

Bayer HealthCare
Consumer Care Division

0035 5 MAY 5 2005



May 4, 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 2005P-0048

Comments to Citizen Petition for Aspirin Professional Labeling Proposed Changes

Dear Dr. Ellenberg:

Reference is made to McNeil Consumer & Specialty Pharmaceuticals' Citizen Petition (CP1) requesting FDA approval for a change in the professional labeling for aspirin dosing for secondary prevention of cardiovascular and cerebrovascular events submitted January 31, 2005.

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

In response to this Petition, Bayer Consumer Care is submitting the attached information to support the current dose range for aspirin approved in the professional labeling for the secondary prevention of cardiovascular and cerebrovascular events. In summary, the data show the following:

- While all doses of aspirin confer some degree of gastrointestinal (GI) bleeding risk, there is no demonstrable difference in the evidence from randomized controlled trials (RCT) and meta-analyses of RCTs among aspirin regimens within the low dose range (75 – 325 mg).
- Different doses of aspirin within the low dose range have shown variability in impacting thromboxane. Thus, a range of doses remains necessary to ensure physicians' choice and appropriate patient care.
- Disease states such as smoking, diabetes and obesity may modify platelet function and aggregation. Consequently, higher doses of aspirin may be needed in these populations.
- While variable platelet function and aggregation changes under aspirin therapy have been observed, more uniform inhibition of platelet function can be achieved in individual patients when higher doses are used.
- Few trials have compared aspirin doses in a randomized, controlled fashion. In those few trials, doses were often outside of low dose range.

2005P 0048

C 2

- Observational evidence may suggest a difference in safety among doses within the low dose range. However, observational evidence is subject to significant confounding. Additionally, the efficacy data in these same observational studies is inconsistent with one trial even suggesting greater efficacy for higher doses.
- Contemporary stroke trials have used higher doses (≥ 650 mg) of aspirin and demonstrated safety and efficacy, thus supporting the acceptance of higher doses in certain secondary prevention populations.
- Professional guidelines, including those from the American Heart Association and the American College of Cardiology, support the entire dose range in both recurrent MI and stroke prevention.
- Guidelines support the higher end of the dose range in other cardiovascular indications such as acute MI and post-procedure prophylaxis.
- Physician survey data demonstrate utilization and support for 325 mg regimen.

Given the current state of the data and the possibility that higher doses of aspirin may be needed for certain populations, we believe that it is appropriate to provide physicians with a range of doses within the professional label from which to choose when treating individual patients.

Thank you very much for your consideration of the attached information as you review this Citizen Petition. Should you have any questions, please feel free to contact me at 973-254-4672 or Catherine Fish, Senior Associate Director, Regulatory Affairs, at 973-254-4793.

Bayer HealthCare
Consumer Care Division



Leonard Baum, RPh
Vice President, Regulatory Affairs

Submitted in duplicate