addyi®
(flibanserin)
100mg tablets



IF SHE'S FRUSTRATED THAT SHE RARELY WANTS SEX IT MAY BE TIME TO BRING UP *THE LITTLE PINK PILL.*



Addyi is indicated for the treatment of premenopausal women with acquired, generalized Hypoactive Sexual Desire Disorder (HSDD), as characterized by low sexual desire that causes marked distress or interpersonal difficulty and is NOT due to a co-existing medical or psychiatric condition, problems within the relationship, or the effects of a medication or other drug substance. Acquired HSDD refers to HSDD that develops in a patient who previously had no problems with sexual desire. Generalized HSDD refers to HSDD that occurs regardless of the type of stimulation, situation or partner. Addyi is not indicated for the treatment of HSDD in postmenopausal women, men or to enhance sexual perfomance.

IMPORTANT SAFETY INFORMATION

WARNING: HYPOTENSION AND SYNCOPE IN CERTAIN SETTINGS
See full prescribing information for complete boxed warning.
• Use of ADDYI and alcohol together close in time increases the risk of severe hypotension and syncope. Counsel patients to wait at least two hours after consuming one or two standard alcoholic drinks before taking ADDYI at bedtime or to skip their ADDYI dose if they have consumed three or more standard alcoholic drinks that evening.
• Severe hypotension and syncope can occur when ADDYI is used with moderate or strong CYP3A4 inhibitors or in patients with hepatic impairment; therefore, ADDYI use in these settings is contraindicated.

See additional Important Safety Information throughout, including Boxed Warning regarding hypotension and syncope in certain settings, and Full Prescribing Information and Medication Guide at addyi.com/pi.

HYPOACTIVE SEXUAL DESIRE DISORDER (HSDD)

Though not fully understood, HSDD is believed to be caused by an imbalance of chemicals in the brain. A PET scan study examined 24 women (age 18-47) with and without HSDD by having them watch neutral, low, and high erotic movies for 2 minutes while lying with their head in a PET scanner. Results showed that the women with HSDD had little to no activation in areas of the brain that normally respond to sexual cues. Increased activation was also viewed in the prefrontal cortex, which blocks the progression of desire.[2-5]



without HSDD*

*Rendering of brain PET scans



with HSDD*

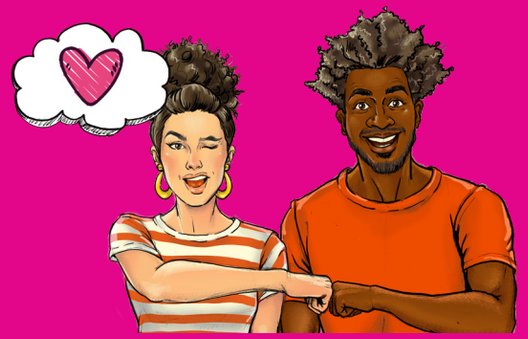
CHARACTERISTICS OF HSDD[6]:

- CHRONICALLY LOW SEXUAL DESIRE
  (which your patients may call low libido or low sex drive)
- ASSOCIATED PERSONAL DISTRESS



MOST PATIENTS WANT YOU TO START THE CONVERSATION[7]

A few simple questions is all it takes to diagnose HSDD. The validated Decreased Sexual Desire Screener (DSDS) can help you make a diagnosis.[8] Add the DSDS, found on addyihcp.com, to your intake forms today.



CLINICAL TRIALS: ADDYI IS PROVEN SAFE & EFFECTIVE[9]

