Joint Meeting of the Bone, Reproductive, and Urologic Drugs and the Drug Safety and Risk Management Advisory Committees

Safety and Efficacy of Flibanserin
June 4, 2015

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I have no financial conflict of interest

Is current evidence about the safety and efficacy of flibanserin significantly different now than June 18, 2010 when a vote was taken?

"Consider the available data on efficacy and safety. Has the applicant demonstrated the overall risk-benefit profile for flibanserin for the treatment of HSDD in premenopausal women is acceptable?"

The vote was 11 no, 0 yes

Prescient reasons 2010 committee voted no

- This is not an effective drug. Where there was improvement in satisfaction with sexual events, a very small effect. But given the *overall percentage of patients that reported adverse events and the concerns about how this would generalize to the population.*
- I am concerned about the *70 percent incidence of adverse events, as well as the potential for interactions with commonly prescribed drugs, as well as substances, including alcohol.*
- I have *concern about the number of exclusions in the trial and the five-page list of medications that were excluded, and then how the drug may be used in a general population.*

Because of these concerns, shared by FDA staff, the agency requested additional safety studies by the company including flibanserin interactions with alcohol and other drugs.

Comparisons between information available in 2010 and now

- The recent efficacy study (Begonia, 511.147) used a new pre-specified primary outcome, 28 day recall instead of daily diary because Sprout, according to FDA "requested to use another instrument [FSFI] to assess desire after the analysis of their first U.S. Phase 3 study indicated that the eDiary desire endpoint was not significantly improved." This newer study again shows very high rate of adverse reactions, such as somnolence:

	2010 data	**somnolence /# women**	**Begonia**
Placebo	40/ 1360 (2.9%)		19/545 (3.5%)
flibanserin 100 qhs	95/ 1001 (9.5%)		78/542 (14.4%)

2010 and current comparisons (cont'd)

"Hypotension and syncope associated with flibanserin alone or when used concomitantly with alcohol is clinically significant and can result in serious, irreversible, or life threatening injuries."*

- "In the phase 1 DDI study, alcohol, consumed over 10 minutes and combined with flibanserin, increased the incidence of somnolence, orthostatic hypotension and syncope….
- study population was predominantly male (23 of 25 subjects). The effect of the combination of flibanserin and ethanol may be more pronounced in females."**

* FDA 2015 briefing document, page 120

**FDA 2015 briefing document, page 61

Benefit Risk Balancing

- If clear evidence of a clinically meaningful benefit existed, accompanied by manageable risks, approval might be appropriate.

- Neither is the case. The placebo-adjusted benefits, though statistically significant, have questionable clinical meaning. Further, FDA concluded: “even the most restrictive REMS may be limited in effectively mitigating the risks of hypotension and syncope alone and when used concomitantly with alcohol in the postmarketing setting, should flibanserin be approved.” (FDA briefing, page 124)

- I strongly urge committee members to again vote NO on whether the overall risk-benefit profile is acceptable.