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 prescribed ADDYI about the importance of waiting at least two hours after consuming alcohol before taking ADDYI.***
- ***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.***

ADDYI is contraindicated:

- With concomitant use with moderate or strong CYP3A4 inhibitors.
- In patients with hepatic impairment.

Summary of Warnings and Precautions

- **Hypotension and Syncope due to an Interaction with Alcohol.** An interaction between *ADDYI* and alcohol when consumed close in time increases the risk of severe hypotension and syncope. Counsel patients to wait at least two hours after consuming alcohol before taking *ADDYI* at bedtime. Alternatively, counsel patients to skip the *ADDYI* dose at bedtime if the patient consumes alcohol in the evening. After taking *ADDYI* at bedtime, advise patients not to use alcohol until the following day.

- **Hypotension and Syncope with CYP3A4 Inhibitors.**
  Moderate and 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.

- **Central Nervous System Depression.** *ADDYI* can cause CNS depression (e.g., somnolence, sedation). In five 24-week, randomized, placebo-controlled, double-blind trials of premenopausal women with HSDD the incidence of somnolence, sedation, or

fatigue was 21% and 8% in patients treated with 100 mg of *ADDYI* at bedtime and placebo, respectively. The risk of CNS depression is increased if *ADDYI* is taken during waking hours, or if *ADDYI* is taken with alcohol or other CNS depressants, or with medications that increase flibanserin concentrations.
Patients should not drive or engage in other activities requiring full alertness until at least 6 hours after taking *ADDYI* and until they know how *ADDYI* affects them.

- **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. In five 24-week, randomized, placebo-controlled, double-blind trials of premenopausal women with HSDD, hypotension was reported in 0.2% and <0.1% of *ADDYI*-treated patients and placebo-treated patients, respectively; syncope was reported in 0.4% and 0.2% of *ADDYI*-treated patients and placebo-treated patients, respectively. The risk of hypotension and syncope is increased if *ADDYI* is taken during waking hours or if higher than the recommended 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 who experience pre-syncope should immediately lie supine and promptly seek medical help if the 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, syncope, and CNS depression. Therefore, *ADDYI* is contraindicated in patients with hepatic impairment.

Most Common Adverse Reactions

- The most common adverse reactions (reactions reported in ≥2% of patients receiving 100 mg ADDYI and at a higher incidence than placebo-treated subjects): dizziness (11.4%; 2.2%), somnolence (11.2%; 2.9%), nausea (10.4%; 3.9%), fatigue (9.2%; 5.5%), insomnia (4.9%; 2.8%), and dry mouth (2.4%; 1.0%).

Summary of Drug Interactions

- *ADDYI* is primarily metabolized by CYP3A4 and, to a lesser extent, by CYP2C19.

- *ADDYI* is contraindicated in women taking a moderate (e.g., fluconazole) or strong (e.g., ketoconazole) CYP3A4 inhibitor.
- The concomitant use of *ADDYI* with CNS depressants (e.g., diphenhydramine, opioids, hypnotics, benzodiazepines) may increase the risk of CNS depression (e.g., somnolence) compared to use of *ADDYI* alone.
- Patients using *ADDYI* with combined oral contraceptives or with weak CYP3A4 inhibitors may experience a higher incidence of adverse reactions.
- Strong CYP2C19 inhibitors (e.g., proton pump inhibitors, selective serotonin reuptake inhibitors, benzodiazepines, antifungals) may increase *ADDYI* exposure, which may increase the risk of hypotension, syncope, and CNS depression.
- Do not use *ADDYI* with strong CYP3A4 inducers (e.g., rifampin, St. John's Wort) as this will substantially reduce the concentration of *ADDYI*.

- *ADDYI* inhibits P-glycoprotein (P-gp). Monitoring of drug concentrations of any narrow therapeutic index drugs that are substrates for P-gp (e.g., digoxin, sirolimus) should be increased if co-administered with *ADDYI*. The concomitant use of *ADDYI* with digoxin, a drug that is transported by P-gp, increases the digoxin concentration. This may lead to digoxin toxicity.

See FULL PRESCRIBING INFORMATION, including Boxed Warning regarding the use of alcohol, hypotension, and syncope in certain settings.