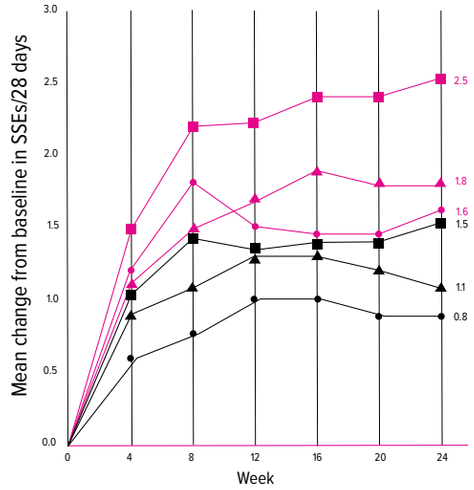
The efficacy of Addyi was established in three 24-week, randomized, double-blind, placebo-controlled trials in premenopausal women with acquired, generalized HSDD. Participants were age 19-55 years (mean 36 years) with an average HSDD and relationship duration of 5 years and 11 years, respectively. Approximately 40% subjects were also taking hormonal contraceptives. Women in these trials were treated with Addyi 100mg (n=1187) once-daily at bedtime, or placebo (n=1188).

	Study 1 ADDYI (n=280) Placebo (n=290)	Study 2 ADDYI (n=365) Placebo (n=372)	Study 3 ADDYI (n=532) Placebo (n=536)
Co-primary endpoints	SSEs eDiary Desire	SSEs eDiary Desire	SSEs FSFI-D
Secondary endpoints	FSFI-D FSDS-R Q13	FSFI-D FSDS-R Q13	FSDS-R Q13

SSEs = satisfying sexual events; FSFI-D = Female Sexual Function Index – Desire Domain; FSDS-R = Female Sexual Distress Scale-Revised Question 13

INCREASED SATISFYING SEXUAL EVENTS

Satisfying Sexual Events (SSEs)[9-12]



- Studies 1, 2, and 3 measured number of monthly SSEs as a co-primary endpoint
- SSEs included sexual intercourse, oral sex, masturbation, or genital stimulation by a partner
- SSEs began to increase between weeks 4 and 8 and the improvement was sustained through week 24

STUDY 1** ● Addyi (n=280) ● Placebo (n=290)
STUDY 2** ▲ Addyi (n=365) ▲ Placebo (n=372)
STUDY 3† ■ Addyi (n=532) ■ Placebo (n=536)

**p<0.01; †*p*<0.0001

Patients may see results as soon as 4 weeks. If improvement is not seen after 8 weeks of treatment, Addyi should be discontinued.

IMPORTANT SAFETY INFORMATION (Continued)

Contraindications

- Moderate or strong cytochrome P450 3A4 (CYP3A4) inhibitors
- Hepatic impairment

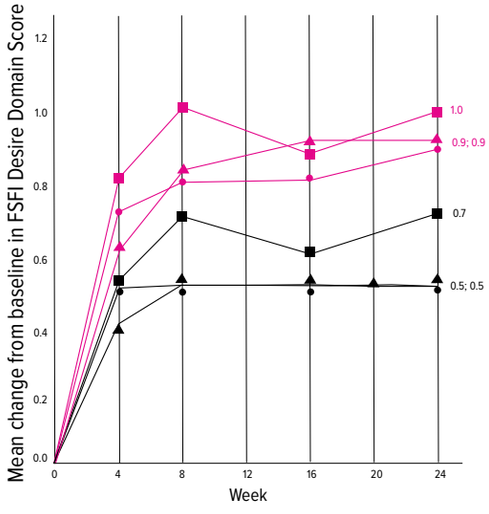
Warnings and Precautions

• Hypotension and Syncope Due to an Interaction with Alcohol: Taking ADDYI within two hours after consuming alcohol increases the risk of severe hypotension and syncope. To reduce this risk, counsel patients to wait at least two hours after drinking one or two standard alcoholic drinks before taking ADDYI at bedtime. Patients who drink three or more standard alcoholic drinks should skip their ADDYI dose that evening. After taking ADDYI at bedtime, advise patients to not use alcohol until the following day.

See additional Important Safety Information throughout, including Boxed Warning regarding hypotension and syncope in certain settings, and Full Prescribing Information and Medication Guide at addyi.com/pi.

