Pharmacy Policy Bulletin

Title: Hypoactive Sexual Desire Disorder (HSDD) Agents

Policy #: Rx.01.177

Application of pharmacy policy is determined by benefits and contracts. Benefits may vary based on product line, group, or contract. Some medications may be subject to precertification, age, quantity, or formulary restrictions (ie limits on non-preferred drugs). Individual member benefits must be verified.

This pharmacy policy document describes the status of pharmaceutical information and/or technology at the time the document was developed. Since that time, new information relating to drug efficacy, interactions, contraindications, dosage, administration routes, safety, or FDA approval may have changed. This Pharmacy Policy will be regularly updated as scientific and medical literature becomes available. This information may include new FDA-approved indications, withdrawals, or other FDA alerts. This type of information is relevant not only when considering whether this policy should be updated, but also when applying it to current requests for coverage.

Members are advised to use participating pharmacies in order to receive the highest level of benefits.

Intent:

The intent of this policy is to communicate the medical necessity criteria for **flibanserin (Addyi®)** and **bremelanotide (Vyleesi™)** as provided under the member's prescription drug benefit.

Description:

Flibanserin is a serotonin 5-HT1A agonist and 5-HT2A antagonist. Flibanserin also has moderate antagonist activities at the 5-HT2B, 5-HT2C, and dopamine D4 receptors. The exact mechanism of flibanserin in the treatment of premenopausal women with hypoactive sexual desire disorder (HSDD) is unknown. Flibanserin was originally studied for depression, but failed to demonstrate efficacy in that area. It was during these clinical trials that researchers recognized the potential benefit of flibanserin for generalized HSDD and continued clinical development in that direction. Although flibanserin has demonstrated improvement in treating HSDD, the overall results of the clinical trials were numerically small, and continued assessment of long-term benefits and risks associated with flibanserin is still warranted.

Bremelanotide is a melanocortin receptor (MCR) agonist that non-selectively activates several receptor subtypes with the following order of potency: MC1R, MC4R, MC3R, MC5R, MC2R. At therapeutic dose levels, binding to MC1R and MC4R is most relevant. Neurons expressing MC4R are present in many areas of the central nervous system (CNS). The mechanism by which VYLEESI improves HSDD in women is unknown. The MC1R is expressed on melanocytes; binding at this receptor leads to melanin expression and increased pigmentation.

HSDD is a disease that represents a subset of symptoms associated with “desire" within the overarching diagnosis of sexual dysfunction. HSDD was a stand-alone diagnosis Diagnostic and Statistical Manual of Mental Disorders (DSM) IV. In DSM V, HSDD is now incorporated into female sexual interest/ arousal disorder (FSIAD). FSIAD is defined as a lack of, or significantly reduced, sexual interest or arousal for 6 months or greater when a patient meets 3 of the 6 diagnostic criteria.

Flibanserin and bremelanotide are indicated for the treatment of premenopausal women with acquired, generalized 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.

Limitations of Use

- Flibanserin and bremelanotide are not indicated for the treatment of HSDD in postmenopausal women or in men

- Flibanserin and bremelanotide are not indicated to enhance sexual performance

Policy:

Hypoactive sexual desire disorder

INITIAL CRITERIA Flibanserin (Addyi®) is approved when ALL of the following are met:

1. Diagnosis of one of the following:
    a. Acquired, generalized hypoactive sexual desire disorder (HSDD); OR
    b. Female sexual interest/arousal disorder; AND
2. Member is premenopausal; and
3. Symptoms of HSDD have persisted for at least 6 months

Initial authorization duration: 3 months

RE-AUTHORIZATION CRITERIA Flibanserin (Addyi®) is re-approved when ALL of the following are met:

1. Positive clinical response to flibanserin (Addyi®) therapy; and
2. Member continues to be premenopausal

Re-authorization duration: 12 months

INITIAL CRITERIA Bremelanotide (Vyleesi™) is approved when ALL of the following are met:

1. Diagnosis of one of the following:
    a. Acquired, generalized hypoactive sexual desire disorder (HSDD); or
    b. Female sexual interest/arousal disorder; AND
2. Symptoms of HSDD or female sexual interest/arousal disorder have persisted for at least 6 months; and
3. Member is premenopausal; and
4. Member does not have either of the following:
    a. Uncontrolled hypertension; or
    b. Known cardiovascular disease

Initial authorization duration: 3 months

REAUTHORIZATION CRITERIA Bremelanotide (Vyleesi™) is re-approved when ALL of the following are met:

1. Documentation of positive clinical response to Vyleesi™ therapy; and
2. Member continues to be premenopausal; and
3. Member does not have either of the following:
    a. Uncontrolled hypertension; or
    b. Known cardiovascular disease

Reauthorization duration: 12 months

Black Box Warning as shown in the drug Prescribing Information:

Addyi®:

WARNING: HYPOTENSION AND SYNCOPE IN CERTAIN SETTINGS

Interaction with Alcohol

The 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.

Contraindicated with Strong or Moderate CYP3A4 Inhibitors

The concomitant use of ADDYI and moderate or strong CYP3A4 inhibitors increases flibanserin concentrations, which can cause severe hypotension and syncope. Therefore, the use of moderate or strong CYP3A4 inhibitors is contraindicated in patients taking ADDYI.

Contraindicated in Patients with Hepatic Impairment

The use of ADDYI in patients with hepatic impairment increases flibanserin concentrations, which can cause severe hypotension and syncope. Therefore, ADDYI is contraindicated in patients with hepatic impairment

Guidelines:

Refer to the specific manufacturer's prescribing information for administration and dosage details and any applicable Black Box warnings.

BENEFIT APPLICATION

Subject to the terms and conditions of the applicable benefit contract, the applicable drug(s) identified in this policy is (are) covered under the prescription drug benefits of the Company's products when the medical necessity criteria listed in this pharmacy policy are met. Any services that are experimental/investigational or cosmetic are benefit contract exclusions for all products of the Company.

References:

Addyi® (flibanserin) [package insert]. Raleigh, NC. Sprout Pharmaceuticals. October 2019. Available at: mk0speedyaddyip6a9xx.kinstacdn.com/wp-content/uploads/2021/03/Full-Prescribing-Information.pdf. Accessed January 13, 2022.

Vyleesi™ (bremelanotide) [package insert]. Waltham, MA. AMAG Pharmaceuticals, Inc. June 2019. Available at https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/210557s000lbl.pdf. Accessed January 13, 2022.

American Psychiatric Association. Diagnostic and Statistical manual of Mental Disorders, 5th edition (DSM V). Washington, DC: In Section II, Sexual Dysfunctions, Female Sexual Interest/Arousal Disorder. Accessed January 13, 2022.

Flibanserin. Micromedex. Available at: http://www.micromedexsolutions.com/. Accessed January 13, 2022.

Applicable Drugs:

Inclusion of a drug in this table does not imply coverage. Eligibility, benefits, limitations, exclusions, precertification/referral requirements, provider contracts, and Company policies apply.

Brand Name	Generic Name
Addyi®	flibanserin
Vyleesi™	bremelanotide

Cross References:

Off Label Use Rx.01.33

Quantity Level Limits for Pharmaceuticals Covered Under the Pharmacy Benefit Rx.01.76

Policy Version Number:	9.00
P&T Approval Date:	December 09, 2021
Policy Effective Date:	April 01, 2022
Next Required Review Date:	December 09, 2022

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