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.:** 2007-000032-68	
Name of active ingredient: Flibanserin, BIMT 17 BS		**Page:** 1 of 4	**Synopsis No.:**
Module:		**Volume:**	
Report date: 06 AUG 2009	**Trial No. / U No.:** 511.77 / U09-1824-01	**Date of trial:** 26 JUN 2007 – 16 MAR 2009	**Date of revision:** Not applicable

Title of trial:	A Twenty-Four Week, Randomized, Double-Blind, Placebo-Controlled, Safety and Efficacy trial of Flibanserin 50 Milligrams Daily and 100 Milligrams Daily in premenopausal European Women With Hypoactive Sexual Desire Disorder
Principal/Coordinating Investigator:	[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 efficacy of Flibanserin 50 Milligrams Daily and 100 Milligrams Daily in 6-month treatment, vs placebo for Hypoactive Sexual Desire Disorder in premenopausal European women; to evaluate safety and tolerability of flibanserin in such patients
Methodology:	Randomized, double-blind, placebo-controlled, 3 parallel-group trial
No. of subjects:	
planned:	entered: 949
actual:	enrolled: 1272 Treatment Flibanserin 50 mg: entered: 314 treated: 311 analysed (for primary endpoint): 305 Treatment Flibanserin 100 mg: entered: 317 treated: 316 analysed (for primary endpoint): 308 Treatment Placebo: entered: 318 treated: 318 analysed (for primary endpoint): 313
Diagnosis and main criteria for inclusion:	Pre-menopausal women with primary generalized acquired Hypoactive Sexual Desire Disorder
Test product:	50 and 100 milligrams (mg) flibanserin tablets
dose:	50 mg daily every evening (q.h.s.), 100 mg q.h.s.
mode of admin.:	by mouth (p.o.)

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batch no.:	Flibanserin 50 mg batch no.: PD-2637 Flibanserin 100 mg batch no.: PD-2639
Reference therapy:	placebo flibanserin tablets to match 50 and 100 mg tablets of flibanserin
dose:	50 mg q.h.s., 100 mg q.h.s.
mode of admin.:	p.o.
batch no.:	placebo 50 mg batch no.: PD-2638 placebo 100 mg batch no.: PD-2554
Duration of treatment:	A 28-day baseline period without study medication, a 24-week double-blind phase with study medication, and a 28 -day follow-up period after discontinuation of study medication
Criteria for evaluation:	
Efficacy / clinical pharmacology:	Primary endpoint: Change from baseline in the number of satisfying sexual events collected daily by an electronic diary (eDiary). First key-secondary endpoint: Change from baseline in the desire items collected from the Female Sexual Function Index (FSFI desire items). Second key-secondary endpoint: Changes from baseline in the Female Sexual Distress Scale –Revised (FSDS-R) ©. Other secondary endpoints include changes from baseline in: eDiary sexual desire score, eDiary distress question, FSFI total score and other domains, Patient's Global Impression (PGI) of Improvement and the final Patient Benefit Evaluation.
Safety:	Blood pressure and pulse, weight, ECG, physical examination, routine laboratory tests, medication compliance, Beck Scale for Suicide Ideation©, concomitant therapy, and adverse events.
Statistical methods:	Frequency counts of sexual activity will be analyzed using the Wilcoxon rank sum test. An analysis of covariance (ANCOVA) model with treatment and center as fixed effects and baseline value as the covariate will be used to analyze other continuous endpoints. The Chi-square test and Cochran Mantel-Haenszel test will be used to analyze dichotomous (responder) endpoints.
SUMMARY – CONCLUSIONS:	
Efficacy / clinical pharmacology results:	There is considerable evidence among the key and secondary endpoints based on the statistical significance of 100 mg q.h.s. flibanserin to support the inference that the 100 mg q.h.s. flibanserin is an efficacious dose. However,

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	the negative results for SSE score prevent the conclusion of efficacy on the pre-specified endpoint taking the *a priori* ordered hierarchical testing strategy into account. For the first key secondary endpoint FSFI desire domain the contrasts for 100 mg q.h.s. flibanserin to placebo were statistically significant at weeks 8 and 16 with a trend toward significance at week 24 (p-value=0.08). For the second key secondary endpoint (FSDS-R© total) as well as for the other secondary endpoints (FSDS-R© item 13, eDiary sexual desire score, PGI-I and PBE) all contrasts for 100 mg q.h.s. flibanserin to placebo were statistically significant and clinically meaningful. Regarding the other secondary endpoints, there is considerable evidence of treatment effect for 100 mg q.h.s. flibanserin dose and significance in responder thresholds for FSDS-R© total, FSDS-R© item 13 and PGI-I. The 50 mg q.h.s. dose was statistically significant compared to placebo for PBE and certain responder thresholds for PGI of improvement.
Safety results:	No deaths were reported in this trial. There were twelve patients with thirteen serious adverse events with onset during the treatment period and none were judged to be related to treatment. There were four frequent adverse events which were more prevalent in the flibanserin 100 mg q.h.s. group compared to placebo. These events of headache, dizziness, fatigue and nausea occurred at rates of 16.8%, 14.6%, 17.1%, and 12.3%, respectively. The most common adverse events that caused patients in the flibanserin 100 mg q.h.s. group to discontinue were dizziness (3.2%), fatigue (2.2%) and nausea (1.9%) and the most common adverse events that caused patients in the placebo group to discontinue were fatigue (0.9%), depression and headache (0.3%). A minority of patients in each treatment group with adverse events experienced severe adverse events (7.4% in the 50 mg q.h.s. flibanserin group, 9.5% in the 100 mg q.h.s. flibanserin group and 6.9% in the placebo group). The most frequently reported severe adverse events in the flibanserin 100 mg q.h.s. treatment group were fatigue (1.3%), headache and nausea (0.9% each) and the most common severe adverse events in the placebo group were headache (1.3%). There were no significant differences between treatment groups in withdrawal effects, suicidality, bleeding. Other safety measures of laboratory tests, ECGs, and vital signs did not reveal any clinically significant differences between flibanserin and placebo.
Conclusions:	In summary, while no flibanserin regimens demonstrated statistically significant separation from placebo for the primary endpoint, there was strong

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evidence of a statistically and clinically significant treatment effect among the supporting secondary endpoints for the flibanserin 100 mg q.h.s. dose. Dose regimens of 50 mg flibanserin q.h.s. and 100 mg flibanserin q.h.s. were well tolerated over 24 weeks of treatment in this population of pre-menopausal women with HSDD.