

NDA 022512/S-042

## **SUPPLEMENT APPROVAL**

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

Dear Mr. Mazzarella:

Please refer to your supplemental new drug application (sNDA) dated and received April 9, 2021, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Pradaxa (dabigatran etexilate) Tablets.

We also refer to our letter dated February 19, 2021, notifying you, under Section 505(o)(4) of the FDCA, of new safety information that we believe should be included in the labeling for the novel oral anticoagulant (NOAC) class. This information pertains to the risk of serious uterine bleeding associated with the use of NOACs, such as Pradaxa.

This supplemental new drug application provides for revisions to the labeling for Pradaxa as well as revisions to the Medication Guide, consistent with our February 19, 2021 letter requiring removal of all references to site specific bleeding in Section 6.2 of the approved label; and addition of section 8.3 to describe the risk of clinically significant uterine bleeding in females of reproductive potential. The Medication Guide was also updated with the language from section 8.3.

### **APPROVAL & LABELING**

We have completed our review of this application. 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](http://www.fda.gov).<sup>1</sup> Content of labeling must be identical to the enclosed labeling (text for the Prescribing Information), 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. If the content of labeling in SPL format initially submitted with

---

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

this CBE-0 labeling supplement is identical to the attached approved labeling, an additional submission of content of labeling in SPL format is not required.

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(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).

## **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, please call Lori Anne Wachter, RN, BSN, RAC, Acting Regulatory Project Manager for Safety, at 301 796-3975

Sincerely,

*{See appended electronic signature page}*

Rosanna Setse, MD, PhD.  
Deputy Director for Safety  
Division of Non-malignant Hematology  
Office of Oncology, Hematology, Endocrinology  
and Nephrology  
Center for Drug Evaluation and Research

### ENCLOSURE(S):

- Content of Labeling
  - Prescribing Information
  - Medication Guide

---

<sup>2</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>.

-----  
**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/  
-----

ROSANNA W SETSE  
04/20/2021 11:30:24 AM