Mazzarella:

Please refer to your supplemental new drug application (sNDA) dated and received September 21, 2020, and your amendments, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Pradaxa (dabigatran etexilate) Capsules.

We acknowledge receipt of your major amendment dated March 19, 2021, which extended the goal date by three months.

This Prior Approval supplemental new drug application provides for the following:

- Treatment of venous thromboembolic events (VTE) in pediatric patients 8 to less than 18 years of age who have been treated with a parenteral anticoagulant for at least 5 days

- To reduce the risk of recurrence of VTE in pediatric patients 8 to less than 18 years of age who have been previously treated

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

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

Prescribing Information and Medication Guide), 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).

CARTON AND CONTAINER LABELING

Submit final printed carton and container labeling that are identical to the carton and container labeling submitted on February 23, 2021, 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 022512/S-041**." 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 all relevant pediatric age groups for this application.

[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 submission dated September 21, 2020, containing the final reports for the following postmarketing requirements listed in the April 4, 2014, approval letter for NDA 022512/S-018.

2139-2 Conduct an open-label, randomized, parallel-group, active-controlled, multicenter, non-inferiority efficacy study of dabigatran etexilate versus standard of care for venous thromboembolism treatment in children from birth to less than 18 years of age. Include PK/PD (sparse sampling) in all patients. The anticipated enrollment is 240 evaluable patients for the efficacy analysis. Enroll adequate numbers of patients in 3 age groups, from 12 to <18 years of age, from 2 to <12 years of age, from birth to <2 years of age. Submit the clinical study report with datasets.

Patients from birth to <2 years of age may be enrolled only after data from a planned interim analysis have shown efficacy and safety of dabigatran in the older pediatric age groups.

2139-3 Conduct an open label, single arm trial to evaluate safety of dabigatran etexilate for secondary prevention of venous thromboembolism in children aged 0 to less than 18 years. The anticipated enrollment is 100 patients. Submit the clinical study report with datasets.

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

This completes all of your postmarketing requirements acknowledged in our April 4, 2014, approval letter.

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]

You must submit final promotional materials and Prescribing Information, accompanied by a Form FDA 2253, at the time of initial dissemination or publication

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

[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]

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 information [21 CFR 314.70(a)(4)]. The revisions in your promotional materials should include prominent disclosure of the important new safety 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).

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, contact Brittany Garr-Colón, MPH, Regulatory Project Manager, at (301) 796-6153 or via email at Brittany.Garr-Colon@fda.hhs.gov.

Sincerely,

{See appended electronic signature page}

Albert Deisseroth, MD, PhD
Deputy Division 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

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

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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.

/s/

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