



Cindy Eckert  
Chief Executive Officer  
Sprout Pharmaceuticals, Inc.  
4350 Lassiter at North Hills Avenue, #260  
Raleigh, NC 27609

**RE: NDA 022526**  
ADDYI (flibanserin) tablets, for oral use  
MA 241

## WARNING LETTER

Dear Ms. Eckert:

The Office of Prescription Drug Promotion (OPDP) of the U.S. Food and Drug Administration (FDA) has reviewed a direct-to-consumer (DTC) radio advertisement (radio ad) (US—1900289.03) for ADDYI (flibanserin) tablets, for oral use (Addyi) submitted by Sprout Pharmaceuticals (Sprout) under cover of Form FDA 2253. This radio ad makes false or misleading claims about the risks associated with Addyi and omits other material facts. Thus, the radio ad misbrands Addyi within the meaning of the Federal Food, Drug and Cosmetic Act (FD&C Act) and makes its distribution violative. 21 U.S.C. 352(n); 321(n); 331(a). See 21 CFR 202.1(e)(3)(ii) and (iii); (e)(5). These violations are concerning from a public health perspective because they create a misleading impression about the safety and effectiveness of Addyi, a drug that bears a Boxed Warning due to the risk of severe hypotension and syncope in certain settings.

### Background

Below are the indication and summary of the most serious and most common risks associated with the use of Addyi.<sup>1</sup> According to the FDA-approved product labeling (PI) (emphasis original):

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

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<sup>1</sup> This information is for background purposes only and does not necessarily represent the risk information that should be included in the promotional piece cited in this letter.

- 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.

#### Limitations of Use

- ADDYI is not indicated for the treatment of HSDD in postmenopausal women or in men.
- ADDYI is not indicated to enhance sexual performance.

The PI for Addyi contains a Boxed Warning regarding hypotension and syncope in certain settings. Addyi is contraindicated with concomitant use with moderate or strong CYP3A4 inhibitors and in patients with hepatic impairment. The PI for Addyi includes warnings and precautions regarding hypotension and syncope due to an interaction with alcohol, hypotension and syncope with CYP3A4 inhibitors, central nervous system depression, hypotension and syncope with Addyi alone, syncope and hypotension in patients with hepatic impairment and mammary tumors in female mice. Most common adverse reactions reported with Addyi were dizziness, somnolence, nausea, fatigue, insomnia and dry mouth.

#### Prior Communication

OPDP notes that our advisory comments dated August 11, 2016 to VALEANT Pharmaceuticals International (Valeant)

(b) (4)

We are concerned that, in the radio ad, Sprout is continuing promotion of Addyi in a manner that does not adequately convey the FDA-approved indication nor the important risk information for the drug.

#### **False or Misleading Risk Presentations**

Promotional materials misbrand a drug if they are false or misleading with respect to risk. The determination of whether promotional materials are misleading includes, among other things, not only representations made or suggested in promotional materials, but also failure to reveal facts material in light of the representations made or with respect to consequences that may result from the use of the drug as recommended or suggested in the materials.

The radio ad includes numerous claims and presentations regarding the benefits of using Addyi for acquired, generalized HSDD in premenopausal women. However, it completely omits all the contraindications associated with the use of Addyi.

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<sup>2</sup> We note that, at the time of the advisory comments, Sprout, the holder of NDA 022526, was a wholly-owned subsidiary of Valeant. On January 8, 2018, FDA acknowledged receipt of Sprout's correspondence notifying FDA of its change of address and contact information following divestiture from Valeant.

Furthermore, while the radio ad presents some risk information from the Boxed Warning such as, “. . . low blood pressure and fainting in certain settings . . . [,]” it omits material information pertaining to these risks. Specifically, the radio ad fails to disclose material information from the Boxed Warning that the use of Addyi and alcohol together close in time increases the risk of severe hypotension and syncope. For example, according to the Boxed Warning and the Medication Guide, patients should wait at least 2 hours after drinking 1 or 2 standard alcoholic drinks before taking ADDYI at bedtime.

Additionally, the radio ad fails to disclose material information from the Boxed Warning that the use of Addyi with certain prescription medications or in patients with liver problems increases the risk of severe hypotension and syncope.

The radio ad also omits the warning and precaution regarding central nervous system depression, and it fails to include material information that the use of ADDYI – without other concomitant medications known to cause hypotension or syncope – can cause hypotension and syncope.

