FOOD AND DRUG ADMINISTRATION (FDA)

Center for Drug Evaluation and Research (CDER)

Joint Meeting of the Nonprescription Drugs Advisory Committee and the Endocrinologic and Metabolic Drugs Advisory Committee

HILTON WASHINGTON, DC/SILVER SPRING
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QUESTIONS TO ADVISORY COMMITTEE

DECEMBER 13, 2007

1. The NCEP ATP-III guidelines use LDL-C as the basis for determining therapeutic targets and selecting populations for drug treatment and ongoing management. The FDA advisory committee that convened in January 2005 to discuss nonprescription lovastatin 20 mg agreed that the population of subjects selected using an LDL-based label paradigm was appropriate for drug treatment.

   Do you believe that a total cholesterol-based label paradigm is an appropriate approach to selecting patients for use of nonprescription lovastatin and ongoing management? Please state the reasons for your position.

2. At previous joint Nonprescription Drug Advisory Committee (NDAC) and Endocrine and Metabolic Drugs Advisory Committee meetings, the difficulty in developing a label which adequately conveys to consumers all the information necessary to make a correct self-selection has been discussed. The NDAC members, in September, 2006, at an advisory committee meeting devoted to consumer study design issues stated that it was reasonable to use hierarchies based on safety and efficacy consideration, to assess appropriate self-selection for products that have multiple self-selection criteria. Since that meeting we have been advising sponsors to use the hierarchy approach. You have seen examples of different hierarchies used to assess self-selection of nonprescription lovastatin 20-mg.

   Was there a hierarchy presented today that should be used for the basis of a regulatory decision? Please state which one and provide your reasoning. Is there another hierarchy that you would suggest for this purpose? If so, please state the elements that should be part of that hierarchy.

3. Do the results from the SELECT self-selection study demonstrate that OTC consumers could make an appropriate self-selection decision?

   In your deliberation please consider how these groups should be factored into our thinking about appropriate self-selection.

   a. Those who receive little benefit because they are at lower risk for CHD
   b. Those who receive sub-optimal benefit because they are at higher risk for CHD than the population identified on the label
   c. Those who might switch from a prescription statin such as atorvastatin, simvastatin, or rosuvastatin to lovastatin 20 mg, a less potent alternative.
   d. Those who might take their prescription statin or other prescription lipid-altering drug in addition to the OTC statin

4. To address the safety of lovastatin in the nonprescription setting:

   a. Does the data support adequate consumer understanding of the warning concerning pregnancy and appropriate self-selection by women of childbearing potential? If not, what further data would be needed?

   b. Does the data support adequate consumer understanding of the muscle pain warning? If not, what further data would be needed? When answering, please consider the self-selection responses of those who were already on statins and chose to switch to the OTC product or to take both products.

   c. Does the data demonstrate that consumers with common asymptomatic liver disease can safely use lovastatin 20 mg without liver function monitoring? If not, could labeling minimize this risk?

   d. FDA and others have observed a data mining signal for amyotrophic lateral sclerosis (ALS) with statins. Retrospective analyses of data from large, long-term trials of primary and secondary CAD prevention revealed similar incidence rates of ALS in statin and placebo-treated patients. There is an ongoing case-control study examining the question of whether statins increase the risk for ALS. This study is expected to be completed in mid-to-late 2008. Considering the self-selection data and risk versus benefit of taking a statin for coronary heart disease prevention, how does the ALS data mining signal impact on OTC availability of statins?

5. Subjects in the CUSTOM actual use study used a different label then subjects in the SELECT label comprehension studies and SELECT self-selection study. In the absence of actual use data from the SELECT label, can we bridge the actual use data from the CUSTOM actual use study to the following consumer behaviors:
    - follow-up cholesterol testing
    - consumer action if the LDL target is not met
    - consumer action if a side effect such as muscle pain develops

    If not, what additional data are needed? Address this question for the LDL–C Label and, if your answer to question 1 is yes, address this question for the Total-C label.

6. Should FDA approve nonprescription lovastatin based on the data presented at this meeting? Why or why not? What additional data is needed, if any?