THE MAGAZINE FOR INTERNATIONAL HEALTHCARE & MEDICAL TOURISM

GlobalHealth AND TRAVEL

DUBAI
Ripe and ready for medical tourism

THAILAND ON TOP
Bernstein-GHT index demines Asia's top medical tourism destination

SPROUTING CONTROVERSY
Medication designed to restore women's sexual appetite takes a beating

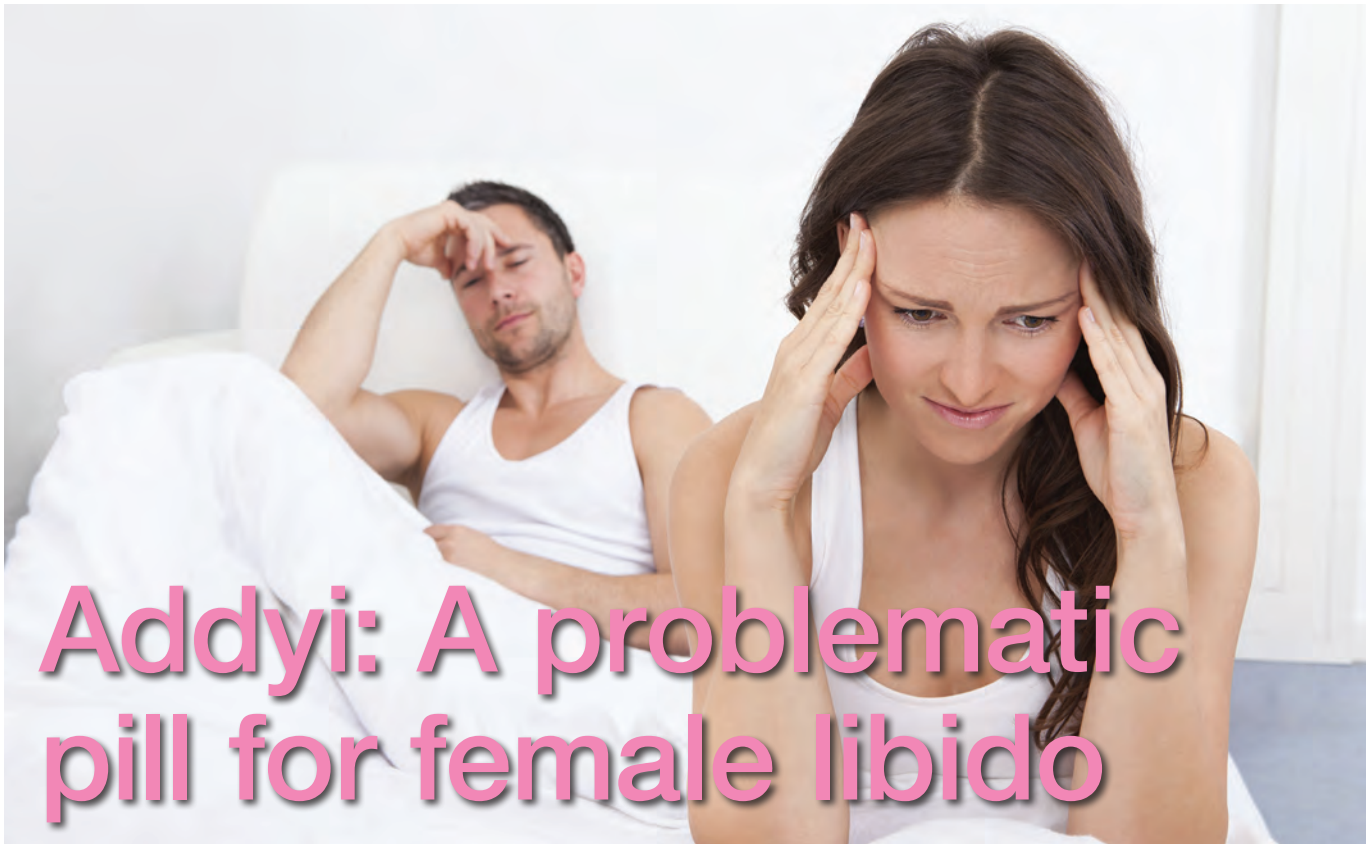
THE BEEF WITH PROCESSED MEAT
Will it give you cancer?