INCREASED SEXUAL DESIRE

Female Sexual Function Index - Desire Domain[9-12 §]



STUDY 1
- Addyi (n=280)
- Placebo (n=290)

STUDY 2
- Addyi (n=365)
- Placebo (n=372)

STUDY 3*
- Addyi (n=532)
- Placebo (n=536)

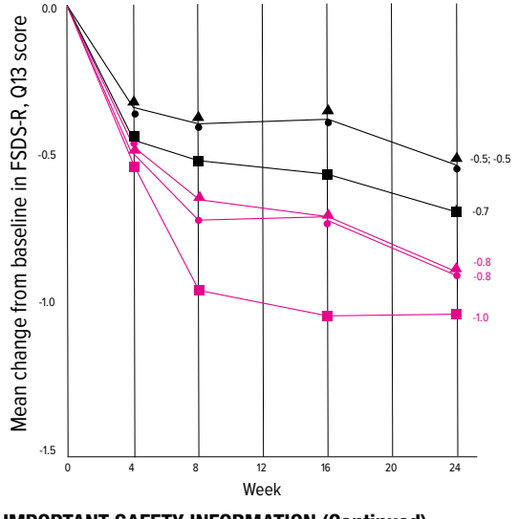
*p<0.0001

- FSFI-Desire domain was a co-primary endpoint in Study 3, and secondary endpoint in Studies 1 and 2
  - The FSFI-D consists of 2 questions: "Over the past 4 weeks, how often did you feel sexual desire or interest?" and "Over the past 4 weeks, how would you rate your level of sexual desire or interest?"[6,7]
  - A score of ≤3 may indicate the presence of HSDD[6,7]
  - Sexual desire began to increase between weeks 4 and 8 and the improvement was sustained through week 24

E-Diary
- Studies 1 and 2 measured desire using eDiary scores as a co-primary endpoint
  - Every day, patients rated their level of sexual desire from a scale of 0 to 3
  - The eDiary responses were summed over a 28-day period to yield the calculated monthly sexual desire score, which ranged from 0 to 84
  - P value not reported for secondary endpoints because the trial failed on the eDiary desire co-primary efficacy endpoint

REDUCED DISTRESS ASSOCIATED WITH LOW SEXUAL DESIRE

Female Sexual Distress Scale-Revised Question 13 (FSDS-R, Q13)[9-12 §]



- Studies 1, 2, and 3 measured the decrease in distress with the FSDS-R, Q13 as a secondary endpoint
- The FSDS-R, Q13 measures distress based on the question, "How often did you feel bothered by low sexual desire?"
- Distress with associated low desire began to decrease between weeks 4 and 8 and the improvement was sustained through week 24

STUDY 1*
- Addyi (n=280)
- Placebo (n=290)

STUDY 2*
- Addyi (n=365)
- Placebo (n=372)

STUDY 3**
- Addyi (n=532)
- Placebo (n=536)

**p* value not reported for secondary endpoints because the trial failed on the eDiary Desire co-primary efficacy endpoint; ***p*=0.0001

§ Patients may see results as soon as 4 weeks. If improvement is not seen after 8 weeks of treatment, Addyi should be discontinued.

IMPORTANT SAFETY INFORMATION (Continued)

• Hypotension and Syncope with CYP3A4 Inhibitors: Moderate or strong CYP3A4 inhibitors significantly increase ADDYI concentrations, which can lead to hypotension and syncope. Concomitant use of ADDYI with a moderate or strong CYP3A4 inhibitor is contraindicated. Concomitant use of multiple weak CYP3A4 inhibitors that may include herbal supplements (e.g., ginkgo, resveratrol) or non-prescription drugs (e.g., cimetidine) could also lead to clinically relevant increases in flibanserin concentrations that may increase the risk of hypotension and syncope.

CLINICAL TRIAL SAFETY PROFILE

ADVERSE REACTIONS LEADING TO DISCONTINUATION

	Placebo (n=1556)	Addyi (n=1543)
Dizziness	0.1%	1.7%
Nausea	0.1%	1.2%
Insomnia	0.2%	1.1%
Somnolence	0.3%	1.1%
Anxiety	0.3%	1.0%

In 4 randomized, double-blind, placebo-controlled trials in premenopausal women with HSDD, the discontinuation rate due to adverse reactions† was 13% among patients treated with 100mg Addyi at bedtime and 6% among patients treated with placebo.

