Boehringer Ingelheim

Clinical Study Synopsis for Public Disclosure

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The synopsis - which is part of the clinical study report - had been prepared in accordance with best practice and applicable legal and regulatory requirements at the time of study completion.

The synopsis may include approved and non-approved uses, doses, formulations, treatment regimens and/or age groups; it has not necessarily been submitted to regulatory authorities.

A synopsis is not intended to provide a comprehensive analysis of all data currently available regarding a particular drug. More current information regarding a drug is available in the approved labeling information which may vary from country to country..

Additional information on this study and the drug concerned may be provided upon request based on **Boehringer Ingelheim's Policy on Transparency and Publication of Clinical Study Data**.

Name of company: Boehringer Ingelheim		**Tabulated Trial Report**	Boehringer Ingelheim
Name of finished product: Not applicable		**EudraCT No.:** 2007-004076-38	
Name of active ingredient: Flibanserin, BIMT 17 BS		**Page:** 1 of 4	**Synopsis No.:**
Module:		**Volume:**	
Report date: 26 APR 2010	**Trial No. / U No.:** 511.118 / U10-1696-01	**Date of trial:** 09 JAN 2008 – 23 OCT 2009	**Date of revision** (if applicable)**:** Not applicable

Title of trial:	A Twenty-Eight Week, Open-Label, Safety Study of Flibanserin 50 milligrams to 100 milligrams daily in Premenopausal European Women With Hypoactive Sexual Desire Disorder
Principal/Coordinating Investigator:	Professor [redacted], MD, PhD
Trial sites:	Multicentre Study, cf. Appendix 16.1.4
Publication (reference):	Data of this study has not been published
Clinical phase:	III
Objectives:	To establish the long-term safety and tolerability of flibanserin for Hypoactive Sexual Desire Disorder (HSDD) in European women who have completed a prior clinical trial of flibanserin, for 28 weeks of treatment
Methodology:	Open-label design of 4 flibanserin dosage regimens over 6 months of treatment
No. of subjects:	
planned:	entered: 480
actual:	enrolled: 480
	Treatment flibanserin: entered: 480 treated: 480 analysed (for primary endpoint): 479
Diagnosis and main criteria for inclusion:	Female patients with primary HSDD
Test product:	25, 50, and 100 milligram (mg) flibanserin tablets
dose:	flexible dosing of 50 or 100 mg once daily at bedtime (q.h.s.), or 25 mg or 50 mg twice daily (b.i.d.)
mode of admin.:	by mouth (p.o.)
batch no.:	25 mg - 059052A
	50 mg - 059053A; 059054A; 059055A

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Reference therapy:	none
dose:	none
mode of admin.:	none
batch no.:	none
Duration of treatment:	A 28-week treatment period with flibanserin and a four week follow-up period without study medication
Criteria for evaluation:	
Efficacy / clinical pharmacology:	Female Sexual Function Index©, Female Sexual Distress Scale-Revised©, Clinical Global Impression (CGI) of severity, CGI of efficacy Index (Therapeutic Effects), Patient's Global Impression (PGI) of Improvement and the final Patient Benefit Evaluation
Safety:	Beck Scale for Suicide Ideation® (BSS®), blood pressure, pulse, weight, electrocardiogram (ECG), routine laboratory tests, CGI of Efficacy Index (Side Effects), concomitant medication(s) and adverse events (AEs).
Statistical methods:	Descriptive statistics on safety, adverse events, and efficacy endpoints.

SUMMARY – CONCLUSIONS:

Efficacy / clinical pharmacology results:

The study objectives were to assess the long-term safety and tolerability of flibanserin for HSDD in pre-menopausal women as well as to assess the maintenance of efficacy. All efficacy results serve the descriptive purpose only.

For patients in FSFI remission at baseline, there is considerable evidence that they maintained treatment effect during the treatment. Based on FSDS-R total and Item 13, decreasing trends are observed, indicating patients improved in the study. FSFI related measurements also demonstrate the maintenance of treatment effect based on the big proportion of patients in FSFI remission at every visit and overall increasing trend in FSFI total and desire scores. Besides, patients did not worsen their disease severity based on the CGI of Severity ratings. CGI of Efficacy Index shows that side effects did not interfere with patients' functioning while the treatment effects were maintained. At the end of treatment, a majority (59.4%) of patients responded positively on the meaningful benefit from the flibanserin treatment. For PGI of improvement assessments increasing trend of

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	improvement was observed throughout the trial with nearly half (47.7%) recording a score of 1 (very much improved) or 2 (much improved). For patients not in FSFI total remission at baseline, all the results consistently show that patients improved their sexual functioning during the treatment. Decreasing trends are observed in the FSDS-R total and Item 13 scores, indicating benefits to those entering the trial not in FSFI remission. Compared with those in FSFI remission at baseline, FSFI total non-remitters showed greater improvement in FSFI total and desire scores on average. 27.2% improved their FSFI total to the remission level (greater or equal to 26.55) at the end of treatment. From the three components in CGI ratings, the overall severity of illness reduces and the relief from illness symptoms is observed. The side effects did not interfere with patients' functioning. In addition, patient benefit evaluation reports that 37.6% of patients received meaningful benefits from the flibanserin treatment. For PGI of improvement assessments increasing trend of improvement was observed throughout the trial with 19.9% recording a score of 1 (very much improved) or 2 (much improved) at the end of the trial.
Safety results:	The mean duration of exposure (including exposure from parent trial) was 263.0 days. A total of 144 patients (30%) had at least 351 days of flibanserin, including the treatment that they received in their parent trial. A total of 301 patients (62.7%) had been treated with any dose of flibanserin for at least 180 days in Trial 511.118 only (i.e., excluding exposure in their parent trial). No deaths were reported in this trial. There were 12 SAE preferred terms (PTs) (in ten patients) that occurred during the treatment period; two SAEs (ovarian cyst and uterine polyp) were judged by the investigator to be related to treatment. The most commonly reported AEs were fatigue (14.4%), headache (10.4%), nasopharyngitis (9.8%), nausea (8.5%), dizziness (8.3%) and somnolence (5.6%). The most common AEs that led to discontinuation were fatigue (1.5%), dizziness and insomnia (1.3% each) and nausea (1.0%). A minority of patients (10.6%) experienced severe AEs and slightly less than half of patients with AEs had AEs that were considered by investigators to be related to study treatment. The most common AEs that were considered related to treatment were fatigue (13.3%), nausea (7.7%), dizziness (7.3%), somnolence (5.6%) and headache (5.0%). There were no clinically relevant findings in the evaluation of suicidality, haemorrhage AEs, eye AEs, AEs related to liver

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function abnormalities or accidental injury AEs. Other safety measures (routine laboratory tests, ECG, vital signs) did not demonstrate any clinically important findings.

Conclusions: Among the patients comprising the FAS, a high rate of response to flibanserin and maintenance of efficacy was observed. Overall, flibanserin was well-tolerated with no new or unexpected safety findings were observed in patients with HSDD who were treated for up to 28 weeks.