

The Science of **DESIRE** New Discoveries in HSDD



Flibanserin Background Information

- 1. What is flibanserin?**
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1. What is flibanserin?

Boehringer Ingelheim is currently investigating flibanserin[†] as the first CNS-acting compound to restore the sexual desire which was lost in pre-menopausal women suffering from the medical condition, generalised, acquired Hypoactive Sexual Desire Disorder (HSDD).¹ HSDD is characterised by a decrease in sexual desire that causes marked personal distress and/or interpersonal difficulties.²

There are a number of potential causes and contributing factors to HSDD. Current medical research suggests that neurotransmitters in the brain particularly dopamine, norepinephrine and serotonin play a key role in modulating sexual desire.^{3,4,5,6} Sexual dysfunction could occur when the balance of these neurotransmitters is disrupted. Diminished function of the dopamine system, which increases sexual desire and excitement, and norepinephrine system, which affects arousal and orgasm, could lead to the inability to begin the sexual response cycle. An overactive serotonin system, which can decrease desire and delay orgasm could also lead to inhibition of sexual response.

2. How does flibanserin work?

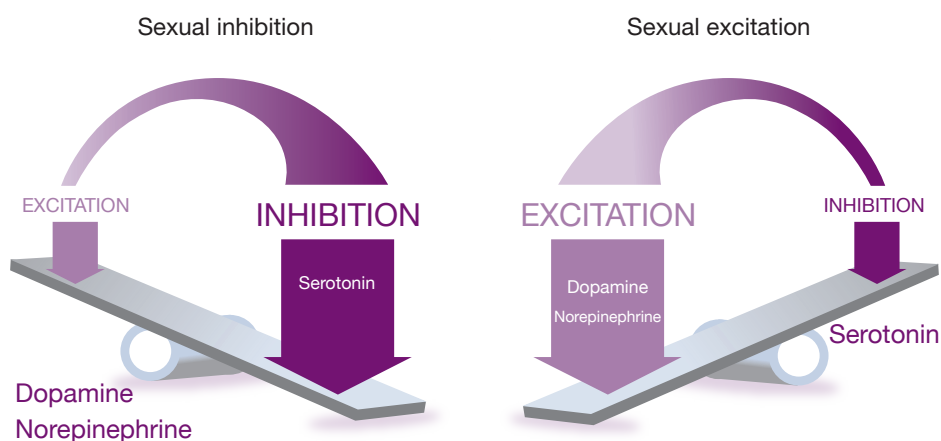
Boehringer Ingelheim is investigating flibanserin[†] as a novel, non-hormonal treatment for HSDD. Our current understanding from pre-clinical research is that flibanserin[†] has two main pharmacological targets in the brain, 5-HT_{1A} receptors (agonism) and 5-HT_{2A} receptors (antagonism). Flibanserin targets these receptors preferentially in selective brain areas. Flibanserin affects the neurotransmitters dopamine, norepinephrine and serotonin which play a role in the

[†] This compound is an investigational agent. Its safety and efficacy have not yet been fully established.

sexual response cycle. Boehringer Ingelheim believes that by modulating these neurotransmitter systems in selective brain areas flibanserin might help to restore a balance between inhibitory and excitatory factors which could lead to a healthier sexual response.¹ See Figure 1.

Figure 1:

Balance of neurotransmitter systems is necessary in the sexual response cycle:



The figure illustrates how a relative lack of dopamine and norepinephrine and excess serotonin can inhibit the sexual response cycle. Natural sexual excitation is possible when these neurotransmitters are appropriately balanced.

3. The Bouquet® Study Programme

The Bouquet® Study Programme is an umbrella term for the flibanserin Phase III clinical trial programme conducted by Boehringer Ingelheim. Currently five Phase III studies have been completed in North America and Europe involving over 5,000 pre-menopausal women with generalised acquired Hypoactive Sexual Desire Disorder.⁸ The overall aim of the programme is to evaluate the safety and efficacy of flibanserin, an investigational, non-hormonal compound that is being investigated as a potential treatment for this condition.

The current study programme consists of seven trials:

- The ROSE study was a randomised withdrawal trial of flibanserin in premenopausal women with HSDD. (For results please refer to the fact sheet on the Bouquet® Study Programme)
- The DAHLIA®, VIOLET®, DAISY® and ORCHID® trials were randomised placebo-controlled trials designed to assess the safety and efficacy of 24 weeks' treatment with flibanserin in premenopausal women with HSDD. The DAHLIA®, VIOLET®, and DAISY® trials were conducted in North America and the ORCHID® trial was conducted in Europe.
- The SUNFLOWER® and MAGNOLIA® trials are ongoing open-label extension trials of flibanserin in North America and Europe, respectively.

Overall flibanserin has demonstrated in Phase III clinical trials significant improvements in women suffering with HSDD as it relates to the hallmarks of the condition, decreased sexual desire and marked associated distress.

The results of the phase III North American pivotal trials have confirmed that flibanserin 100 mg once-daily, taken at bedtime, is a well-tolerated, and effective treatment for pre-menopausal women with HSDD. The 100 mg once-daily North American pooled data (VIOLET® and DAISY®) demonstrated that women experienced a statistically significant increase in satisfying sexual events over placebo, a statistically significant improvement in the frequency and intensity level of sexual desire and a statistically significant reduction in HSDD related distress.¹ Data from the Phase III European pivotal trial ORCHID® shows that flibanserin (100 mg once daily) significantly increases sexual desire and reduces distress associated with sexual dysfunction. There is also a numerical increase in Satisfying Sexual Events (SSE).

In all studies of the Bouquet® study programme that have been concluded so far, flibanserin was shown to be well-tolerated in pre-menopausal women with HSDD.

References

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