



NDA 022512/S-018

SUPPLEMENT APPROVAL

Boehringer Ingelheim Pharmaceuticals, Inc.
Attention: Dawn Collette, Associate Director
900 Ridgebury Road
P.O. Box 368
Ridgefield, CT 06877

Dear Ms. Collette:

Please refer to your Supplemental New Drug Application (sNDA) dated June 6, 2013, received June 6, 2013, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Pradaxa[®] (dabigatran etexilate mesylate) 75 mg and 150 mg Capsules for oral use.

We acknowledge receipt of your amendments dated June 19, July 22, August 5, 21, 28, September 3, 4, 11, October 4, 9, 28, December 20, 2013, January 14, February 11, 12, 13, 25, March 5, 6, 24, 31, and April 3, 2014.

This Prior Approval[™] supplemental new drug application provides for two new indications:

- For the treatment of deep venous thrombosis (DVT) and pulmonary embolism (PE) in patients who have been treated with a parenteral anticoagulant for 5-10 days.
- To reduce the risk of recurrence of DVT and PE in patients who have been previously treated.

APPROVAL & LABELING

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

WAIVER OF HIGHLIGHTS SECTION

We acknowledge your request to waive the requirements of 21 CFR 201.57(d)(8) regarding the length of Highlights of prescribing information. As previously discussed with you, we are denying your 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 <http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm>. Content of labeling must be identical to the enclosed labeling (text for the package insert and Medication Guide), with the addition of any labeling changes in pending “Changes Being Effectuated” (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 titled “SPL Standard for Content of Labeling Technical Qs and As at <http://www.fda.gov/downloads/DrugsGuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf>.

The SPL will be accessible from publicly available labeling repositories.

Also within 14 days, amend all pending supplemental applications that includes 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 MS Word format, that includes the changes approved in this supplemental application, as well as annual reportable changes and annotate each change. To facilitate review of your submission, 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, 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(s) in pediatric patients unless this requirement is waived, deferred, or inapplicable.

We are deferring submission of your pediatric studies, because this product is ready for approval for use in adults and the pediatric studies have not been completed.

Your deferred pediatric studies required under section 505B(a) of the FDCA are required postmarketing studies. The status of these postmarketing studies must be reported annually according to 21 CFR 314.81 and section 505B(a)(3)(B) of the FDCA. These required studies are listed below.

PMR 2139-1 Conduct an open-label, single dose, single arm, tolerability, PK/PD and safety study of dabigatran etexilate given at the end of standard anticoagulant therapy in children aged less than 1 year old.

Final Protocol Submission:	10/31/2014
Study Completion:	12/31/2016
Final Report Submission:	06/30/2017

PMR 2139-2 Conduct an open-label, randomized, parallel-group, active-controlled, multi-center, 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.

Final Protocol Submission: 12/31/2014
Study Completion: 06/30/2018
Final Report Submission: 06/30/2019

PMR 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.

Final Protocol Submission: 12/31/2014
Study Completion: 12/31/2018
Final Report Submission: 12/31/2019

Submit the protocols to your IND 063267, with a cross-reference letter to this NDA.

Reports of these required pediatric postmarketing studies must be submitted as a new drug application (NDA) or as a supplement to your approved NDA with the proposed labeling changes you believe are warranted based on the data derived from these studies. When submitting the reports, please clearly mark your submission "**SUBMISSION OF REQUIRED PEDIATRIC ASSESSMENTS**" in large font, bolded type at the beginning of the cover letter of the submission.

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 package insert(s) to:

Food and Drug Administration
Center for Drug Evaluation and Research
Office of Prescription Drug Promotion (OPDP)
5901-B Ammendale Road
Beltsville, MD 20705-1266

You must submit final promotional materials and package insert(s), 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

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

Information and Instructions for completing the form can be found at

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

more information about submission of promotional materials to the Office of Prescription Drug Promotion (OPDP), see <http://www.fda.gov/AboutFDA/CentersOffices/CDER/ucm090142.htm>.

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 package labeling. Within 7 days of receipt of this letter, submit your statement of intent to comply with 21 CFR 314.70(a)(4) to the address above or by fax to 301-847-8444.

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 Elleni Alebachew, Regulatory Project Manager, at (301) 796-5225.

Sincerely,

{See appended electronic signature page}

Ann T. Farrell, M.D.
Director
Division of Hematology Products
Office of Hematology and Oncology Products
Center for Drug Evaluation and Research

ENCLOSURE(S):
Content of Labeling

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

ANN T FARRELL
04/04/2014