July 9, 2015

Janet Woodcock, MD
Director
Center for Drug Evaluation and Research
Food and Drug Administration
Department of Health and Human Services

Dear Dr. Woodcock,

We, the undersigned nonprofit organizations and individuals, represent patients, consumers, women's health advocates, healthcare providers, scientists and researchers. We are writing to express our deep concern that the FDA's independent, evidence-based evaluation of flibanserin is being undermined by an aggressive marketing and public relations campaign, and to urge you not to approve flibanserin at this time. We strongly support the independent decision-making of the reviewers within the Center for Drug Evaluation and Research. We believe that the Advisory Committee vote in favor of approval did not fully take into account the sponsor's responsibility to include adequate numbers of women in the alcohol-flibanserin interaction study. As a result, we firmly believe that flibanserin should not be granted FDA approval until a well-controlled drug-alcohol interaction study is conducted that adequately assesses the possibility of clinically significant adverse events in premenopausal women.

Since its founding, the National Women's Health Network has worked in collaboration with the undersigned organizations to ensure that women and their healthcare providers receive complete and accurate information about the medical products available to them, particularly the specific benefits a drug or device might offer and risks it might pose to women. In furtherance of this goal, the Network has worked long and hard in partnership with the women's health community to demand the greater inclusion of women in clinical trials for all FDA approved drugs and devices. We have also stressed the need for demographic data, analysis of sub-group differences, and availability of accessible and consumer-friendly information that women and their health care providers can use to make informed health care decisions.

Since women are less likely than men to be included in clinical trials, we often do not discover if a drug or device is unsafe or less effective for women until after it is on the market. To address this pervasive problem, we have advocated for the establishment of more rigorous inclusion standards and improved reporting requirements as seen in Section 907 of the Food and Drug Administration Safety and Innovation Act.

Given our concern for the inclusion of women in clinical trials, we are concerned about the insufficient number of women in Sprout's alcohol-flibanserin interaction study. After expressing concerns "regarding the additive sedative and hypotensive effects of concomitant use of alcohol" in its 2013 *Complete Response letter*, the FDA recommended that Sprout Pharmaceuticals conduct a study assessing drug-drug interactions between alcohol and flibanserin.

Inexplicably, in their 25 person study, Sprout included only two women. For a product whose indicated use is solely in women, studying this interaction in a group comprised of mostly men makes little sense and invalidates this study.

This alcohol-flibanserin study demonstrated that somnolence, orthostatic hypotension, and syncope were significantly worsened by the concomitant use of alcohol and flibanserin compared to flibanserin administration alone in men.
However, an alcohol-flibanserin interaction study primarily in men is not adequate to evaluate its safety in women. There are known differences between how men and women metabolize alcohol. For the purposes of an evidence-based assessment of the risks to women of drinking alcohol while taking flibanserin, the study has not yet been done.

In the real world, alcohol consumption by women is common, and a risk mitigation and management strategy is simply not enough to reduce the risks of using this drug with alcohol. There is no known intervention or REMS that can ensure people abstain from alcohol in the long term when consumption significantly increases serious risks from other medications. Thus, including alcohol use as a contraindication in product labeling is not sufficient for protecting the health of women using this drug on a chronic, daily basis.

Approving flibanserin at this time, when the impact of alcohol has not been adequately tested in women, would be directly counter to the intent of Section 907 of the Food and Drug Administration's Safety and Innovation Act, which aims to improve the inclusion of women and other demographic subgroups in clinical trials to ultimately enhance health and safety.

Women need and want answers to sexual problems, and we strongly support and advocate for sexual health research to explore biomedical and non-biomedical solutions to these problems. Unfortunately, the drug's sponsors have on three occasions been unable to present sufficient documentation of the drug's safety and efficacy. The current sponsor is now pressuring the FDA to approve the drug based on unfounded claims of sexism in the handling of the drug's application. We do not believe that the FDA and the review staff within it are sexist; indeed, we recognize that the reproductive health division has provided unbiased reviews on many women's health products, including flibanserin. We recommend that the FDA withhold approval of flibanserin until the sponsor completes an adequate alcohol study assessing its safety profile.

As patient, consumer and women's health organizations long engaged with the FDA, we support the agency's concern for drug safety as shown in its handling of the flibanserin applications, and look forward to its continuing support for women's health and safety.

Sincerely,

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