†Adverse reactions leading to discontinuation of ≥ 1% of patients receiving 100 mg Addyi at bedtime and at a higher incidence than placebo-treated patients.

MOST COMMON ADVERSE REACTIONS

	Placebo (n=1556)	Addyi (n=1543)
Dizziness	2.2%	11.4%
Somnolence	2.9%	11.2%
Nausea	3.9%	10.4%
Fatigue	5.5%	9.2%
Insomnia	2.8%	4.9%
Dry Mouth	1.0%	2.4%

Common adverse reactions‡ in 4 randomized, double-blind, placebo-controlled trials in premenopausal women with HSDD.

The majority of these adverse reactions began within the first 14 days of treatment.[9]

‡ Adverse reactions reported in ≥ 2% of patients receiving 100 mg Addyi at bedtime and at a higher incidence than placebo-treated patients.



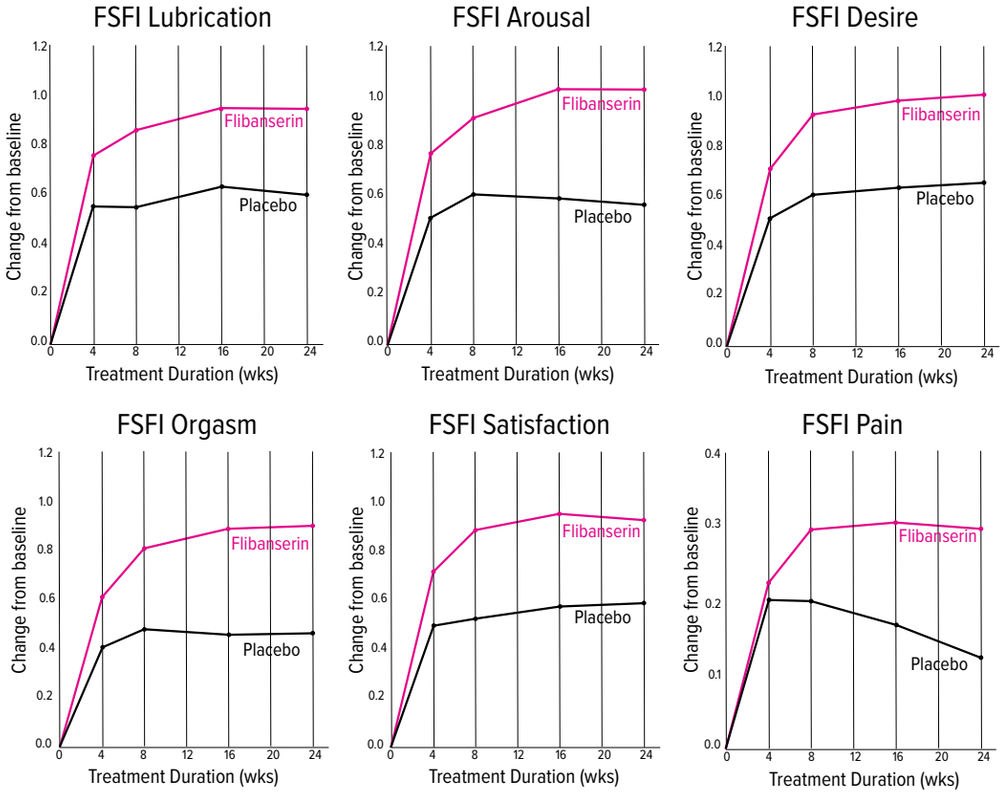
IMPORTANT SAFETY INFORMATION (Continued)

• Central Nervous System (CNS) Depression (e.g., Somnolence, Sedation): Can occur with ADDYI alone and is exacerbated by other CNS depressants including alcohol, and in settings where flibanserin concentrations are increased such as CYP3A4 inhibitors. The risk of CNS depression is also increased if ADDYI is taken during waking hours. Patients should avoid activities requiring full alertness (e.g., operating machinery or driving) until at least six hours after each dose and until they know how ADDYI affects them.