January 2016

S$ 10.90 (inc. GST)
₹300
THB 300
RM 21.50 (inc. GST)
DHS25 (Dubai)
US$15 (USA)
€ 12 (Europe)

ISSN 2223465-9

GlobalHealthAndTravel.com



Addyi: A problematic pill for female libido

The first medication to restore women's sexual appetite has been hailed as a breakthrough and lambasted as a form of over-medicalisation

The approval of the first drug to boost women's sexual drive by the US Food and Drug Administration (FDA) last August marked a tipping point in the treatment of female sexual dysfunctions and brought with it a storm of controversy over the new medication's adequacy to treat low libido in women.

Addyi, the brand name of Flibanserin, has been engineered by Sprout Pharmaceuticals to treat hypoactive sexual desire disorder (HSDD), defined as a recurrent lack of sexual desire causing marked distress or interpersonal difficulty not due to mental disorder, medication, stress or other medical conditions.

Several studies report that HSDD is one of the most common sexual problems in women, and before Addyi received the green light there wasn't any specific pharmacological treatment for women or men.

Supporters of the drug have therefore hailed its FDA approval as a tremendous step forward in the treatment of female sexual dysfunction.

"It's a huge breakthrough for women not just because Flibanserin is good but because it will keep the door open for research on other treatments for female sexual problems as well," Dr. Sheryl Kingsberg, a clinical psychologist and behavioural medicine division chief in OB/GYN with University Hospitals Case Medical Center in Cleveland who has been involved in the development of Flibanserin since 2006, told *Global Health and Travel*.

By contrast, critics have said it treats the common ups and downs of sexual desire as a physiological condition in order to market a new medication that holds uncertain effectiveness but significant side effects.

"This is an example of medicalisation of female sexuality," said Dr. Barbara Mintzes, a research scientist in pharmaceutical policy at the University of Sydney. "There are many non-medical reasons for lower sexual desire, including relationship problems. So, many people who do not have a medical problem are likely being labelled as having a medical problem."

Modest efficacy but immediate side effects

The studies supporting Addyi's market approval comprise three, 24-week-long, and placebo-controlled clinical trials.

"Across the three trials, about 10 percent more Addyi-treated patients than placebo-treated patients reported meaningful improvements in satisfying sexual events, sexual desire or

> **"It is unfair to expect Addyi to push women with HSDD to have sex more often than a woman without the disorder. What we want is to restore women to what their normal was"**
>
> — Dr. Sheryl Kingsberg
> Clinical psychologist and behavioural medicine division chief in OB/GYN with University Hospitals Case Medical Center in Cleveland

distress," according to a press release by the FDA.

On average, Addyi increased the amount of satisfying sexual events (SSE) by 0.5 to one additional event per month over the placebo.

In the third trial, the primary method to measure desire was the Female Sexual Function Index, which asked women how often they felt sexual desire or interest and to rate its intensity. The Index score ranged from 1.2 to 6.

Starting from a baseline of 1.9, at the end of the 24-week trial women on Addyi improved their score by one extra point while women on placebo increased it by 0.7.

These improvements don't come without side effects and the most common adverse reactions are sleepiness, dizziness and nausea. In addition, the interaction between Flibanserin and alcohol has been associated with low blood pressure and faintness. As a result, only certified healthcare professionals and pharmacies are approved to dispense the drug to ensure women are properly informed that the use of Addyi is severely contraindicated with alcohol.

The pill is to be taken daily for at least eight weeks before the supposed benefits kick in, while side effects start immediately. Patients are recommended to discontinue the treatment after two months if they don't perceive any benefit.

Drawing on these data, several observers have lambasted Addyi for its poor results.

PHOTO CREDITS: SPROUT PHARMACEUTICALS

ADDYI PACKAGING

"The difference between the benefits experienced by patients who received Addyi and those experienced by patients on placebo is particularly small," says Dr. Mintzes. "This points to the drug being very ineffective."

She concludes the drug has such mild effectiveness that the potential for harm for an individual woman outweighs the potential for benefit.

Meaningful benefits

Dr. James A. Simon, a reproductive endocrinologist based in Washington D.C. and one of the investigators in the clinical trials for Flibanserin, disagrees with the idea that Addyi's risk-to-benefit ratio is not favourable.

He says while Flibanserin average results are not on the surface extraordinary women who did respond to the treatment (about 60 percent of those studied) managed to double their number of SSEs up to about five per month. The average was lower because many women didn't experience any increase at all.

"Looking at the mean of the results is what the FDA requires, but it is not fair in characterising the efficacy of the drug," Simon says.

Kingsberg agrees and adds any increase is significant because the range of the scale was small to begin with.

"It is unfair to expect Addyi to push women with HSDD to have sex more often than a woman without the disorder," she says. "What we want is to restore women to what their normal was."

