DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Silver Spring, MD 20993

Nada Glavan, Associate Director, Drug Regulatory Affairs
Boehringer Ingelheim Pharmaceuticals Inc.
900 Ridgebury Road
P.O. Box 368
Ridgefield, CT 06877-0368

RE: NDA # 022512
Pradaxa® (dabigatran etexilate mesylate) capsules
MA #2,5,7 (MACMIS # 19197, 19201, 19202)

Dear Ms. Glavan:

Pursuant to the provisions of 21 CFR 202.1 (j)(4), we are changing our opinion regarding Pradaxa® (dabigatran etexilate mesylate) capsules' (Pradaxa) direct-to-consumer promotional materials which include the following claim:

- "In a clinical trial, PRADAXA 150 mg reduced stroke risk 35% more than warfarin."

As presented, the 35% relative risk reduction claim is misleading because it does not inform consumers about the absolute magnitude of the benefit of the drug, an important consideration when weighing benefits against risks. Without useful numeric contextual information, relative risk reduction can suggest a magnitude of benefit much greater than demonstrated. According to the Clinical Studies section of the approved product labeling (PI) for Pradaxa, "Relative to warfarin and PRADAXA 110 mg, Pradaxa 150 mg twice daily significantly reduced the primary composite endpoint of stroke and systemic embolism," **with a relative risk reduction of 35% (based on incidences of 2.2% for Pradaxa 150 mg vs. 3.4% for warfarin)**. (emphasis added)

We recommend adding numeric context to prominently convey the absolute risk reductions for stroke between patients treated with Pradaxa and patients treated with warfarin, to accompany the 35% relative risk reduction claims. The purpose of this additional disclosure to the promotional pieces is to provide consumers with pertinent information to more accurately interpret the relative benefit Pradaxa may provide in reducing the risk of a stroke.

We acknowledge that revising the 35% stroke relative risk reduction claim to add this context involves presenting three different percentage concepts, and as such, creates an unusual challenge to successfully transmit all of the important numeric information in a compressed-format broadcast ad. For example, the following information should be disclosed in addition to the 35% efficacy presentation, "That means that in a large clinical study, 3.4% of patients taking warfarin had a stroke compared to 2.2% of patients taking Pradaxa." To reinforce the

important contextual information, we recommend presenting the absolute risk reduction percentages in both the audio and video of the TV ads, to parallel the 35% relative risk reduction claim that appears in both the voice-over and a large on-screen graphic; and to present this combined efficacy claim in a manner that is slow and clear enough to describe these risk reduction concepts. In addition, we recommend revising all other direct-to-consumer Pradaxa promotional materials which include the same or similar 35% stroke relative risk reduction claim, to include the absolute risk reduction percentages to accompany the quantitative relative risk reduction claim, or to add some other contextual information understandable to consumers so that they may more accurately interpret the relative benefit Pradaxa provides in reducing the risk of a stroke.

Because this constitutes a change in our position, you will be provided a reasonable period of time to revise any promotional materials currently in use that contain this or similar claims and presentations. Accordingly, the revisions should be completed within 90 days of receipt of this letter or at next printing, whichever comes first. Please submit a written response to this letter by June 5, 2013, stating whether you intend to comply with our request and the specific date the revisions will be implemented.

If you have any questions or comments, please direct your response to the undersigned by facsimile at (301) 847-8444, or at the **Food and Drug Administration, Center for Drug Evaluation and Research, Office of Prescription Drug Promotion, 5901-B Ammendale Road, Beltsville, Maryland 20705-1266.** To ensure timely delivery of your submissions, please use the full address above and include a prominent directional notation (e.g. a sticker) to indicate that the submission is intended for OPDP. Please refer to MA numbers 2, 5, and 7 in addition to the NDA number in all future correspondence relating to this particular matter. OPDP reminds you that only written communications are considered official.

Sincerely,

{See appended electronic signature page}

Zarna Patel, Pharm.D.
Regulatory Review Officer
Office of Prescription Drug Promotion

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

/s/

ZARNA PATEL
05/22/2013