



NDA 22512/S-032

**SUPPLEMENT APPROVAL**

Boehringer Ingelheim Pharmaceuticals, Inc.  
Attention: Michelle Kliewer  
Director, Drug Regulatory Affairs  
900 Ridgebury Road  
P.O. Box 368  
Ridgefield, CT 06877

Dear Ms. Kliewer:

Please refer to your Supplemental New Drug Application (sNDA) dated 15 October 2015, received 15 October 2015, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Pradaxa (dabigatran etexilate mesylate) 75 and 150 mg Capsules.

This Prior Approval supplemental new drug application proposes changes to include information regarding Praxbind (idarucizumab), an approved PRADAXA specific antidote

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 agreed-upon labeling text. These changes are as follows:

- In Section 2, **DOSAGE AND ADMINISTRATION**, subsection 2.6 **Discontinuation for Surgery and Other Interventions**, the following text was added:  
  
“Use a specific reversal agent in case of emergency surgery or urgent procedures when reversal of the anticoagulant effect of dabigatran is needed. Refer to the idarucizumab prescribing information for additional information. Restart PRADAXA as soon as medically appropriate.”
- In Section 5, **WARNINGS AND PRECAUTIONS**, subsection 5.1 **Increased Risk of Thrombotic Events after Premature Discontinuation**, the following text in red was added:  
  
“If PRADAXA is discontinued for a reason other than pathological bleeding or completion of a course of therapy, consider coverage with another anticoagulant and restart PRADAXA as soon as medically appropriate [see Dosage and Administration (2.4, 2.5, 2.6)].”

- Also under Section 5, subsection 5.2. **Risk of Bleeding**, “*Reversal of Anticoagulant Effect*” was amended to read:

“A specific reversal agent (idarucizumab) for dabigatran is available when reversal of the anticoagulant effect of dabigatran is needed:

- For emergency surgery/urgent procedures
- In life-threatening or uncontrolled bleeding”

- In Section 10, **OVERDOSAGE**, the following sentence was added:

“A specific reversal agent (idarucizumab) is available.”

- The above mentioned changes to Sections 2 and 5 were included in Highlights under **RECENT MAJOR CHANGES**.

### **LABELING**

Submit final printed labeling, as soon as they are available, but no more than 30 days after they are printed. The final printed labeling (FPL) must be identical to the enclosed labeling, and must be in the “Drug Facts” format (21 CFR 201.66), where applicable.

The final printed labeling should be submitted electronically according to the guidance for industry titled “Providing Regulatory Submissions in Electronic Format – Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications (June 2008).” Alternatively, you may submit 12 paper copies, with 6 of the copies individually mounted on heavy-weight paper or similar material. For administrative purposes, designate this submission “**Final Printed Labeling for approved NDA 22512/S-032.**” Approval of this submission by FDA is not required before the labeling is used.

### **DRUG REGISTRATION AND LISTING**

All drug establishment registration and drug listing information is to be submitted to FDA electronically, via the FDA automated system for processing structured product labeling (SPL) files (eLIST). At the time that you submit your final printed labeling (FPL), the content of labeling (Drug Facts) should be submitted in SPL format as described at <http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm>. 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/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf>. In addition, representative container or carton labeling, whichever includes Drug Facts, (where differences exist only in the quantity of contents statement) should be submitted as a JPG file.

### **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.

Because none of these criteria apply to your application, you are exempt from this requirement.

**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 contact:

Alison Blaus, RAC  
Regulatory Project Manager  
(301) 796-1138

Sincerely,

*{See appended electronic signature page}*

Norman Stockbridge, MD, PhD  
Director  
Division of Cardiovascular and Renal  
Products  
Office of Drug Evaluation I  
Center for Drug Evaluation and Research

ENCLOSURE:  
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/  
-----

NORMAN L STOCKBRIDGE  
10/23/2015