Clinical Policy: Desmopressin Acetate (DDAVP, Stimate, Nocdurna)

Reference Number: CP.PHAR.214
Effective Date: 05.01.16
Last Review Date: 02.25
Line of Business: Commercial, HIM, Medicaid

Coding Implications
Revision Log

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

Description

Desmopressin acetate (DDAVP®, Stimate®, Nocdurna®) is a synthetic vasopressin analog.

FDA Approved Indication(s)

DDAVP and Stimate are indicated for the treatment of patients with:

- Mild to moderate classic von Willebrand's disease (VWD; type I) with factor VIII (FVIII) levels greater than 5%
- Hemophilia A with FVIII coagulant activity levels greater than 5% *without FVIII antibodies (DDAVP only)*

DDAVP is also indicated for the management of central (cranial) diabetes insipidus and for the management of the temporary polyuria and polydipsia following head trauma or surgery in the pituitary region.

Nocdurna is indicated for the treatment of nocturia due to nocturnal polyuria in adults who awaken at least 2 times per night to void.

Limitation(s) of use:

- Stimate is not indicated for the treatment of hemophilia A with FVIII coagulant activity levels equal to or less than 5%, or for the treatment of hemophilia B, or in patients who have FVIII antibodies.
- DDAVP and Stimate are not indicated for the treatment of severe classic VWD (type I) and when there is evidence of an abnormal molecular form of FVIII antigen.
- DDAVP is ineffective and not indicated for the treatment of nephrogenic diabetes insipidus.

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 DDAVP injection/generic, Stimate/generic, and Nocdurna are **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Polyuria and Central Diabetes Insipidus (must meet all)**:**

1. Request is for DDAVP injection;

2. Diagnosis of one of the following (a or b):
   a. Central (cranial) diabetes insipidus (referred to as arginine vasopressin deficiency);
   b. Temporary polyuria and polydipsia following head trauma or surgery in the pituitary region;
3. Prescribed by or in consultation with an endocrinologist;
4. Age ≥ 12 years;
5. Failure of desmopressin tablets, unless contraindicated, clinically significant adverse effects are experienced, or documentation supports inability to swallow tablets;
6. For brand DDAVP injection requests, member must use desmopressin injection, unless contraindicated or clinically significant adverse effects are experienced;
7. Dose does not exceed 4 mcg per day.

Approval duration:
Medicaid/HIM – 6 months
Commercial – 6 months or to member's renewal date, whichever is longer

B. Congenital Hemophilia A (must meet all)**:**
1. Diagnosis of congenital hemophilia A (FVIII deficiency);
2. Prescribed by or in consultation with a hematologist;
3. Age ≥ 3 months;
4. Request is for DDAVP injection or Stimate for one of the following uses (a, b, or c):
   a. Control and prevention of bleeding episodes;
   b. Perioperative management;
   c. Routine prophylaxis to prevent or reduce the frequency of bleeding episodes;
5. FVIII coagulant activity levels are > 5%;
6. Member does not have FVIII antibodies;
7. For brand DDAVP injection requests, member must use desmopressin injection, unless contraindicated or clinically significant adverse effects are experienced;
8. Dose does not exceed any of the following (a or b):
   a. DDAVP injection: 0.3 mcg/kg per dose;
   b. Stimate: 300 mcg per day.

Approval duration:
Medicaid/HIM – 6 months (*12 months for prophylaxis for HIM Texas*)
Commercial – DDAVP injection: 6 months or to member's renewal date, whichever is longer; Stimate: 12 months

C. Von Willebrand Disease (must meet all)**:**
1. Diagnosis of VWD type 1 or type 2;
2. Prescribed by or in consultation with a hematologist;
3. Age ≥ 3 months;
4. Request is for DDAVP injection or Stimate for one of the following uses (a, b, or c):
   a. Control and prevention of bleeding episodes;
   b. Perioperative management;
   c. Routine prophylaxis to prevent or reduce the frequency of bleeding episodes;
5. FVIII coagulant activity levels are > 5%;

6. For brand DDAVP injection requests, member must use desmopressin injection, unless contraindicated or clinically significant adverse effects are experienced;
7. Dose does not exceed any of the following (a or b):
   a. DDAVP injection: 0.3 mcg/kg per dose;
   b. Stimate: 300 mcg per day.

