Clinical Policy: Bremelanotide (Vyleesi)

Reference Number: CP.PHAR.434
Effective Date: 08.07.19
Last Review Date: 11.25
Line of Business*: Commercial, Medicaid

Revision Log

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

Description

Bremelanotide (Vyleesi®) is a melanocortin receptor agonist.

**For Health Insurance Marketplace (HIM), drugs in this class are excluded from the benefit per the Evidence of Coverage, unless specifically listed on the formulary.*

FDA Approved Indication(s)

Vyleesi 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 NOT due to:

- A co-existing medical or psychiatric condition,
- Problems with the relationship, or
- The effects of a medication or drug substance.

Limitation(s) of use:

- Vyleesi is not indicated for treatment of HSDD in postmenopausal women or in men.
- Vyleesi 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 Vyleesi 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. HSDD is not attributed to any of the following (a, b, or c):
   a. A co-existing medical or psychiatric condition;
   b. Problems within the relationship;
   c. Effects of a medication or other drug substance;

6. Vyleesi is not prescribed concurrently with Addyi®;
7. Dose does not exceed both of the following (a and b):
   a. 1.75 mg (1 injection) per day;
   b. 8 doses per month.

Approval duration: 3 months

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

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial and CP.PMN.53 for Medicaid.

II. Continued Therapy

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

1. Member meets one of the following (a or b):
   a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
   b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B*);
2. Member is responding positively to therapy;
3. If request is for a dose increase, new dose does not exceed both of the following (a and b):
   a. 1.75 mg (1 injection) per day;
   b. 8 doses per month.

Approval duration:
Medicaid – 12 months
Commercial – 6 months or duration of request, whichever is less

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

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial and CP.PMN.255 for Medicaid; or

b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial and CP.PMN.16 for Medicaid; or

2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial 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 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®, Wellbutrin SR®, Wellbutrin XL®)	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

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): uncontrolled hypertension or known cardiovascular disease
- Boxed warning(s): none reported

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 Vyleesi 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.
- Examples of co-existing psychiatric conditions include a history of major depressive disorder within the previous six months, a current diagnosis of mild to severe depression using a validated depression scale.
- Examples of co-existing medical condition that could contribute to sexual dysfunction include pelvic inflammatory disease, cervicitis, interstitial cystitis, vulvodynia, significant vaginal atrophy, sexual pain.
- Examples of medications associated with low sexual desire among women:
    - Cardiac and antihypertensive: lipid-lowering medications, beta-blockers, clonidine, digitalis, methyldopa, spironolactone
    - Hormonal: androgen antagonists, gonadotropin-releasing hormone agonists and analogs, oral contraceptives, tamoxifen
    - Opioids: any opioids used chronically, methadone
    - Psychotropic: antipsychotics, barbiturates, benzodiazepines, lithium, monoamine oxidase inhibitors, selective serotonin reuptake inhibitors, serotonin-norepinephrine reuptake inhibitors, tricyclic antidepressants
    - Other: aromatase inhibitors, chemotherapy, histamine 2 receptor blockers, nonsteroidal anti-inflammatory agents, ketoconazole

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
HSDD	1.75 mg SC in abdomen or thigh, as needed, at least 45 minutes before anticipated sexual activity	1.75 mg/day (max 8 doses/month)

VI. Product Availability

Single-dose prefilled autoinjector: 1.75 mg/0.3 mL

VII. References

1. Vyleesi Prescribing Information. Cranbury, NJ: Palatin Technologies, Inc.; March 2024. Available at: https://vyleesi.com. Accessed July 17, 2025.

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 4, 2025.
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.
6. Pachano Pesantez GS and Clayton AH. Treatment of hypoactive sexual disorder among women: General considerations and pharmacological options. Focus 2021; 19(1):39-45.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
4Q 2021 annual review: added criterion for symptom persistence of 6 months per DSM-5 diagnostic criteria; removed HIM line of business from continued therapy approval duration; references reviewed and updated.	08.01.21	11.21
Revised continued therapy approval duration for Commercial line of business from length of benefit to 12 months or duration of request, whichever is less	10.18.21	02.22
4Q 2022 annual review: added to initial criteria that HSDD is not due to a co-existing medical or psychiatric condition, problems with the relationship, or the effects of a medication or drug substance per PI; appendix D updated with examples of co-existing medical or psychiatric conditions and medications associated with low sexual desire; references reviewed and updated. Template changes applied to other diagnoses/indications and continued therapy section.	08.11.22	11.22
4Q 2023 annual review: for Commercial line of business revised continued therapy from 12 months to 6 months or duration of request, whichever is less; references reviewed and updated.	06.30.23	11.23
4Q 2024 annual review: no significant changes; references reviewed and updated.	07.31.24	11.24
4Q 2025 annual review: no significant changes; references reviewed and updated.	08.04.25	11.25

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.

This clinical policy does not constitute medical advice, medical treatment, or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

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.