By omitting risks associated with Addyi, the radio ad fails to provide material information about the consequences that may result from the use of the drug and create a misleading impression about the drug’s safety. This is particularly concerning from a public health perspective due to the serious risks associated with the drug.

### **Omission of Material Facts**

The radio ad includes the following claims:

- “1 in 10 premenopausal women suffer from frustrating low libido, also known as HSDD.”
- “Meet Addyi – the first and only FDA-approved non-hormonal pill for acquired, generalized HSDD in premenopausal women. In other words: An FDA-approved pill for women frustrated by their low libido.”
- “Ladies, add your desire back with Addyi.”

These claims create a misleading impression regarding the scope of the approved use of Addyi by omitting material information about the product’s approved indication and the limitations of its use. Specifically, the “**What is ADDYI?**” section of the Medication Guide states the following (in pertinent part, bolded emphasis in original, underlined emphasis added):

ADDYI is a prescription medicine used to treat hypoactive (low) sexual desire disorder (HSDD) in women who have not gone through menopause, who have not had problems with low sexual desire in the past, and who have low sexual desire no matter the type of sexual activity, the situation, or the sexual partner. Women with HSDD have low sexual desire that is troubling to them. Their low sexual desire is **not** due to:

- a medical or mental health problem
- problems in the relationship

- medicine or other drug use

. . .

ADDYI is not for use to improve sexual performance.

By failing to adequately communicate the indication and limitations of use associated with Addyi, the radio ad creates a misleading impression about the FDA-approved indication. This is particularly concerning given the serious risks of this product and the suggestion that Addyi is approved for all women “frustrated by their low libido” when this is not the case.

### **Conclusion and Requested Action**

For the reasons discussed above, the radio ad misbrands Addyi within the meaning of the FD&C Act and makes its distribution violative. 21 U.S.C. 352(n); 321(n); 331(a). See 21 CFR 202.1(e)(3)(ii) and (iii); (e)(5).

OPDP requests that Sprout immediately cease misbranding Addyi and/or cease introducing the misbranded drug into interstate commerce. Please submit a written response to this letter on or before September 15, 2020, stating whether you intend to comply with this request, listing all promotional materials (with the 2253 submission date) for Addyi that contain statements such as those described above, and explaining your plan for discontinuing use of such materials, or, in the alternative, for ceasing distribution of Addyi. Because the violations described above are serious, we request, further, that your submission include a comprehensive plan of action to disseminate truthful, non-misleading, and complete corrective messages about the issues discussed in this letter to the audience that received the violative promotional material. In order to clearly identify the violative promotional piece and/or activity and focus on the corrective messages, OPDP recommends that corrective piece include a description of the violative promotional piece and/or activity, include a summary of the violative messages, provide information to correct each of the violative message, and be free of promotional claims and presentations. To the extent possible, corrective messaging should be distributed using the same media, and generally for the same duration of time and with the same frequency that the violative promotional material was disseminated. If you believe that your product is not in violation of the FD&C Act, include your reasoning and any supporting information for our consideration.

Please direct your response to the undersigned at the **Food and Drug Administration, Center for Drug Evaluation and Research, Office of Prescription Drug Promotion, 5901-B Amundson Avenue, Beltsville, Maryland 20705-1266**. A courtesy copy can be sent by facsimile to (301) 847-8444. To ensure timely delivery of your submissions, please use the full address above and include a prominent directional notation (e.g. a sticker) to indicate that the submission is intended for OPDP. Please refer to MA 241 in addition to the NDA number in all future correspondence relating to this particular matter. All correspondence should include a subject line that clearly identifies the submission as a Response to Warning Letter.

The violations discussed in this letter do not necessarily constitute an exhaustive list. It is your responsibility to ensure that your promotional materials for Addyi comply with each applicable requirement of the FD&C Act and FDA implementing regulations.

Failure to correct the violations discussed above may result in FDA regulatory action, including seizure or injunction, without further notice.

Sincerely,

*{See appended electronic signature page}*

Robert Dean  
Director  
Division of Advertising & Promotion Review 2  
Office of Prescription Drug Promotion

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**This is a representation of an electronic record that was signed electronically. Following this are manifestations of any and all electronic signatures for this electronic record.**  
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/s/  
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