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Division of Dockets Management (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, MD 20852

Submitted via http://www.regulations.gov at Docket No. FDA 2013-S-0610

CITIZEN PETITION

The Physicians Committee for Responsible Medicine submits this petition pursuant to 21 C.F.R. § 10.30 to request that the Commissioner of the Food and Drug Administration ("FDA") require that all product packaging and labeling for erectile dysfunction drugs disclose information on the role of cardiovascular disease in erectile dysfunction and the role of diet and lifestyle in cardiovascular health.

A. ACTION REQUESTED

The Physicians Committee requests that the Commissioner require manufacturers to include the following notice on the product packaging and labeling of erectile dysfunction drugs:

Erectile dysfunction is caused by artery disease, a condition that this drug will not improve. Artery disease can lead to heart attacks, strokes, and early death. A plant-based diet, moderate exercise, stress management, and lack of smoking can, in combination, improve and often reverse artery disease.

B. STATEMENT OF GROUNDS

Between 18 and 30 million men in the United States have erectile dysfunction. Although some cases result from prostate surgery or from medications, such as antidepressants in the selective serotonin reuptake inhibitor category (e.g., fluoxetine (Prozac), sertraline (Zoloft), or citalopram (Celexa)), most cases are caused by artery disease.

The male sexual anatomy is a hydraulic system that relies on good blood flow to work properly. If the arteries are wide open and healthy, the system functions correctly. But if the arteries have been narrowed by atherosclerosis, blood flow will be impaired. As cholesterol particles circulate in the bloodstream, some can irritate the artery wall, causing a plaque to form in the inner lining of the artery. The plaques narrow the passageway for blood, slowly choking off the blood supply to the organs. When atherosclerosis narrows the arteries to the male sexual organ, the reduced blood flow leads to erectile dysfunction.

A middle-aged man with erectile dysfunction is at serious risk of a heart attack or stroke. Researchers have found that after the beginning of erectile dysfunction, symptoms of cardiovascular disease can be expected within two to three years.[1] The risk factors for heart disease—high cholesterol, high blood pressure, diabetes, obesity, and smoking—are essentially

identical to the risk factors for erectile dysfunction. This is because they are symptoms of the same underlying condition—damaged arteries.

In a review published in 2019, researchers found a "wealth of evidence" linking erectile dysfunction and cardiovascular disease. Among men with erectile dysfunction, the researchers observed an increased prevalence and incidence in myocardial infarction, ischemic heart disease, hypertension, stroke, angina, arteriosclerosis, and peripheral vascular disease. They also found a relationship between erectile dysfunction and mortality. The researchers noted, however, that most of the studies that they examined were cross-sectional population studies that showed only association instead of cause and effect.[2]

A recent meta-analysis of studies on more than 150,000 men found that men with erectile dysfunction have a 59 percent higher risk of coronary heart disease or atherosclerosis, a 34 percent higher risk of stroke, and a 33 percent higher risk of dying from any cause, compared with men without symptoms of erectile dysfunction.[3]

Erectile dysfunction drugs widen the arteries temporarily but do nothing to fix damaged arteries. Diet and lifestyle changes can improve cardiovascular health and address erectile dysfunction, however. For example, the Massachusetts Male Aging Study tracked a large group of men ranging in age from 40 to 70. Those who stayed physically active or started a new program of physical activity cut their risk of erectile dysfunction in half, compared with sedentary men.[4]

In a case study published in the *Journal of the American Dietetic Association*, a previously healthy 51-year-old man developed high cholesterol, atherosclerosis, and erectile dysfunction after starting the Atkins Diet, a low-carbohydrate diet that emphasizes high-fat meat and dairy products. Eventually, he ended up in an emergency room with chest pain caused by a near total blockage of a coronary artery. Two months after discontinuing the diet, his health problems, including his erectile dysfunction, were resolved.[5]

In a 2004 study, 100 obese men averaging about 43 years in age and 225 pounds in weight, participated in a study to determine the effect of weight loss on erectile dysfunction. Most had high cholesterol levels, and all had erectile dysfunction. Over a two-year span, half of the men reduced their meal portions and started regular exercise, eventually reducing their weight by an average of 33 pounds and slightly lowering their cholesterol levels. About one-third of these men regained their sexual function. The men whose sexual function improved the most were those who lost the most weight, exercised the most, and had the biggest drops in C-reactive protein, an inflammation indicator that is often elevated in overweight people. A control group received no specific advice and made no significant progress on any of these measures.[6]

A study in the journal *Urology* evaluated the association between fruit and vegetable consumption and erectile dysfunction among Canadian men with diabetes. Each additional daily serving reduced erectile dysfunction risk by 10 percent.[7]

A 1990 study demonstrated that heart disease can be reversed via a program based on a plant-based diet, regular exercise, stress management, and no smoking. After following this program for a year, participants had an angiogram, and the results were compared to the same test done

when the study began. The comparison showed that participants' arteries were reopening so much that a measurable difference was seen in 82 percent of the participants—with no medication and no surgery.[8] Diet played a key role in that plants have effectively no cholesterol and lack animal fat, the latter being high in saturated fat, which in turn boosts cholesterol levels.

In a study published in the *American Journal of Clinical Nutrition* in 2016, researchers followed the diets of 25,096 men and monitored incidence of erectile dysfunction. Participants with the highest intakes of anthocyanins, flavones, and flavanones, phytonutrients found in fruit, lowered their risk for erectile dysfunction by 14 percent when compared to those who consumed the least. Researchers suspect a diet rich in fruits aids prevention and early treatment of cardiovascular disease by improving vascular conditions.[9]

Approximately 44 percent of men with heart disease risk factors—such as erectile dysfunction—are unaware of their risk, according to a study published in the *Journal of Sexual Medicine*. If men with erectile dysfunction were screened for heart disease, 5.8 million cases would be identified over 20 years. Even a 20 percent decrease in heart attacks or strokes as a result of screening and treatment could help avoid 1.1 million heart attacks and strokes, saving $21.3 billion over 20 years. More than 1 million cases of erectile dysfunction would also be treated, saving $9.7 billion.[10]

To ensure that physicians and patients understand the health risks, including the risk for early mortality, associated with erectile dysfunction, as well as basic lifestyle and diet steps that can address those risks without medication, the Commissioner should require erectile dysfunction drug manufacturers to prominently place the above notice on all product packaging and labeling.

C. ENVIRONMENTAL IMPACT

The requested action is excluded under the provisions of 21 C.F.R. § 525.30 because the action will not result in the introduction of any substance into the environment.

D. ECONOMIC IMPACT

Pursuant to 21 C.F.R. § 10.30(b)(3), this information will be submitted if requested by the Commissioner following review of the petition.

E. CERTIFICATION

The undersigned certifies, that, to the best knowledge and belief of the undersigned, this petition includes all information and views on which the petition relies, and that it includes representative data and information known to the petitioner which are unfavorable to the petition.

Respectfully Submitted,

Neal D. Barnard, MD
Physicians Committee for Responsible Medicine
5100 Wisconsin Ave., NW, Suite 400
Washington, DC 20016
202-686-2210

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