Approval duration:
Medicaid/HIM – 6 months (*12 months for prophylaxis for HIM Texas*)
Commercial – DDAVP injection: 6 months or to member's renewal date, whichever is longer; Stimate: 12 months

D. Nocturia (must meet all)**:**
1. Diagnosis of nocturia due to nocturnal polyuria;
2. Age ≥ 18 years;
3. Request is for Nocdurna;
4. Dose does not exceed 1 tablet per day and one of the following (a or b):
   a. 27.7 mcg for women;
   b. 55.3 mcg for men.

Approval duration: 12 months

E. 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, HIM.PA.33 for health insurance marketplace, 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, HIM.PA.103 for health insurance marketplace, 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, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy

A. All Indications in Section I (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. For brand DDAVP injection requests, member must use desmopressin injection, unless contraindicated or clinically significant adverse effects are experienced;
4. If request is for a dose increase, new dose does not exceed any of the following (a, b, or c):
   a. DDAVP injection: 4 mcg per day for polyuria or diabetes insipidus and 0.3 mcg/kg per dose for hemophilia A or VWD;
   b. Stimate: 300 mcg per day;
   c. Nocdurna: 1 tablet per day and one of the following (i or ii):
      i. 27.7 mcg for women;
      ii. 55.3 mcg for men.

Approval duration:
Medicaid/HIM – 12 months
Commercial – DDAVP injection: 6 months or to member's renewal date, whichever is longer; Stimate/Nocdurna: 12 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, HIM.PA.33 for health insurance marketplace, 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, HIM.PA.103 for health insurance marketplace, 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, 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

DDAVP: 1-deamino-8-D-arginine vasopressin
eGFR: estimated glomerular filtration rate
FDA: Food and Drug Administration
FVIII: factor VIII
SIADH: syndrome of inappropriate antidiuretic hormone
VWD: von Willebrand disease

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
desmopressin acetate oral tablets (DDAVP®)	**Polyuria and Central Diabetes Insipidus** 0.05 mg PO BID, titrated to a maintenance dose in the range of 0.1-1.2 mg divided into 2-3 daily doses as needed to obtain adequate antidiuresis	1.2 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):
  - Stimate: none reported
  - DDAVP injection, Nocdurna: hyponatremia or a history of hyponatremia; polydipsia; concomitant use with loop diuretics or systemic/inhaled glucocorticoids; renal impairment with an eGFR below 50 mL/min/1.73 m^2; SIADH secretion; during illnesses that can cause fluid or electrolyte imbalance; heart failure; uncontrolled hypertension
  - DDAVP injection: hypersensitivity to desmopressin acetate or to any of the components of DDAVP Injection
- Boxed warning(s):
  - Stimate: none reported
  - DDAVP injection, Nocdurna: hyponatremia

Appendix D: General Information

- The American Urology Association defines nocturnal polyuria as the production of greater than 20 to 33% of total 24-hour urine output during the period of sleep, which is age-dependent with 20% for younger individuals and 33% for elderly individuals.
- In 2022, the Endocrine Society along with various international endocrine societies proposed to change the name of this disorder from central diabetes insipidus to arginine vasopressin deficiency.
- Stimate nasal spray is still listed as affected by a shortage due to packaging issues as of November 1, 2024. Ferring has not estimated a release date for Stimate. A desmopressin acetate nasal spray of the same strength (1.5 mg/mL) is currently available.