See additional Important Safety Information throughout, including Boxed Warning regarding hypotension and syncope in certain settings, and Full Prescribing Information and Medication Guide at addyi.com/pi.

POST HOC ANALYSIS OF FEMALE SEXUAL FUNCTION INDEX (FSFI)[13]

Addyi has not been studied for the treatment of any female sexual dysfunction other than acquired, generalized HSDD. Post hoc analyses of FSFI total and individual domain data were pooled from 3 pivotal, multicenter, randomized, placebo-controlled, double-blind trials in premenopausal women with HSDD who received flibanserin (n=1165) or placebo (n=1204).

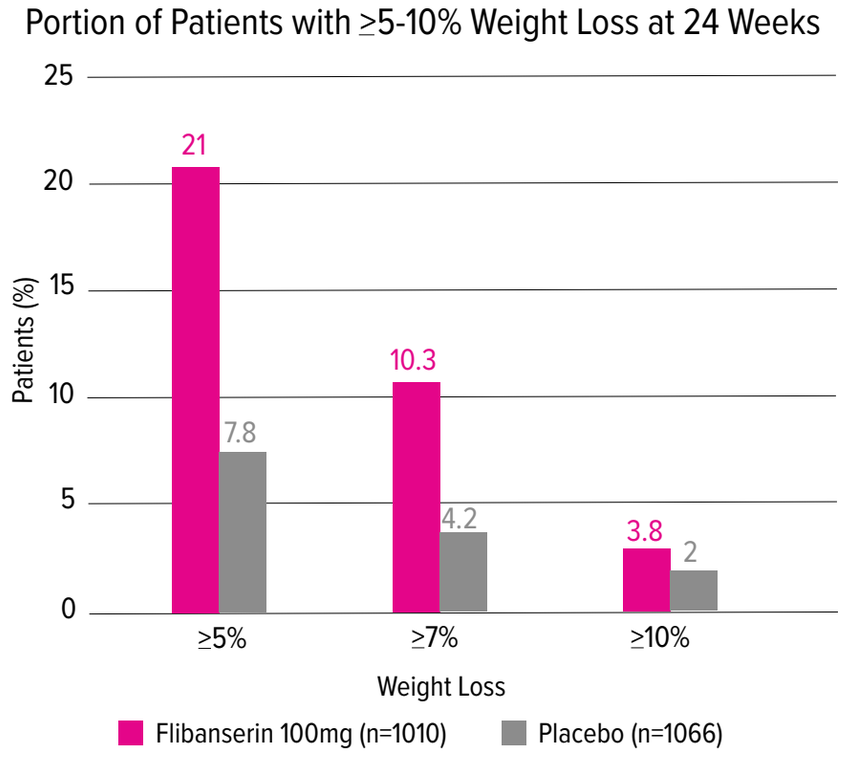


- Post-hoc exploratory analyses compared change from baseline in FSFI scores of flibanserin and placebo groups at each assessment time point by t-test
  - FSFI questionnaire was administered at baseline and Weeks 4,8,16, and 24
  - There was no adjustment for multiple comparisons
  - Missing data were handled using the last observation carried forward (LOCF) method

Post hoc analysis sponsored by Sprout.

POST HOC ANALYSIS OF EFFECT ON WEIGHT[14]

Post hoc analysis of pooled data from 3 pivotal, multicenter, randomized, placebo-controlled, double-blind trials in premenopausal women with HSDD who received flibanserin. **Addyi is not indicated for weight loss.**



- Mean baseline weight was ~73kg (~160lbs)
- Weight gain ≥7% at 24 weeks occurred in 1.8% women receiving flibanserin and 3.4% women receiving placebo
- Higher baseline BMI was associated with greater weight loss
- No association seen between effect on weight and treatment response, contraceptive use, smoking status, SSRI/SNRI use, or occurrence of nausea
- Body weight was measured to assess weight loss and weight gain as potential adverse events
- Study was not designed to evaluate weight loss. Patients were not selected based on obesity status nor did they enter the studies with the goal of losing weight

