



NDA 9-218/S-102

Bristol-Myers Squibb Company  
Attention: David L. Silberstein, Associate Director  
New Opportunities & Product Development  
Pharmaceutical Research Institute  
P.O. Box 4000  
Princeton, NJ 08543-4000

Dear Mr. Silberstein:

Please refer to your supplemental new drug application dated April 29, 2005, received May 2, 2005, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Coumadin<sup>®</sup> (Warfarin Sodium) Injection.

We acknowledge receipt of your submissions dated April 3, May 1 and 3, September 14, and September 26, 2006.

Your submission of April 3, 2006 constituted a complete response to our November 1, 2005 action letter.

This supplemental new drug application provides for revisions to the package insert regarding the risk of major or fatal bleeding and the development of a Medication Guide reflecting the important patient information regarding the bleeding risks.

We 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 and with the editorial revisions listed below and indicated in the enclosed labeling.

1. In the **CLINICAL TRIALS** section, **Myocardial Infarction** subsection, in Table 3 entitled "**WARIS II – Distribution of Separate events According to Treatment Group,**" in the rows labeled "Major Bleeding<sup>c</sup>" and under the fifth column (labeled Rate Ratio), add the phrases "3.35<sup>a</sup> (ND)" and "4.00<sup>b</sup> (ND)".
2. In the **CLINICAL TRIALS** section, **Myocardial Infarction** subsection, in Table 3 entitled "**WARIS II – Distribution of Separate events According to Treatment Group,**" in the rows labeled "Minor Bleeding<sup>d</sup>" and under the fifth column (labeled Rate Ratio), add the phrases "3.21<sup>a</sup> (ND)" and "2.55<sup>b</sup> (ND)".

The final printed labeling (FPL) must be identical to, except for including the revisions listed, the enclosed labeling (text for the package insert, text for the Medication Guide, immediate container and carton labels) and submitted labeling (package insert submitted September 14, 2006, patient package insert submitted September 14, 2006, immediate container and carton labels submitted

September 14, 2006). These revisions are terms of the NDA approval. Marketing the product before making the revisions, exactly as stated, in the product's labeling may render the product misbranded and an unapproved new drug.

Please submit an electronic version of the FPL according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format - NDA*. Alternatively, you may submit 20 paper copies of the FPL as soon as it is available but no more than 30 days after it is printed. Individually mount 15 of the copies on heavy-weight paper or similar material. For administrative purposes, designate this submission "**FPL for approved supplement NDA 9-218/S-102.**" Approval of this submission by FDA is not required before the labeling is used.

If you issue a letter communicating important information about this drug product (i.e., a "Dear Health Care Professional" letter), we request that you submit a copy of the letter to this NDA and a copy to the following address:

MEDWATCH  
Food and Drug Administration  
5515 Security Lane  
HFD-001, Suite 5100  
Rockville, MD 20852

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 Mrs. Diane Leaman, Regulatory Project Manager, at (301) 796-1424.

Sincerely,

*{See appended electronic signature page}*

George Mills, M.D.  
Director  
Division of Medical Imaging and Hematology  
Products  
Office of Oncology Drug Products  
Center for Drug Evaluation and Research

Enclosure

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**This is a representation of an electronic record that was signed electronically and  
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/s/

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George Mills  
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