FDA Panel Rejects OTC Switch for Lovastatin

BY ELIZABETH MECHCATIE
Senior Writer

SILVER SPRING, MD. — For the third time since 2000, Merck & Co. failed to convince Food and Drug Administration advisory panelists that lovastatin should be made available over the counter.

At a joint meeting, the FDA's Nonprescription Advisory Committee and Endocrinologic and Metabolic Drugs Advisory Committee voted 10-2, with one abstention, that lovastatin should not be approved as a nonprescription drug, based on the data provided by the company. The data included the results of a trial evaluating how consumers self-select for treatment with lovastatin. The panelists voted 11-2 that the results of the study did not show that OTC consumers could make an appropriate self-selection decision.

Merck filed for approval for OTC use of a fixed daily 20-mg dose of lovastatin, marketed as Mevacor, "to help lower cholesterol, which may prevent a first heart attack," focusing on a moderate-risk population. This population, identified using National Cholesterol Education Program (NCEP) ATP III guidelines, comprised men aged at least 45 years and women aged at least 55 years with moderately high LDL cholesterol (130 mg/dL to 170 mg/dL) and one additional CHD risk factor. Merck's main argument was that the OTC availability of lovastatin would increase access and use among the large, undertreated population of people with high cholesterol, and would result in significant public health benefits.

The panel generally agreed that lovastatin was a safe and effective medication. But they were concerned that the results of the study indicated that a substantial proportion of patients who were actually high risk and should have been on a prescription statin, under a physician's supervision, would self-select for a statin. Likewise, a substantial proportion of people who were low risk and not candidates for therapy would also self-select for a statin. Other concerns were the lack of actual use studies in real-world situations.

"Patients couldn't figure out whether the drug was for them," said Dr. William Shrank of the division of pharmacoepidemiology and pharmacoeconomics at Harvard Medical School, Boston.

"In my view, the benefits greatly outweigh the risks," said Dr. Thomas Pickering, director of the behavioral cardiovascular health and hypertension program at Columbia University, New York. Dr. Pickering voted in favor of approval. Describing the statins as an "incredibly safe" group of drugs, he said there is "a huge, unmet need for people who should be taking statins and who are not, and this offers a plausible way for getting them all to take them."

The FDA usually follows the advice of its advisory panels. This is the third time that the advisory panels have met to vote on approval since 2000. At the second meeting in January 2005, the panels voted 20-3 against approval for the OTC switch, citing problems with the label comprehension study and doubts about whether patients could properly self-select for treatment.

Since then, Merck made substantial changes to the label and accompanying materials, and conducted another self-selection study of more than 1,400 participants at 14 U.S. sites, in a simulated retail setting in which a pharmacist was available to answer questions. The Self-Evaluation of Lovastatin to Enhance Cholesterol Treatment (SELECT) study evaluated two labels (one with LDL cholesterol information and one with total cholesterol information as eligibility criteria) that patients used to determine whether the drug was appropriate for them and whether they would buy the product. Labels also included information on absolute and relative safety warnings and a decision tree.

About 72% of the participants were correct in determining whether lovastatin was appropriate for them, with either label. Most of the correct decisions were that the drug was not appropriate. For example, of the 662 participants who were in the LDL cholesterol label arm, 439 correctly determined that the drug was not appropriate and 34 correctly determined that it was appropriate, for a total of 71.5%.

The materials included in the redesigned package were a refrigerator magnet reminding people to call their physicians if they experienced muscle pains, a "heart healthy" living guide, and cards for consumers to give to pharmacists and physicians saying they were taking lovastatin.

The FDA is expected to make a decision by the end of January. ■