

Bayer HealthCare  
Consumer Care Division

2324 5 JUL 12 09:22



July 11, 2005

Division of Dockets Management  
Food and Drug Administration  
5630 Fishers Lane  
Room 1061 (HFA-305)  
Rockville, Maryland 20852

Leonard Baum, RPh  
Vice President  
Regulatory Affairs

**Re: Docket 77N-0094**

**Aspirin Primary Prevention Professional Labeling (CP16) – Summary of Information Supporting Petition**

Dear Dr. Stockbridge:

Reference is made to Bayer HealthCare, Consumer Care Division's (Bayer) Citizen Petition submitted on 2/11/03 for the use of aspirin in the primary prevention of myocardial infarction (MI) in those at moderate or greater risk of a cardiovascular event. Based on ongoing discussions with the Agency, including the 12/8/03 Advisory Committee Meeting and the 4/30/04 Public Meeting, Bayer has provided information to address the Agency's outstanding questions regarding the Petition, including working with a third party to address the Agency's request to receive the original study data from the Thrombosis Prevention Trial (TPT) and information on silent MI from the TPT study. These data were submitted by Drs. Colin Baigent and Thomas Meade and received by the Agency on 3/14/05 and 5/27/05, respectively.

Bayer HealthCare LLC  
Consumer Care Division  
36 Columbia Road  
P.O. Box 1910  
Morristown, NJ 07962-1910

Phone: (973) 254-4672  
Fax: (973) 254-4875

After a quick topline review of the data received from Dr. Baigent on the TPT study, on 3/30/05 FDA provided Bayer with a letter noting that silent MI data from this study was not provided and that the Cardio-Renal Division would render its conclusions on the Petition within 30 days. As discussed with the Agency on several previous occasions, silent MI was not included as part of the protocol for the TPT trial and therefore the raw data for silent MI was not part of the raw data set for this study and not readily available. Furthermore, silent MI data was not specifically requested at the 4/30/04 public meeting as noted in the Agency's 3/30/05 letter. Importantly, as the Agency is aware, Bayer did not conduct the five studies on which the Petition is based and therefore does not own or have access to the data for these trials. However, Bayer has worked throughout the past 2 years to support the Petition and facilitate the transfer of data from the investigators that has been requested by the Agency.

77N-0094

SUP 56

To better understand the open questions and discuss the data in the Petition as well as new data that continues to become available, Bayer submitted a meeting request on 4/21/05 to the Agency. Bayer continues to believe that, despite the open question surrounding silent MI, the five primary prevention trials support the Petition and can be used to develop labeling to describe the benefits of aspirin in reducing a first MI in those at moderate or greater risk.

On June 7, 2005, however, the Agency denied Bayer's request for a meeting with the Agency noting that there is no new information to discuss.

#### Silent MI

Responding to the Agency's question regarding silent MI, both Drs. Baigent and Meade provided comments to the Agency on the use of silent MI in the analysis of the efficacy of aspirin on primary prevention of MI. Specifically, it was noted that use of these data are problematic in that it is potentially biased by lack of time-to-event data, lack of consistency of measuring the endpoint in all five primary prevention studies, and lack of inclusion of silent MI in the primary outcome measure in the Antiplatelet Trialists' Collaboration.

In order to help bridge the data from the five studies supporting the Petition and the questions raised, Bayer believes that including a discussion of this issue in the clinical trial section of the labeling would provide clinicians with enough information to conduct an individual risk-benefit assessment for their patients.

#### Weight of Evidence

Bayer acknowledges that, while each of the five studies on which the Petition is based were randomized controlled clinical trials conducted by qualified investigators using high standards, they do not represent the "NDA-style" traditionally seen by sponsor-initiated trials. As the Agency is aware, these five studies had different baseline entry criteria and different objectives. However, these five studies and their meta-analysis provide strikingly similar results and support the benefit of aspirin in reducing risk of a first non-fatal MI. Bayer continues to believe that using a "weight-of-evidence" approach to evaluating the efficacy of aspirin is applicable given the consistency in findings of the studies and the long safe history of use.

Additionally, results of the recently-published Women's Health Study (WHS) are consistent with the findings of the five primary prevention trials on which the Petition is based in that the results show aspirin's benefit in the primary prevention of the combined endpoint of MI, vascular death and stroke, as well as MI alone, in women age 65 years of age. As the Agency considers the "weight-of-evidence" for the benefit of aspirin in primary prevention of MI, we hope the WHS will be considered, as we believe that this information can help to further support development of label statements.

Dose

Bayer recognizes that the Agency is evaluating another open Citizen Petition related to aspirin (Docket 2005P-0048, CP1). Specifically, a reduction in the dose allowed in the professional labeling for secondary prevention has been proposed. Bayer has, in fact, provided comments to the Petition on this issue and believes that, as with primary prevention, guidance should be provided to allow physicians to treat individual patients with individual needs, including a range of low doses for treating patients at risk for second MI or stroke.

Summary

Bayer remains committed to working with the Agency on this very important initiative to support the Petition for use of aspirin in the primary prevention of MI in those at moderate or greater risk. As Bayer was denied its request for a meeting, we have prepared a summary of information that supports the Petition and address comments raised on silent MI. Bayer remains committed to support this Petition for the use of aspirin in primary prevention that will align the professional labeling with professional guidelines. We are available anytime to discuss the Petition and would appreciate an update before any final action is taken.

Please contact me at 973-254-4672 or Catherine Fish, Senior Associate Director, Regulatory Affairs at 973-254-4793 if you have any questions.

Bayer HealthCare  
Consumer Care Division



Leonard Baum, RPh  
Vice President, Regulatory Affairs

cc: Dr. C. Ganley