IMPORTANT SAFETY INFORMATION (Continued)

• Hypotension and Syncope with ADDYI Alone: The use of ADDYI – without other concomitant medications known to cause hypotension or syncope – can cause hypotension and syncope. The risk of hypotension and syncope is increased if ADDYI is taken during waking hours or if higher than the recommend dose is taken. Consider the benefits of ADDYI and the risks of hypotension and syncope in patients with pre-existing conditions that predispose to hypotension. Patients with pre-syncope should immediately lie supine and promptly seek medical help if symptoms do not resolve. Prompt medical attention should also be obtained for patients who experience syncope.

• Syncope and Hypotension in Patients with Hepatic Impairment: Any degree of hepatic impairment significantly increases flibanserin concentrations, which can lead to hypotension and syncope. ADDYI is contraindicated in patients with hepatic impairment.

IMPORTANT SAFETY INFORMATION (Continued)

Drug Interactions

• Alcohol: coadministration of ADDYI with alcohol increased the risk of hypotension, syncope, and CNS depression compared to the use of ADDYI alone or alcohol alone. Patients should wait at least two hours after consuming one or two standard alcoholic drinks before taking ADDYI at bedtime or to skip their ADDYI dose if they have consumed three or more alcoholic drinks that evening.

• CNS Depressants: (i.e., diphenhydramine, opioids, hypnotics, benzodiazepines, etc.) Concomitant use with ADDYI may increase the risk of CNS depression compared to use of ADDYI alone.

See additional Important Safety Information throughout, including Boxed Warning regarding hypotension and syncope in certain settings, and Full Prescribing Information and Medication Guide at addyi.com/pi.

COADMINISTRATION WITH SSRI/SNRI

Clinical considerations for taking Addyi with SSRIs and SNRIs

Fluvoxamine (Luvox®)

CONTRAINDICATED[9]

- Fluvoxamine is a moderate CYP3A4 inhibitor[16]

Citalopram (Celexa®)
Escitalopram (Lexapro®)
Fluoxetine (Prozac®)
Paroxetine (Paxil®)
Sertraline (Zoloft®)
Vilazodone (Viibryd®)
Desvenlafaxine (Pristiq®)
Duloxetine (Cymbalta®)
Levomilnacipran (Fetzima®)
Milnacipran (Savella®)
Venlafaxine (Effexor®)

PATIENT COUNSELING RECOMMENDED[9,16]

- Fluoxetine is a strong CYP2C19 inhibitor and weak CYP3A4 Inhibitor and may increase flibanserin exposure
- Concomitant administration with other CNS-acting agents such as SSRI/SNRIs may increase CNS depression

ADVISE PATIENTS

- Concomitant administration may increase risk of adverse reactions.
- Addyi can cause severe hypotension, syncope, and CNS depression (such as somnolence and sedation). The risk is increased if Addyi is taken during waking hours.
- Addyi should be taken only one tablet at bedtime and not any other time of day

Information based on pharmacologic action of products based on respective Prescribing Information as of May 2021. All product names, trademarks and registered trademarks are property of their respective owners.

SAFETY STUDY WITH SSRI/SNRI[15]

12 week randomized, double-blind, placebo-controlled clinical trial in 111 premenopausal women with mild to remitted depression treated with a stable dose of SSRI/SNRI* and symptoms of HSDD.**

RESULT		Flibanserin† + SSRI/SNRI (%) N=72	Placebo + SSRI/SNRI (%) N=37
Primary endpoint: Incidence AEs		65.8	71.1
Depression (QIDS-SR16)	Remission	19.4	10.8
	No change	73.6	67.6
	Worsened	6.9	21.6
Anxiety (Beck Anxiety Inventory)	Remission	16.4	2.7
	No change	82.2	94.6
	Worsened	1.4	2.7

