Addyi
1 Year Later:
What's the Score?

Addyi comes with the strictest possible FDA warning to highlight its life-threatening complications.[1] Meanwhile, clinical trials show that 9 out of 10 women experience no improvement in sexual desire when taking Addyi over placebo.[2] That's a lot of risk for almost no reward. One year later, we went back to see how well Addyi has done.

REPORT CARD FOR: Addyi

AUGUST 2016 (One Year Review)

SUBJECT	GRADE
Provider Education Because of life-threatening complications, the FDA required Addyi's maker to provide safety training for doctors and pharmacists: that training is just a PowerPoint and a 4-question test on the company's website.[3]	D
Practicality The only study of Addyi and alcohol—conducted primarily on men—found serious complications such as severe and sudden drops in blood pressure resulting in loss of consciousness. Now women taking Addyi must promise to avoid alcohol.[4]	D
Promised Studies The FDA required Addyi's maker to conduct three new studies on the effect of alcohol consumption in women taking Addyi. No studies have yet been released.[5]	I
Unknown Risks No studies have looked at the risks of taking Addyi long-term or during pregnancy. Data on these risks won't be available until 2021—if at all.[6]	I
Contraindications Women on Addyi shouldn't take common medicines used to treat yeast infections, chlamydia infections, syphilis, HIV, and Hepatitis C.[7]	D
Birth Control Safety Addyi is marketed to women ages 18–44, but the only available data show that taking hormonal birth control while on Addyi increases the risk of serious complications.[8]	I
Product Demand At its sales peak in March 2016, only 1,500 Addyi prescriptions were written. In contrast, Viagra sold half a million prescriptions in its first month on the market.[9]	F
Affordability Prescriptions run $800 per month, making Addyi costly to take daily as directed.[10]	F

I=Incomplete

Report Card References

1 - Addyi's FDA Warning

Addyi's life-threatening side effects were so grave that they warranted the strictest possible warning by the FDA—a "black box warning." Those side effects include severe, sudden drops in blood pressure that can lead to loss of consciousness for prolonged periods.

2 - 9 Out of 10 Women Experience No Improvement

The drug company's goal with Addyi was to create a drug that promotes spontaneous desire—a noticeable increase in libido. But so far, studies show that Addyi has little to no effect on desire. After two previous rejections, the drug company only won FDA approval for Addyi by changing the question. The FDA noted this maneuvering in a June 2015 briefing document for advisory committee members:

> [During the first review, the] advisory committee voted 10 to 1 that the Applicant had not provided sufficient evidence of efficacy. Of note, both pivotal phase 3 trials failed to show a statistically significant improvement compared to placebo in the pre-specified co-primary efficacy endpoint...
>
> The Applicant stated that the effect of flibanserin on sexual desire was better assessed with the FSFI [Female Sexual Function Index], but most of the advisory committee members did not agree with altering the pre-specified method of assessing sexual desire. ...
>
> The third trial used FSFI as the pre-specified co-primary endpoint for sexual desire… The Applicant and FDA are not in full agreement that the FSFI is optimized for assessing sexual desire.

Even with this questionable change in study design, the drugmaker's own clinical trials showed that 9 out of 10 women experienced *no improvement* in sexual desire when taking Addyi over placebo, and for the remaining 1 out of 10, the number of "sexually satisfying" events only increased slightly per month. As the FDA noted in its approval, "On average, treatment with Addyi increased the number of satisfying sexual events *by 0.5 to 1 additional event per month* over placebo, increased the sexual desire score by 0.3 to 0.4 over placebo, and decreased the distress score related to sexual desire by 0.3 to 0.4 over placebo. … 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 distress. Addyi has not been shown to enhance sexual performance." [Emphasis ours]

3 - Provider Education

To balance grave safety concerns, the FDA required the makers of Addyi to create a Risk Evaluation and Mitigation Strategy, or REMS. The REMS requires that prescribers and pharmacies be certified by enrolling and completing training about the increased risk of severe side effects and the importance of not drinking alcohol during treatment with Addyi. One year later, however, the certification training for clinicians and pharmacies is just a PowerPoint and a 4-question test on the company's website.

4 - Practicality

The FDA asked Addyi's maker to conduct a safety study assessing the risk associated with alcohol consumption, but only 2 of the 25 participants in the alcohol safety study were women. We know women may experience fatigue, low blood pressure, and fainting when using Addyi alone, and those conditions may be exacerbated when drinking alcohol. In fact, following the death of a 54-year-old Addyi patient in another study due to "acute alcohol intoxication," the FDA concluded, "it is not possible to exclude a role of flibanserin [Addyi] in this patient's death." But rather than require the drugmaker to complete additional alcohol safety studies before going on the market, the FDA opted to tell women to abstain from alcohol permanently—despite there being no known strategy to ensure people are able to do this in the long term.

