



The Hot Little Sex Pill That Couldn't

In one year, the so-called
“female Viagra” slid from sizzle to fizzle.

Why are women's libido boosters
such a long time in coming?

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Last August, the FDA made history

by approving flibanserin (Addyi), the first and only treatment for hypoactive sexual desire disorder, or HSDD—translation: low libido—in premenopausal women. In fact, Addyi is the only drug on the market to treat sexual desire in anyone; there's no drug to treat low libido in men. (Viagra, to which Addyi is often compared, treats erectile dysfunction, not lack of desire.)

And the numbers were there. Surveys have reported that about a third of all women have periods of low sexual interest, and as many as 9% meet the medical definition for HSDD (in which lack of interest in sex is distressing and can't be attributed to a medical or psychiatric condition or to a medication side effect). Unlike men with erectile dysfunction, women with HSDD physically can still have sex—and many likely do—but they don't lust for it. "If your

libido issues don't bother you, you don't have HSDD," says Sheryl Kingsberg, chief of behavioral medicine at University Hospitals Case Medical Center in Cleveland, who is past president of the International Society for the Study of Women's Sexual Health (ISSWSH). With so many women reporting distress over their lack of libido, Addyi was expected to fly out of pharmacies.

Yet only 4,000 prescriptions were written for Addyi in its first 4 months on the market. Compare that with sales of Viagra, which was prescribed 600,000 times in the first month it was available. Interest in Addyi among women and their doctors seems as flat as the sex drive the drug is supposed to restore. What happened?

Addyi's Undesirable History

If you've never heard of Addyi until now, there's a reason. Sprout Pharmaceuticals, the manufacturer of Addyi when it was first approved, voluntarily agreed not to advertise the drug for 18 months after it became available. That extraordinary concession

came because the FDA was concerned about the drug's potentially serious side effects. The FDA also required that Addyi carry a "black box warning"—the strongest warning the FDA requires—on the package insert to inform users that

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medical studies indicate the drug carries a serious risk of adverse effects.

The drug's path to approval was rocky. The FDA rejected it twice, saying the side effects outweighed the benefits, before finally granting approval—some say after the manufacturer waged a vigorous public relations campaign. The FDA's analysis showed that Addyi increased desire in about 12% of women and caused side effects in 13%. Two days after the drug's approval, pharmaceutical giant Valeant purchased Sprout for an astounding \$1 billion.

One of Addyi's most worrisome risks involves its interaction with alcohol. Drinking while taking Addyi can lead to extremely low blood pressure, resulting in dizziness, fainting, and accidental

injuries. Before receiving a prescription for the drug, women must sign a waiver promising to abstain from alcohol while they're taking it. And doctors have to pass an online test to become certified to prescribe the drug.

All of this seems rather extreme for a drug that isn't treating a life-threatening illness and doesn't even seem very effective. The most promising clinical trials of Addyi showed an increase of just about one additional satisfying sexual experience a month for women taking the pill every day for 8 weeks. There was also a substantial placebo effect, say Steven Woloshin and Lisa Schwartz, professors and researchers at the Dartmouth Institute for Health Policy and Clinical Practice.



“Some women who take it will feel better, but whether it’s from the drug or the placebo effect is unknown.” Given these results, some people remarked snarkily that rather than forgo alcohol to take Addyi, women would have a better sexual experience after just drinking a glass of wine.

Considering the side effects, disappointing trial results, and lack of advertising, it’s no surprise there’s been minimal demand for the drug. “I’ve talked about Addyi with many patients, and when we finished our discussions, they all said, ‘Not for me!’” says Mary Jane Minkin, a clinical professor of obstetrics and gynecology at Yale University School of Medicine. “I haven’t had a single user.”

Even proponents of Addyi, like Lauren Streicher, medical director of the Center for Sexual Medicine at Northwestern Memorial Hospital in Chicago, who sits on the board of directors of the ISSWSH—an organization sponsored in part by Sprout—haven’t had much success. “I expected the calls to come pouring in,” Streicher says. Instead, she’s written only 10 Addyi prescriptions to date.

Could Addyi Be for You?

Only some women with a disappearing sex drive are potential candidates for Addyi. If you can check at least four boxes on this list, it might be something to bring up with your doctor.

