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June 26, 2012

Margaret A. Hamburg, M.D.
Commissioner
Food and Drug Administration
Department of Health and Human Services
WO 2200
10903 New Hampshire Ave.
Silver Spring, MD 20993-0002

Dear Dr. Hamburg:

Tomorrow is the user fee (Prescription Drug User Fee Act) deadline for the Food and Drug Administration's (FDA's) decision on whether to approve the new diet drug lorcaserin (Lorqess), manufactured by Arena Pharmaceuticals. I strongly urge you to take personal responsibility and make a preventive public health decision not to approve the drug.

From a review of the just- posted transcript of the May 10, 2012, FDA advisory committee meeting at which lorcaserin was discussed, it is now clear that although the committee voted 18-4 for approval, it did so quite reluctantly, particularly because of widely shared concerns about evidence of heart valve damage in people using the drug in clinical trials. This same adverse effect led the FDA to ban fenfluramine and dexfenfluramine, the "fen" components of Fen-Phen, in 1997.

A key discussion point at the meeting was "whether the phase 3 echocardiography [a test for abnormal heart valves] data are sufficient to rule out a clinically meaningful increase in the risk for valvular heart disease in patients treated with lorcaserin." The committee chair summed up the comments of the other advisory committee members on this question by stating, "There's probably not sufficient data at this time to rule out a clinically meaningful increase in the risk for valvular heart disease."

The FDA, in its briefing package for the committee, had stated that "in the pooled analysis of the Phase 3 echocardiographic data, the relative risk for FDA-defined valvular heart disease (VHD) … was 1.16, with a 95% confidence interval (CI) of 0.81 to 1.67. This upper bound exceeds the 1.5 upper bound requested by FDA to rule out an excess risk of VHD." This means that the upper bound of 1.67 — a possible increase in valvular heart disease of 67 percent above that seen in people getting a placebo — was more than that which FDA had indicated as acceptable (an upper limit of a 50 percent increase).

Regarding the drug's benefits, after a year of exposure, patients experienced an approximately 3 percent weight loss beyond the weight loss seen in those using a placebo alone, meaning that a woman weighing 200 pounds would lose an average of six pounds by using the drug, a man weighing 300 pounds would lose an average of nine pounds.

Cardiologist Sanjay Kaul, voting against approval, stated, "Given the totality of evidence, the potential benefits of lorcaserin do not, in my opinion, outweigh the potential risks when used long term in a population of overweight and obese individuals."

Although evidence of heart valve damage with fenfluramine was only apparent after approval, in the case of lorcaserin, there is the above-mentioned pre-approval conclusion that "[t]here's probably not sufficient data at this time to rule out a clinically meaningful increase in the risk for valvular heart disease."

Faced with this serious concern, it would be dangerous and unconscionable for you to allow the FDA to disregard the available evidence and subject large numbers of obese patients, already at risk of cardiovascular disease, to the added risk of damaged heart valves. Just say no.

Sincerely,

Sidney M. Wolfe, M.D.
Director, Public Citizen's Health Research Group

CC: Dr. Janet Woodcock, Director, Center for Drug Evaluation and Research, Food and Drug Administration