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RE: FDA Joint Meeting of the Nonprescription Drugs Advisory Committee and the Endocrinologic and Metabolic Drugs Advisory Committee

Pfizer welcomes the Food and Drug Administration's (FDA) commitment to exploring new ways to reduce the burden of cardiovascular disease (CVD), the leading cause of death in the United States.

Effective use of HMG-CoA reductase inhibitors (statins) can lower the risk of cardiovascular events that often lead to costly hospitalization, disabilities, and in some cases, death. The fact that the FDA is considering statins in an over-the-counter (OTC) setting reaffirms the safety profile of this class of drugs. However, given the complexity of managing a chronic, asymptomatic and potentially life-threatening disease such as CVD, we have concerns that we wish to raise regarding the question of the suitability of OTC statins.

Over the past decade, the Nonprescription Drugs Advisory Committee and the Endocrinologic and Metabolic Drugs Advisory Committee have considered the issues around the use of cholesterol-lowering therapies in an OTC setting. During its meeting in 1997, and again in 2000, the Advisory Committee concluded that hypercholesterolemia is not a disease that lends itself to OTC treatment but rather one that requires an accurate diagnosis, ongoing clinical testing, and careful medical management directed by a prescribing healthcare practitioner. In both cases, the Center for Drug Evaluation and Research (CDER) agreed that these drugs were inappropriate for OTC distribution.

Although the proposed OTC products are purportedly intended for a different and arguably healthier target population than those with diagnosed hypercholesterolemia, their availability would raise the same issues and risks that were addressed during the 1997 and 2000 meetings. In these meetings, the Committee underscored the importance of involving a prescribing healthcare practitioner in the management of CVD. These issues remain valid today, particularly in light of new clinical evidence and recent changes to medical treatment guidelines for CVD management.

We believe that, based on the following issues, statins are most appropriate for use as prescription-only medications:

- *Cardiovascular disease is a multi-factorial disease; it is not only about cholesterol*

Cardiovascular disease is a chronic and potentially life-threatening disease that most frequently occurs as a result of *multiple risk factors*, including high blood pressure, elevated lipid levels, diabetes mellitus,

obesity, smoking, and family history. The United States is under serious threat of decreased life expectancy due to simultaneous epidemics of diabetes mellitus and obesity, both significant contributors to cardiovascular disease. CVD risk management must therefore be based on a thorough assessment of **all** of a patient's personal risk factors, with treatment plans tailored to the individual.

- *Availability of OTC statins would shift the burden of complex disease management to consumers*

Cardiovascular disease is complex to manage and requires the expertise of a prescribing healthcare practitioner, who can counsel patients on important lifestyle changes, help them control multiple risk factors, and steer them to the correct therapeutic options and most appropriate doses of medicine. People who self-select an OTC cholesterol-lowering drug instead of entering the healthcare system could make important medical decisions without appropriate medical guidance. Attempting to treat a life-threatening disease such as CVD without achieving a clinically meaningful individual goal may create a false sense of security for patients. By not seeking the counsel of a prescribing healthcare professional, these people might not receive the best treatment options available or be screened and treated for other CVD risk factors. As a result, they may not be addressing, treating, and effectively managing all of their risk factors for heart disease, such as high blood pressure, which would otherwise be recommended or could be prescribed by a healthcare practitioner. The potential to negatively impact their cardiovascular health is enormous.

- *Statins are intended for chronic treatment of an asymptomatic but life-threatening disease*

CDER has stated that OTC drugs are generally used for self-recognizable conditions that are symptomatic, require short-term treatment, and can be treated without the oversight and intervention of a prescribing healthcare practitioner. In contrast, statins are used to treat an asymptomatic condition that requires long-term treatment and monitoring (not only with drug therapy but also therapeutic lifestyle changes) under the care and expertise of a prescribing healthcare professional. The prescribing healthcare practitioner not only diagnoses and prescribes the right treatment for a patient's CVD risk factors, but also provides continuous monitoring to evaluate the success of the treatment. This allows the prescribing healthcare professional to make changes, such as increasing the dosage or switching therapies, to provide the patient with the optimal treatment regimen.

- *OTC availability will supplant non-drug intervention choices and decrease emphasis on the behavioral modifications needed to create life-long health improvements*

A low-fat, low-cholesterol diet, regular exercise and smoking cessation are all important steps in lowering an individual's risk of CVD. When medical therapy is warranted, it should be administered concomitantly with lifestyle changes. Making lipid-lowering drugs readily available in an OTC setting may mislead individuals into thinking that they can avoid making beneficial lifestyle changes in favor of the "quick fix" of immediate drug therapy.

- *OTC availability is not the solution to poor compliance and persistency as is seen with current prescription regimens*

Circumventing the prescribing healthcare professional will likely have a negative impact on compliance and persistence by signaling to the public that the disease is not significant enough to warrant the care of a prescribing healthcare professional. Even when under a physician's care, achieving target levels for cholesterol and other risk factors can be challenging, and often requires drug titration and combination therapy. For example, an analysis of longitudinal prescription data from Verispan shows that approximately half of the patients prescribed statin therapy stop taking their

cholesterol medication within one year. Anecdotal evidence indicates that people believe that once a target LDL cholesterol level is achieved, medication is no longer required.

- *Clinical treatment guidelines are trending toward lower goals, suggesting the need for more intensive lipid-lowering therapy*

Evolving clinical evidence from trials such as HPS, ASCOT and PROVE-IT – available since the last Advisory Committee meeting – suggest that additional cardiovascular benefits can be achieved with even lower LDL cholesterol levels for certain individuals. Recently, the National Cholesterol Education Program’s Adult Treatment Panel (ATP III) updated its guidelines, highlighting the importance of intensive LDL cholesterol lowering. The report underscored the need for reducing LDL cholesterol by at least 30% to 40% to reduce coronary heart disease risk by the same percentage over a five-year period. Recent clinical evidence validates that even lower LDL reductions than recommended in the most recent guidelines may be required for optimal outcomes. This level of reduction, and corresponding CV benefit, is unlikely to be achieved with low-dose therapy.

Statin drugs are clearly safe and effective prescription drug therapies in the hands of knowledgeable prescribing healthcare practitioners for reducing cholesterol in individuals at an increased risk for CVD. However, the proposal to introduce these medications into the OTC market for a “low risk” population is troubling, in that it places an undue burden on consumers to make complex medical decisions without the extensive medical training or expertise of a prescribing healthcare practitioner. The degree of benefit in the proposed OTC population is unproven, but modest at best, while the consequences of inappropriate use (such as using these drugs to avoid the healthcare system by those at high risk for heart disease) can produce significant adverse consequences to the public health. We firmly believe that the health of the American public is better served by keeping these medications available by prescription only.

Respectfully,



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