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

Reference Number: PA.CP.PHAR.214
Effective Date: 01/2018
Last Review Date: 01/2024

Coding Implications
Revision Log

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 PA Health & Wellness that desmopressin acetate - DDAVP injection, Stimate 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. Diagnosis of one of the following:
   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;
2. Prescribed by or in consultation with an endocrinologist;
3. Age ≥ 12 years;

4. Request is for DDAVP injection;
5. Failure of a trial of desmopressin tablets, unless contraindicated or clinically significant adverse effects are experienced, or documentation supports inability to swallow tablets;
6. Dose does not exceed 4 mcg per day.

Approval duration: 6 months

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. Does not have FVIII antibodies;
6. FVIII coagulant activity levels are >5%;
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: 6 months

C. Von Willebrand Disease (must meet all)**:**
1. Diagnosis of von Willebrand disease (VWD), Type 1 or Type 2 *(off-label)*;
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 use (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. 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: 6 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: Refer to PA.CP.PMN.53

II. Continued Approval

A. All indications listed in section I (must meet all)**:**

1. Currently receiving medication via PA Health & Wellness benefit or member has previously met all initial approval criteria or the Continuity of Care Policy (PA.LTSS.PHAR.01) applies;
2. Member is responding positively to therapy.
3. 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 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: 12 months

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

1. Currently receiving medication via PA Health & Wellness benefit and documentation supports positive response to therapy or the Continuity of Care Policy (PA.LTSS.PHAR.01) applies.

Approval duration: Duration of request or 6 months (whichever is less); or

2. Refer to PA.CP.PMN.53

III. 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.

IV. Dosage and Administration

Drug Name	Indication	Dosing Regimen	Maximum Dose
Desmopressin injection (DDAVP)	Central diabetes insipidus	2 to 4 mcg IV or SC daily, usually 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
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

V. 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

VI. 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 October 28, 2023.
2. Nocdurna Prescribing Information. Parsippany, NJ: Ferring Pharmaceuticals; November 2020. Available at: www.nocdurna.com. Accessed October 10, 2023.
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 October 10, 2023.
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 October 25, 2023.
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. 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.

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
Removed the requirement for CrCl at least 50 mL/min and serum sodium at least 35 mEq/L to adhere to the accepted approach re: inclusion of safety precautions in PA policies. References reviewed and updated.	02/2018
1Q 2019 annual review: added Noctiva; references reviewed and updated.	01/2019
1Q 2020 annual review: added Nocdurna to policy; references reviewed and updated.	01/2020
1Q 2021 annual review: references reviewed and updated.	01/2021
1Q 2022 annual review: updated product availability; references reviewed and updated.	01/2022

Reviews, Revisions, and Approvals	Date
1Q 2023 annual review: removed Noctiva from policy as it has been discontinued by manufacturer; references reviewed and updated.	01/2023
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.	01/2024