Moreover, both the investigators stress that a significant number of participants rated their improvement as meaningful. Across the three pivotal trials, 28.9 to 47.9 percent of women on the drug ranked their improvement as "at least much improved" compared to 14.5 to 37.9 percent for women on placebo.

As for the limited difference in efficacy between the drug and the placebo, Simon explains that this is a well-known issue for the class of drugs affecting the central nervous system, including Addyi.

"In all medication treatments where you are dealing with mental, cognitive or neurological disorders, there is a high placebo effect because the patient really wants to get better. This automatically tends to reduce the treatment effect above and beyond placebo."

Mintzes recognises that this is true for several drugs, like those prescribed for Alzheimer's, but she stresses that "no one doubts that Alzheimer's is a real disease, while this is not the case for hypoactive sexual desire disorder."

Pharmacology or psychology?

Indeed, HSDD presently has no clear biological markers, which makes diagnosis itself a challenge.

"When it comes to low sexual desire we really don't have a measure of what is a normal level of sexual desire for a woman to have," explains Mintzes.

Dr. Anna Ng, a Hong Kong-based sex therapist, agrees that any degree of desire could be low for one woman, but totally acceptable – and hence normal - for another. In fact, before diagnosing HSDD she says she has to be sure patients feel distressed about their sexual appetite.

"If a woman doesn't care about having a low interest in sex and her partner doesn't care either, there is no sexual dysfunction."

Flibanserin alters brain chemistry by reducing serotonin levels, which are thought to be responsible for inhibiting desire, and promoting dopamine along with norepinephrine, which are believed to intensify sexual desire and the excitement of sexual response.

"This is the theoretical mechanism by which Flibanserin appears to act in vitro and in animal models," says Simon. "But we don't know why and exactly how these neurotransmitters influence sexual desire in women."

On these grounds, Mintzes remains sceptical of Addyi, and any other pharmacological approach to HSDD.

"Although there are sexual problems that are very distressing, the idea that desire is something that requires drug treatment is not sufficiently proven."

Dr. Laurie Mintz, a psychology professor at the University of Florida and the author of *A Tired Woman's Guide to Passionate Sex*, is of the same opinion.

"Except in rare cases where blood tests confirm that there is a biological reason for the low sexual desire (i.e., low testosterone), I do not believe that a pharmacological approach is the appropriate or best treatment."

She says there are several social, individual and environmental factors behind low sexual desire and a variety of psychological treatments have demonstrated to be effective in dealing with it. Mindfulness and cognitive behavioural therapy – where women engage in group discussions and meditation, and are provided with information on responsive desire – is a promising example of treatments that helped some women improve sexual desire and satisfaction.

However, while Kingsberg agrees that desire is influenced by a mix of biological, interpersonal and psychological components, she says a biological cause is the best guess for a sizeable portion of her patients with HSDD.

"About 50 percent of my patients seem to have a biological aetiology for lack of sexual desire because they don't have any cultural or religion prohibition, they are in a good relationship, they are not overly stressed. So, I cannot find any external or interpersonal factor leading to HSDD."

In her view, it's this segment of HSDD women who could potentially benefit from taking Addyi as a first-line treatment.

The thrust of the controversy: How to interpret desire

Disagreements about the role desire plays in female sexual cycle is at the heart of the controversy surrounding Addyi's approval.

Kingsberg believes it is key, saying that women involved in clinical trials lacked desire but were fully functional from a sexual point of view.

"Before starting the trial, they were already having sex and achieving an orgasm," she says. "But, what was missing is the motivation, the desire to do it again, the anticipation, the wanting to want."

This approach implies that desire is a crucial stepping stone to wanting to have sex. It's a linear model that goes from desire to sex, then arousal and finally orgasm.

However, many argue that this is not a one-size-fits-all paradigm for every woman.

According to Mintz, "research demonstrates that female sexual response cycle doesn't have to and often doesn't start with desire."

She explains that in many cases desire can be the result of arousal, meaning that engaging in any sexual activity or getting stimulated are common ways that spark and reinforce desire.

"Being less interested in sex is a normal change with age and length of relationship, not a disorder," Mintz added. "If women knew this and made use of receptive desire, they'd be less concerned about their lack of spontaneous desire." **GHT**

> **"Being less interested in sex is a normal change with age and length of relationship, not a disorder. If women knew this and made use of receptive desire, they'd be less concerned about their lack of spontaneous desire"**
>
> **— Dr. Laurie Mintz**
> A psychology professor at the University of Florida and the author of *A Tired Woman's Guide to Passionate Sex*

FDA.GOV

SPROUTPHARMA.COM