Prior Authorization Review Panel

CHC-MCO Policy Submission

A separate copy of this form must accompany each policy submitted for review.
Policies submitted without this form will not be considered for review.

Plan: PA Health & Wellness	**Submission Date: 02/01/2020**
Policy Number: PA.CP.PHAR.214	**Effective Date: 01/01/2018** **Revision Date: 01/15/2020**
Policy Name: Desmopressin Acetate (DDAVP, Stimate, Noctiva)	

Type of Submission – Check all that apply:

- ☐ **New Policy**
- ✓ **Revised Policy***
- ☐ **Annual Review - No Revisions**
- ☐ **Statewide PDL -** *Select this box when submitting policies for Statewide PDL implementation and when submitting policies for drug classes included on the Statewide PDL.*

***All revisions to the policy must be highlighted using track changes throughout the document.**

Please provide any changes or clarifying information for the policy below:

Added Nocdurna to policy; references reviewed and updated.

Name of Authorized Individual (Please type or print):	**Signature of Authorized Individual:**
Francis G. Grillo, MD	Francis Gregory Grillo M.D

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

Reference Number: PA.CP.PHAR.214
Effective Date: 01/18
Last Review Date: 01/20

Coding Implications
Revision Log

Description
Desmopressin acetate (DDAVP®, Stimate®, Noctiva™) 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 levels greater than 5%
- Hemophilia A with factor VIII coagulant activity levels greater than 5%

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 and Noctiva 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:
- DDAVP and Stimate are not indicated for the treatment of hemophilia A with factor VIII coagulant activity levels equal to or less than 5%, or for the treatment of hemophilia B, or in patients who have factor VIII 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 factor VIII antigen.
- DDAVP is ineffective for the treatment of nephrogenic diabetes insipidus.
- Noctiva has not been studied in patients less than 50 years of age.

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 Pennsylvania Health and Wellness that desmopressin acetate - DDAVP injection, is **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;
   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 (factor VIII 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 factor VIII antibodies;
6. Factor VIII coagulant activity levels are >5%;
7. Dose does not exceed the following (a or b):
   1. DDAVP injection: 0.3 mcg/kg per dose;
   2. 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. Factor VIII coagulant activity levels are >5%;
6. Dose does not exceed the following (a or b):
   1. DDAVP injection: 0.3 mcg/kg per dose;
   2. 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 or Noctiva;
4. Dose does not exceed one of the following (a or b):
   a. Nocdurna: 1 tablet per day (27.7 mcg for women, 55.3 mcg for men);
   b. Noctiva: 1.66 mcg per day (1 bottle per 30 days).

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 Pennsylvania Health and 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 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 (27.7 mcg for women, 55.3 mcg for men);
   d. Noctiva: 1.66 mcg per day (1 bottle per 30 days).

Approval duration: 6 months

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

1. Currently receiving medication via Pennsylvania Health and 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
FDA: Food and Drug Administration
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®)	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):
  - DDAVP injection: moderate to severe renal impairment (creatinine clearance < 50 mL/min), hyponatremia or a history of hyponatremia

- Stimate: none reported
- Noctiva: primary nocturnal enuresis; hyponatremia or a history of hyponatremia; polydipsia; concomitant use with loop diuretics or systemic/inhaled glucocorticoids; renal impairment with an estimated glomerular filtration rate (eGFR) below 50 mL/min/1.73 m^2; known or suspected syndrome of inappropriate antidiuretic hormone (SIADH) secretion, during illnesses that can cause fluid or electrolyte imbalance, such as gastroenteritis, salt-wasting nephropathies, or systemic infection; congestive heart failure (New York Heart Association class II to IV); uncontrolled hypertension
- 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; syndrome of inappropriate antidiuretic hormone (SIADH) secretion, during illnesses that can cause fluid or electrolyte imbalance, heart failure; uncontrolled hypertension

- Boxed warning(s):
  - DDAVP injection, Stimate: none reported
  - Nocdurna and Noctiva: 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.
- Nocturnal polyuria was defined in the Noctiva clinical trials as nighttime urine production exceeding one-third of the 24-hour urine production.
- Noctiva is contraindicated in the treatment of primary nocturnal enuresis because of reports of hyponatremic-related seizures in pediatric patients treated with other intranasal forms of desmopressin. Desmopressin acetate tablets, however, are FDA-approved for this use.

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 in 2 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

Drug Name	Indication	Dosing Regimen	Maximum Dose
Desmopressin nasal spray (Noctiva)	Nocturnal polyuria	One spray in either nostril approximately 30 minutes before bedtime; dose varies by age and hyponatremia risk: • Patients < 65 years without increased risk for hyponatremia: 1.66 mcg/spray • Patients ≥ 65 years or younger patients at risk for hyponatremia: 0.83 mcg/spray (may titrate to 1.66 mcg after at least 7 days with normal sodium levels)	1.66 mcg/day

V. Product Availability

Drug Name	Availability
Desmopressin injection (DDAVP)	Ampules: 4 mcg/mL (1 mL) Vials: 4 mcg/mL (10 mL)
Desmopressin nasal spray (Stimate)	Bottle with spray pump: 25 sprays of 150 mcg (2.5 mL)
Desmopressin nasal spray (Noctiva)	Nasal spray: 3.5 mL bottle (30 effective 0.1 mL doses of either 0.83 mcg or 1.66 mcg)

VI. References

1. DDAVP Injection Prescribing Information. Parsippany, NJ: Ferring Pharmaceuticals; August 2018. Available at: https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=651f6fee-a2c7-431b-8d5d-58b156c72244. Accessed October 29, 2019.
2. Stimate Prescribing Information. King of Prussia, PA: CSL Behring LLC; June 2013. Available at: http://labeling.cslbehring.com/PI/US/Stimate/EN/Stimate-Prescribing-Information.pdf. Accessed October 29, 2019.
3. Desmopressin tablets Prescribing Information. Parsippany, NJ: Actavis Pharmaceuticals, Inc.; September 2014. Available at: https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=43bd65ca-0b1c-42c9-bbcd-7a97d3287581. Accessed October 29, 2019.
4. Srivastava A, Brewer AK, Mauser-Bunschoten EP, et al. Guidelines for the management of hemophilia. *Haemophilia.* Jan 2013; 19(1): e1-47.
5. Medical and Scientific Advisory Council (MASAC) of the National Hemophilia Foundation (NHF): Database of treatment guidelines. Available at https://www.hemophilia.org/Researchers-Healthcare-Providers/Medical-and-Scientific-Advisory-Council-MASAC/MASAC-Recommendations. Accessed October 29, 2019.
6. Noctiva Prescribing Information. Chesterfield, MO: Avadel Specialty Pharmaceuticals, LLC; December 2017. Available at: www.noctiva.com. October 29, 2019.

7. Van Kerrebroeck P, Abrams P, Chaikin D et al. The standardisation of terminology in nocturia: Report from the standardization sub-committee of the International Continence Society. Neurourol Urodyn 2002; 21: 179.
8. Nocdurna Prescribing Information. Parsippany, NJ: Ferring Pharmaceuticals; June 2018. Available at: www.nocdurna.com. Accessed October 29, 2019.

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	Approval 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.	02/18	
1Q 2019 annual review: added Noctiva; references reviewed and updated.	01/19	
1Q 2020 annual review: added Nocdurna to policy; references reviewed and updated.	01/2020	