- Overall, no increased risk of adverse events, including depression and anxiety were observed
- No instances of suicidality (C-SSRS)
- AEs ≥3% with Addyi and higher than placebo: dry mouth, insomnia, back pain, dizziness
- This study was designed to assess flibanserin safety; No conclusions regarding efficacy can be made

*citalopram, escitalopram, fluoxetine, paroxetine, sertraline, desvenlafaxine, duloxetine, venlafaxine
**Planned sample size was 200 patients; study was terminated early due to commercial reasons
†Includes 28 patients on fixed 100 mg qhs dose and 45 patients on up-titrated dose (50 mg qhs first two weeks, followed by 100 mg qhs)
C-SSRS = Columbia-Suicide Severity Rating Scale; QIDS-SR16 = 16-item Quick Inventory of Depressive Symptomology-Self Report

IMPORTANT SAFETY INFORMATION (Continued)

• Moderate or Strong CYP3A4 Inhibitors: ADDYI is contraindicated in women taking moderate (e.g., fluconazole, etc.) or strong (e.g., ketoconazole, etc.) CYP3A4 inhibitors

• Oral Contraceptives and Other Weak CYP3A4 Inhibitors: In combination with ADDYI may increase the risk of adverse reactions

ABOUT ADDYI

SETTING EXPECTATIONS

Patients may start to notice the effects of Addyi in as little as 4 weeks but be sure to give Addyi 8 full weeks to experience continuously improving results[10-12‡]...



DOSING

Once-daily only at bedtime, 100mg qhs

It is important for your patients to take Addyi as prescribed to help decrease the risks of hypotension, syncope, accidental injury and fatigue.

"I'm fantasizing about having sex again!"

ADDYI + ALCOHOL

If patients consume up to 2 standard alcoholic drinks§ in the evening instruct her to wait 2 hours before taking Addyi at bedtime.



Advise patients skip their Addyi dose if they have consumed 3 or more standard alcoholic drinks§ that evening.



‡Some women may see results in as early as 4 weeks. Addyi should be discontinued if there is no improvement after 8 weeks.

§A standard alcoholic drink includes: one 12-ounce regular beer, 5 ounces of wine, 1.5 ounces of distilled spirits or shot.

IMPORTANT SAFETY INFORMATION (Continued)

• Strong CYP2C19 Inhibitors: (i.e., proton pump inhibitors, SSRI's, benzodiazepines, antifungals, etc.) Increase flibanserin exposure which may increase risk of hypotension, syncope, and CNS depression

• CYP3A4 Inducers: (i.e., carbamazepine, phenobarbital, etc.) Concomitant use substantially decreases flibanserin exposure compared to the use of ADDYI alone and is not recommended.

See additional Important Safety Information throughout, including Boxed Warning regarding hypotension and syncope in certain settings, and Full Prescribing Information and Medication Guide at addyi.com/pi.

CHEAT SHEET: DOSING, CODING, PRESCRIBING, & SAVINGS

CODING FOR HSDD*

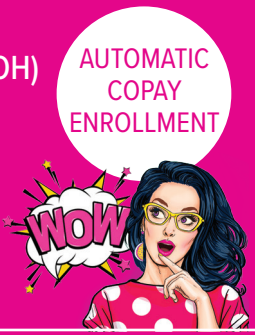
- ICD-10-CM HSDD is F52.0
- ICD-11 HSDD is HA00.2
- DSDS/FSFI screeners, if administered, are CPT 96127

*Coding is at the discretion of the HCP and does not guarantee reimbursement

addyi®
(flibanserin)
100mg tablets

PHARMACY (phil)

- Phil eRX: **PhilRX (Columbus, OH)**
- Phil Fax: **888-975-0603**
- NCPDP: **3685508**
- Phil Support: **855-652-7445**
- Free HOME DELIVERY & ONLY $20/mo with commercial insurance coverage**



- Phil will TEXT PATIENT with instructions (please include patient mobile phone number on eRX)
- Phil Email: **md-help@phil.us**


(actual size)

RETAIL CARD PICKUP / COPAY CARD NEEDED

- A copay card for the pharmacy must be downloaded at: **addyi.com/savings**



"I WANT sex again :-) I cannot believe I'm saying that!!"