V. Dosage and Administration

Drug Name	Indication	Dosing Regimen	Maximum Dose
Desmopressin injection (DDAVP)	Central diabetes insipidus	2 to 4 mcg IV or SC daily, as one or two divided doses	4 mcg/day
	Hemophilia A, VWD	0.3 mcg/kg IV or SC as needed	0.3 mcg/kg/dose

Drug Name	Indication	Dosing Regimen	Maximum Dose
Desmopressin nasal spray (Stimate)	Hemophilia A, VWD	One spray per nostril	300 mcg/dose
Desmopressin sublingual tablet (Nocdurna)	Nocturnal polyuria	Women: 27.7 mcg PO QD one hour before bedtime Men: 55.3 mcg PO QD one hour before bedtime	Women: 27.7 mcg/day; Men: 55.3 mcg/day

VI. Product Availability

Drug Name	Availability
Desmopressin injection (DDAVP)	Single-dose ampule: 4 mcg/mL (1 mL) Multi-dose vial: 4 mcg/mL (10 mL)
Desmopressin nasal spray (Stimate)	Bottle with spray pump: 25 sprays of 150 mcg (2.5 mL)
Desmopressin sublingual tablet (Nocdurna)	Sublingual tablets: 27.7 mcg, 55.3 mcg

VII. References

1. DDAVP Injection Prescribing Information. Parsippany, NJ: Ferring Pharmaceuticals; September 2022. Available at: https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=651f6fee-a2c7-431b-8d5d-58b156c72244. Accessed November 1, 2024.
2. Nocdurna Prescribing Information. Parsippany, NJ: Ferring Pharmaceuticals; November 2020. Available at: www.nocdurna.com. Accessed November 1, 2024.
3. Stimate Prescribing Information. King of Prussia, PA: CSL Behring LLC; June 2013. Available at: https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=30d4c387-b99c-49f8-a8bd-de23fdafb739. Accessed November 1, 2024.
4. Srivastava A, Santagostino E, Dougall A, et al. WFH Guidelines for the Management of Hemophilia, 3rd edition. *Haemophilia*. 2020;26 Suppl 6:1-158.
5. Medical and Scientific Advisory Council (MASAC) of the National Bleeding Disorders Foundation (formerly National Hemophilia Foundation): Database of treatment guidelines. Available at: www.hemophilia.org/healthcare-professionals/guidelines-on-care/masac-documents. Accessed November 18, 2024.
6. Van Kerrebroeck P, Abrams P, Chaikin D et al. The standardization of terminology in nocturia: Report from the standardization sub-committee of the International Continence Society. Neurourol Urodyn 2002; 21: 179.
7. Tomkins M, Lawless S, Martin-Grace J, et al. Diagnosis and management of central diabetes insipidus in adults. *J Clin Endocrinol Metab*. 2022;107(10):2701-2715.
8. Arima H, Cheetham T, Christ-Crain M, et al. Changing the Name of Diabetes Insipidus: A Position Statement of the Working Group for Renaming Diabetes Insipidus. *J Clin Endocrinol Metab*. 2022;108(1):1-3.
9. Drug shortages list. American Society of Health-System Pharmacists. Available at: https://www.ashp.org/drug-shortages/current-shortages/drug-shortages-list. Accessed November 30, 2024.

Coding Implications
Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
J2597	Injection, desmopressin acetate, per 1 mcg

Reviews, Revisions, and Approvals	Date	P&T Approval Date
1Q 2021 annual review: no significant changes; removed reference to non-formulary HIM policy for Nocdurna and Noctiva requests; references to HIM.PHAR.21 revised to HIM.PA.154; references reviewed and updated.	11.04.20	02.21
1Q 2022 annual review: no significant changes; references reviewed and updated.	11.27.21	02.22
Template changes applied to other diagnoses/indications.	10.03.22	
1Q 2023 annual review: removed Noctiva from policy as it has been discontinued by manufacturer; references reviewed and updated.	11.07.22	02.23
Extended initial authorization duration for hemophilia and von Willebrand disease prophylaxis from 6 months to 12 months for HIM Texas.	08.28.23	
1Q 2024 annual review: no significant changes; added update that central diabetes insipidus is referred to as arginine vasopressin deficiency with further information in Appendix D; references reviewed and updated.	10.27.23	02.24
1Q 2025 annual review: added the generic versions of DDAVP and Stimate to the "Policy/Criteria" section to clarify that criteria are applicable to the generic versions; for brand DDAVP injection requests, added redirection to generic desmopressin injection for both initial and continued criteria; added Appendix D reference for Stimate brand shortage; references reviewed and updated.	11.01.24	02.25

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.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members, and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

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.