One year after going on the market, anecdotal evidence suggests just how impractical this approach has been. As one example, in a Vogue piece about Addyi last December, the author explicitly ignores this precaution.

> I had already signed a consent form vowing not to drink and promising to lie down if I felt light-headed (nausea, sleepiness, and low blood pressure are other risks). ...
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> [My husband] and I try not to talk about our children and flirt, tentatively, over a bottle of Saint-Émilion. (Despite the pharmacist's warnings, I decide to drink; none of Addyi's worst side effects have materialized, and my husband is driving.) At home, I take my nightly pill and get into bed, wondering if desire will strike at last. Unfortunately, I fall asleep almost instantly—it turns out that Addyi taken with half a bottle of red wine can, indeed, result in extreme sleepiness.

5 - Promised Studies

As a condition of its approval, the FDA required Addyi's maker to conduct three post-market studies on the effect of alcohol consumption in women taking Addyi, after the alcohol study conducted prior to approval only included two women. The first post-market study—the easiest of the three—was supposed to be completed August 2016, with a final report produced by December 2016. One year later, all of the flibanserin studies required by the FDA, including the alcohol study due to be completed this month, are listed as "pending," the official designation for a study that "has not been initiated (i.e., no subjects have been enrolled or animals dosed)." (Search results for "flibanserin" retrieved August 16, 2016.)

Having already missed their completion deadline for the easiest study to conduct, we have little faith that they will meet the deadlines for the other safety studies promised to the FDA.

6 - Unknown Risks

As a condition of its approval, the FDA required Addyi's maker to conduct two studies on the safety of taking Addyi during pregnancy, but data on these risks won't be available until 2021. One year later, the failure of the drugmaker to even initiate the easiest of its post-market studies (see #5) suggests that the 2021 deadline for studying Addyi's effects on pregnant women and their fetuses will not be met. Meanwhile, no studies have been conducted that examine the safety of taking Addyi long-term even though Addyi must continue to be taken daily to have an effect.

7 - Contraindications

The use of Addyi with common antibiotics and antifungals used to treat a host of infections—including urinary tract infections, respiratory tract infections, yeast infections, chlamydia infections, syphilis, HIV, Hepatitis C, and many more—significantly increases flibanserin concentrations, which raises the risk for sudden drops in blood pressure and fainting.

Many other commonly used medications may also significantly increase Addyi exposure, including antiepileptic drugs, benzodiazepines, antidepressants, antipsychotics, mood stabilizers, narcotics, vaginal lubricants, and even St. John's wort, all of which were excluded from Addyi's phase 3 studies.

8 - Birth Control Safety

Addyi is only approved for premenopausal women —i.e. those most likely to use hormonal birth control—but the only available data show that taking hormonal birth control while on Addyi increases the risk of serious complications. Some adverse events, including sleepiness (somnolence), dizziness and fatigue, were reported more often in women who used hormonal contraceptives. Hormonal contraceptives are known to affect a certain enzyme (CYP3A4) which may increase Addyi exposure by 40%.

9 - Product Demand

One year later, Addyi's market performance has been underwhelming, perhaps due to its high risks and low benefit. At its sales peak in March 2016, it is estimated that only 1,500 Addyi prescriptions were written. In contrast, Viagra sold half a million prescriptions in its first month on the market. Current estimates put the number of Addyi prescriptions at 1,000 in May 2016, suggesting that interest in the drug is falling among consumers.

10 - Affordability

One year later, Addyi's costs range anywhere between $800 per month to $1000 per month. As of August 2016, Drugs.com lists it as $856 per month. Due to its high costs, serious side effects, and underwhelming effectiveness, insurance companies have been hesitant to cover Addyi.

The drug is prescribed to be taken every day, and positive effects—if any—are not usually experienced until about six to eight weeks after beginning the medication.

While Addyi's maker boasts of a patient assistance program, consumers should beware. The offer is only valid at Walgreens and select "independent pharmacies," even though major pharmacies like CVS, Rite Aid, Walmart, Target, and many more are all certified under the REMS process to disburse Addyi. For women whose commercial insurance already covers Addyi, the program reduces their monthly co-pay to $50/month, but only for 7 months. For women paying out of pocket, because they are uninsured or their insurance doesn't cover Addyi, the coupon enables women to get their prescription for $125/month but only for 3 months. Also worth remembering: "This offer is not valid in Massachusetts or Minnesota or where otherwise prohibited, taxed, or otherwise restricted." And, of course, "Valeant Pharmaceuticals reserves the right to rescind, revoke, terminate, or amend this offer at any time, without notice."