Drug Coverage Policy

Effective Date.....4/15/2025
Coverage Policy Number.....IP0116
Policy Title.....Addyi

Hypoactive Sexual Desire Disorder – Addyi

- Addyi™ (flibanserin tablets - Sprout)

INSTRUCTIONS FOR USE
The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Each coverage request should be reviewed on its own merits. Medical directors are expected to exercise clinical judgment and have discretion in making individual coverage determinations. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

Cigna Healthcare Coverage Policy

OVERVIEW
Addyi is indicated for the **treatment of premenopausal women with acquired, generalized hypoactive sexual desire disorder (HSDD)** that is 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.[1]

Addyi is not indicated for the treatment of HSDD in postmenopausal women or in men. It is also not indicated to enhance sexual performance. The prescribing information notes that Addyi should be discontinued after 8 weeks if the patient does not report any improvement in HSDD symptoms.[1] In the Addyi clinical studies, one of the coprimary efficacy endpoints was assessed by the median increase in the number of satisfying sexual events standardized over a 28-day period.

Safety
Addyi contains a Boxed Warning regarding the use of alcohol and the increase in risk of severe hypotension and syncope.[1] Patients should be counseled to wait at least two hours after consuming one or two standard alcoholic drinks before taking Addyi or skip the dose if they have consumed three or more standard alcoholic drinks that evening.

Guidelines
The American College of Obstetricians and Gynecologists guideline on Female Sexual Dysfunction (2019) notes the importance of recognizing if the loss of sexual interest is due to a co-morbid or undiagnosed condition, or medication.[4] The guidelines note that Addyi was approved in 2015 by the FDA to treatment hypoactive sexual desire disorder in premenopausal women without depression. Addyi is noted as a treatment option for HSDD in premenopausal women without depression who are appropriately counseled about the risk of alcohol use during treatment.[4] The guidelines also discuss that systemic review and meta-analysis of existing studies with Addyi show that although the studies were randomized, their overall quality of evidence for efficacy and safety was very low.

Medical Necessity Criteria

Addyi is considered medically necessary when the following are met:

FDA-Approved Indication

1. **Hypoactive Sexual Desire Disorder (HSDD)/Female Sexual Interest/Arousal Disorder (FSIAD).** Approve for the duration noted if the patient meets ONE of the following (A or B):
   - **A)** Initial Therapy. Approve for 8 weeks if the patient meets the following (i, ii, iii, iv, v, and vi):
     - **i.** Patient is premenopausal; AND
     - **ii.** Patient's symptoms of HSDD/FSIAD have persisted for a minimum of 6 months; AND
     - **iii.** Patient has had normal sexual desire in the past, prior to the diagnosis of HSDD/FSIAD; AND
     - **iv.** Patient does **not** have a diagnosis of depression; AND
     - **v.** Other known causes of HSDD/FSIAD, such as co-existing medical or psychiatric conditions, problems within a relationship, effects of medications (e.g., antidepressants), or drug abuse have been ruled out by the prescriber; AND
     - **vi.** The prescriber has counseled the patient regarding the interaction with alcohol and Addyi, and the increased risk of hypotension and syncope.
   - **B)** Patient is Currently Receiving Addyi. Approve for 6 months if the patient meets the following (i, ii, and iii):
     - **i.** Patient is premenopausal; AND
     - **ii.** The prescriber confirms that since initiating Addyi therapy, the patient reports a significant improvement in sexual desire and/or a decrease in sexual distress; AND
     - **iii.** Patient has not reported any serious or concerning adverse events (e.g., hypotension, syncope, dizziness) while taking Addyi.

When coverage is available and medically necessary, the dosage, frequency, duration of therapy, and site of care should be reasonable, clinically appropriate, and supported by evidence-based literature and adjusted based upon severity, alternative available treatments, and previous response to therapy.

Receipt of sample product does not satisfy any criteria requirements for coverage.

Conditions Not Covered

Any other use is considered experimental, investigational, or unproven, including the following (this list may not be all inclusive; criteria will be updated as new published data are available):

1. **<u>Postmenopausal</u> Patients.** Two published Phase III trials assessed the efficacy of Addyi in postmenopausal women with HSDD.[2,3] In the SNOWDROP trial though there was statistical significance in the primary endpoints (number of satisfying sexual events over 28 days and increase in desire score), the treatment difference between Addyi and placebo was very minimal.[2] The PLUMERIA study was discontinued early by the study sponsor for commercial reasons; however, published data are available for up to Week 16.[3] The improvement from baseline to Week 16 in the Female Sexual Function Index desire domain was significantly greater with Addyi compared with placebo, but the other co-primary endpoint of sexually satisfying events was not significantly different between Addyi and placebo. Addyi is currently not approved for use in postmenopausal women with HSDD/FSIAD symptoms.

References

1. Addyi™ tablets [prescribing information]. Raleigh, NC: Sprout; September 2021.
2. Simon JA, Kingsberg SA, Shumel B, et al. Efficacy and safety of flibanserin in postmenopausal women with hypoactive sexual desire disorder: results of the SNOWDROP trial. *Menopause.* 2014;21:633-640.
3. Portman DJ, Brown L, Yuan J, et al. Flibanserin in postmenopausal women with hypoactive sexual desire disorder: results of the PLUMERIA study. *J Sex Med.* 2017;14:834-842.
4. Female Sexual Dysfunction. *ACOG Practice Bulletin.* Clinical Management Guidelines for Obstetrician-Gynecologists. Number 213; July 2019. Available at: https://www.acog.org/. Accessed on January 16, 2025.

Revision Details

Type of Revision	Summary of Changes	Date
Annual Revision	**Updated** policy title, was previously Flibanserin. **Hypoactive Sexual Desire Disorder (HSDD)/Female Sexual Interest/Arousal Disorder (FSIAD):** Removed "Female at birth;" updated "Not currently being treated for active depression" to "Patient does not have a diagnosis of depression;" added clarification to patient counseling requirement to specifically address the increased risk of hypotension and syncope with Addyi and alcohol. Added to Patient is Currently Receiving Addyi criteria the following: "Patient has not reported any serious or concerning adverse events (e.g., hypotension, syncope, dizziness) while taking Addyi."	7/15/2024
Annual Revision	No criteria changes.	4/15/2025

The policy effective date is in force until updated or retired.