Clinical Policy: Flibanserin (Addyi)

Reference Number: CP.PHAR.446
Effective Date: 03.01.20
Last Review Date: 11.21
Line of Business: Commercial, HIM, Medicaid

Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description

Flibanserin (Addyi®) is a serotonin 5-HT1A receptor agonist and a 5-HT2A receptor antagonist.

FDA Approved Indication(s)

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.

Limitation(s) 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.

Policy/Criteria

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with Centene Corporation® that Addyi is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Hypoactive Sexual Desire Disorder (must meet all)**:**

1. Diagnosis of HSDD in premenopausal women;
2. Age ≥ 18 years;
3. Failure of a 3-month trial of bupropion at up to maximally studied effective doses (*see Appendix B*), unless contraindicated or clinically significant adverse effects are experienced;
4. HSDD symptoms have persisted for a minimum of 6 months;
5. Addyi is not prescribed concurrently with Vyleesi;
6. Dose does not exceed 100 mg (1 tablet) per day.

Approval duration: 3 months

B. Other diagnoses/indications

1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is

NOT authorized): CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy

A. Hypoactive Sexual Desire Disorder (must meet all)**:**

1. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
2. Member is responding positively to therapy;
3. If request is for a dose increase, new dose does not exceed 100 mg (1 tablet) per day.

Approval duration:
HIM/Medicaid – 12 months
Commercial – Length of Benefit

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy.
   Approval duration: Duration of request or 12 months (whichever is less); or
2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key
DSM: Diagnostic and Statistical Manual of Mental Disorders
FDA: Food and Drug Administration
HSDD: hypoactive sexual desire disorder

Appendix B: Therapeutic Alternatives
This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
bupropion (Aplenzin®, Budeprion SR® , Budeprion XL®, Forfivo XL®, Wellbutrin®,	Varies	Immediate-release: 450 mg/day (300 mg/day if pediatric) Sustained-release: 400 mg/day Extended-release (HCl): 450 mg/day Extended-release (HBr): 522 mg/day

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Wellbutrin SR®, Wellbutrin XL®)		

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s):
  - Moderate or strong CYP450 3A4 inhibitors
  - Hepatic impairment
- Boxed warning(s): hypotension and syncope in certain settings (e.g., alcohol with Addyi)

Appendix D: General Information

- HSDD is characterized by a deficiency or absence of sexual fantasies and desire for sexual activity which causes marked distress or interpersonal difficulty, and is not better accounted for by another psychiatric disorder or due exclusively to the direct physiological effects of a substance or to the direct physiological effects of another medical condition. HSDD does not encompass normal (e.g., daily or weekly) fluctuations in levels of desire.
- There is currently no published data demonstrating the efficacy of Addyi in the treatment of HSDD in postmenopausal women or in men.
- Treatment should be discontinued after 8 weeks if there is no improvement in symptoms.
- In the DSM-5, female hypoactive sexual desire disorder was merged with female arousal dysfunction and is now reclassified as one disorder: female sexual interest/arousal disorder.
- All of the DSM-5 sexual dysfunctions (except substance-/medication-induced sexual dysfunction) now require a minimum duration of approximately 6 months and more precise severity criteria to improve precision regarding duration and severity criteria and to reduce the likelihood of over-diagnosis. These changes provide useful thresholds for making a diagnosis and distinguish transient sexual difficulties from more persistent sexual dysfunction.
- Two randomized trials (Segraves RT, et al. and Safarinejad MR, et al.) of premenopausal women with HSDD and without underlying depression reported increased sexual pleasure, desire, arousal, and orgasm with bupropion compared with placebo.

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
HSDD	100 mg PO QD at bedtime	100 mg/day

VI. Product Availability

Tablets: 100 mg

VII. References

1. Addyi Prescribing Information. Raleigh, NC: Sprout Pharmaceuticals, Inc; October 2019. Available at: www.addyi.com. Accessed November 12, 2020.

2. American Psychiatric Association. Highlights of changes from DSM-IV-TR to DSM-5. Available at: https://www.psychiatry.org/File%20Library/Psychiatrists/Practice/DSM/APA_DSM_Changes_from_DSM-IV-TR_-to_DSM-5.pdf. Accessed August 8, 2019.
3. Segraves RT, Clayton A, Croft H, et al. Bupropion sustained release for the treatment of hypoactive sexual desire disorder in premenopausal women. J Clin Psychopharmacol. 2004;24(3):339.
4. Safarinejad MR, Hosseini SY, Asgari MA, et al. A randomized, double-blind, placebo-controlled study of the efficacy and safety of bupropion for treating hypoactive sexual desire disorder in ovulating women. BJU Int. 2010 Sep;106(6):832-9.
5. American College of Obstetricians and Gynecologists' Committee on Practice Bulletins - Gynecology. Female Sexual Dysfunction: ACOG Practice Bulletin Clinical Management Guidelines for Obstetrician-Gynecologists, Number 213. Obstet Gynecol. 2019;134 (1):e1-e18.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created; Policy adopted from CP.CPA.214; retired CP.CPA.214. Added Medicaid line of business; added 3-month trial and failure of bupropion; added Vyleesi is not prescribed concurrently with Addyi; references reviewed and updated.	11.19.19	02.20
1Q 2021 annual review: added HIM line of business; revised Medicaid line of business continued therapy approval duration from length of benefit to 12 months; updated reference for HIM off-label use to HIM.PA.154 (replaces HIM.PHAR.21); references reviewed and updated.	11.12.20	02.21
Clarified language of bupropion trial requirement from "up to maximally indicated doses" to "up to maximally studied effective doses."	03.18.21	
4Q 2021 annual review: Added criterion for symptom persistence of 6 months per DSM-5 diagnostic criteria.	08.15.21	11.21

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

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Note:
For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

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