- I've had a healthy libido in the past.
- My stress levels are manageable.
- My lack of desire causes me distress.
- I have a clean bill of health, including no underlying conditions that affect my libido.
- I'm in a loving and satisfying relationship.
- I've talked to my doctor about possible sexual side effects of the other medications I'm taking.
- I'm getting adequate sleep.

Among the women who have opted to take the drug, many gave up after experiencing no benefit. Judith Reid-Haff, 68, from Temecula, CA, knew about the warnings but was relieved to finally have something to try. “I was aware of the possible side effects but very hopeful that Addyi would help,” she says. Within days of taking the drug, which she was prescribed off-label because of her age, her brain felt foggy. She started waking up each morning with a dull headache. “I stuck with it for 3 months, hoping it would work, but the headaches got more

intense, and I was getting irritable,” she says. “Plus, my sex drive was still low. Since there was no significant improvement, I decided to quit.”

The Mysteries of Desire

Part of the reason there’s never been another medical treatment for low libido is that “the biology of women’s libido is not well understood,” says JoAnn Pinkerton, executive director of the North American Menopause Society. Desire is complicated, and sex drive involves everything from hormones and brain chemicals to the ability to communicate with your partner and the way you feel when you look in the mirror. Female desire “is much more subjective and difficult to measure than having an erection,” says Kingsberg.

Addyi is considered almost a last resort after other possible reasons for low desire have been addressed. “Addyi works on the brain to increase dopamine and other neurotransmitters, but not everyone has the same biology,” says Pinkerton. The trouble is, it’s impossible to predict who needs that dopamine lift. For one subset of women, neurotransmitters may indeed be the key to desire. And for all the naysayers, there are women who feel Addyi has been a godsend.

Lynette Stone* is one of these women. After 15 years of passionate

marriage, her libido vanished. The 46-year-old from Lyndhurst, OH, says she used to desire her husband constantly. Confused and frustrated by the change, she tried therapy, OTC aphrodisiacs, even re-creating sexy movie scenes. Several weeks after she starting taking Addyi, she noticed a shift. “It wasn’t sudden or intense—it was a gradual return—but my desire was back,” she says. “I was back.”



Comparing Addyi with Viagra is misguided. Addyi is a libido drug, while Viagra is a performance drug.



It’s women like Stone, who had exhausted other options, who helped win over the FDA. “In general, those recommending approval acknowledged the small treatment effects and substantial safety concerns but considered the unmet medical need,” FDA officials wrote in a January 2016 editorial in the *New England Journal of Medicine*. In other

words, they were swayed by the fact that there was a need for something to address the problem of low sexual desire, even if this option wasn’t ideal.

Getting Your Groove Back

Addyi’s proponents have pointed out that it’s the only “sexual” drug on the market for women, while there are 26 options for men. But comparing Addyi with drugs that increase blood flow to the penis is misguided. “Viagra and similar drugs are not libido drugs like Addyi; they’re performance drugs,”



testosterone-based drugs are being studied for women, including a nasal spray and a lozenge that mixes testosterone with an anti-anxiety medicine. In Europe, testosterone has already been approved for women.

Despite its underwhelming success, Addyi’s status as the first and only medication that addresses desire rather than the mechanics of sex is groundbreaking. Its approval by the FDA and the clamor of drug companies to own it prove that the industry is finally acknowledging female sexual dysfunction. But the complexity of female desire means there may

never be a one-size-fits-all solution. “Addyi isn’t the magic pill we were hoping for,” Minkin says, “and I don’t think there’s ever going to be a magic pill.”

In the meantime, says Stacy Tessler Lindau, director of integrative sexual medicine at the University of Chicago, at least Addyi got us talking. “Female sexual dysfunction is commonly thought of as a quality-of-life issue, not a medical issue, and is commonly absent from doctor-patient discussions,” she says. “The greatest value of Addyi is that it has opened the door for much-needed dialogue between women and their doctors.”

Minkin says. Women do have options to help them handle the physical aspects of sex. Especially for older women dealing with the effects of menopause, estrogen creams and lubricants can make sex more comfortable.

Many ob-gyns who spurn Addyi turn to a different, off-label option to help boost women’s libidos: testosterone. As with estrogen, testosterone levels drop as women approach midlife, and some women notice a dip in sex drive as a result. Without an FDA-approved version specifically for women, doctors are forced to alter formulas and dosages designed for men. Several promising

*Name has been changed.