1. IQVIA Monthly Total Prescriptions Volume Data Comparing Addyi vs Vyleesi in the US. December 2020.
2. Arnow BA, Millheiser L, Garrett A, et al. Women with hypoactive sexual desire disorder compared to normal females: a functional magnetic resonance imaging study. *Neuroscience* 2009;158:484-502.
3. Woodard TL, Nowak NT, Balon R, et al. Brain activation patterns in women with acquired hypoactive sexual desire disorder and women with normal sexual function: a cross-sectional pilot study. *Fertil Steril* 2013;100:1068-1076.
4. Bianchi-Demicheli F, Cojan Y, Waber L, et al. Neural basis of hypoactive sexual desire disorder in women: an event-related fmri study. *J Sex Med*. 2011;8:2546-2559.
5. Holstege G. How the emotional motor system controls the pelvic organs. *Sex Med Rev.* 2016: 4;303-328.
6. American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders. 4th ed., Text Revision. Washington, DC: *American Psychiatric Press*; 2000.
7. Association of Reproductive Health Professionals. ARHP and Healthy Women (2009). Women's Sexual Health Survey (online in the US). Harris Interactive.
8. Clayton AH, Goldfischer ER, Goldstein I, et al. Validation of the Decreased Sexual Desire Screener (DSDS): a brief diagnostic instrument for generalized acquired female hypoactive sexual desire disorder (HSDD). *J Sex Med*. 2009;6(3):730-738.
9. Addyi Prescribing Information.
10. Derogatis LR, Komer L, Katz M, et al. Treatment of hypoactive sexual desire disorder in premenopausal women: efficacy of flibanserin in the VIOLET Study. *J Sex Med*. 2012;9(4):1074-1085.
11. Thorp J, Simon J, Dattani D, et al. Treatment of hypoactive sexual desire disorder in premenopausal women: efficacy of flibanserin in the DAISY study. *J Sex Med*. 2012;9(3):793-804.
12. Katz M, Derogatis LR, Ackerman R, et al. Efficacy of flibanserin in women with hypoactive sexual desire disorder: results from the BEGONIA Trial. *J Sex Med*. 2013;10(7):1807-1815.
13. Simon JA, Millheiser L, Clayton AH, et al. Improvements in Female Sexual Function Index (FSFI) domains over time after flibanserin treatment in premenopausal women with hypoactive sexual desire disorder (HSDD). Poster presented at the International Society for the Study of Women's Sexual Health (ISSWSH) 2020 Annual Meeting; March 5-8, 2020; Orlando, FL.(A084).
14. Kornstein SG, James JA, Apfel SC, et al. Effect of flibanserin treatment on body weight in premenopausal and postmenopausal women with hypoactive sexual desire disorder: A post hoc analysis. *J Women's Health*. 2017;26(11):1161-1168.
15. Clayton AH, Harry AC, Yuan J, et al. Safety of flibanserin in women treated with antidepressants: A randomized, placebo-controlled study. *J Sex Med* 2018;15(1):43-51.
16. https://www.fda.gov/drugs/drug-interactions-labeling/drug-development-and-drug-interactions-table-substrates-inhibitors-and-inducers

**Eligible patients only. Restrictions apply. Please see Terms and Conditions at addyi.com/savings.

IMPORTANT SAFETY INFORMATION (Continued)

• Digoxin or other P-glycoprotein (P-gp) substrates: Increases digoxin concentration, which may lead to digoxin toxicity. Increase monitoring of drugs transported by P-gp that have a narrow therapeutic index.

Most Common Adverse Reactions

• Most common adverse reactions (ADDYI incidence ≥2% and higher than placebo) are dizziness, somnolence, nausea, fatigue, insomnia, and dry mouth.

See additional Important Safety Information throughout, including Boxed Warning regarding hypotension and syncope in certain settings, and Full Prescribing Information and Medication Guide at addyi.com/pi.