Clinical Policy Title:	desmopressin acetate
Policy Number:	RxA.94
Drug(s) Applied:	DDAVP®, Stimate®, Nocdurna®, Noctiva™
Original Policy Date:	02/07/2020
Last Review Date:	03/09/2021
Line of Business Policy Applies to:	All lines of business

Background

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

Dosing Information

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 Less than 50 kg: one spray in one nostril	300 mcg/dose
desmopressin sublingual tablet (Nocdurna®)	Nocturnal polyuria	Women: 27.7 mcg PO once daily one hour before bedtime	Women: 27.7 mcg/day; Men: 55.3 mcg/day

		Men: 55.3 mcg PO once daily one hour before bedtime	
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 risk for hyponatremia: 1.66 mcg/spray in either nostril • Patients ≥ 65 year or 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

Dosage Forms

- desmopressin injection (DDAVP®): Single dose ampules - 4 mcg/mL (1 mL)
  Multiple dose vials - 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
- 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)

Clinical Policy

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

I. Initial Approval Criteria

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

1. Diagnosis of one of the following (a or b):
   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 desmopressin tablets, unless contraindicated, clinically significant adverse effects are experienced, or documentation supports inability to swallow tablets;
6. Dose does not exceed 4 mcg per day.

Approval Duration

Commercial: 6 months

Medicaid: 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. Factor VIII coagulant activity levels are > 5%; 6. Member does not have factor VIII antibodies; 7. Dose does not exceed (a or b):
   a. DDAVP® injection: 0.3 mcg/kg per dose;
   b. Stimate®: 300 mcg per day.

Approval Duration
Commercial: DDAVP® Injection: 6 months; Stimate®: 12 months
Medicaid: DDAVP® Injection: 6 months; 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. Factor VIII coagulant activity levels are > 5%;
6. Dose does not exceed (a or b):
   a. DDAVP® injection: 0.3 mcg/kg per dose;
   b. Stimate®: 300 mcg per day.

Approval Duration
Commercial: DDAVP® Injection: 6 months; Stimate®: 12 months
Medicaid: DDAVP® Injection: 6 months; Stimate®: 12 months

D. Nocturia (must meet all):
1. Diagnosis of nocturia due to nocturnal polyuria;
2. Age ≥ 18 years;
3. Member has normal serum sodium concentration prior initiation of therapy;
4. Request is for Nocdurna® or Noctiva™;
5. 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
Commercial: 12 months
Medicaid: 12 months

II. Continued Therapy Approval

A. All Indications in Section I (must meet all):
1. Member is currently receiving medication that has been authorized by RxAdvance or member has

previously met initial approval criteria listed in this policy;
2. Member is responding positively to therapy;
3. For Nocdurna®, Noctiva™: Member has normal serum sodium concentration;
4. If request is for a dose increase, new dose does not exceed (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 (27.7 mcg for women, 55.3 mcg for men);
   d. Noctiva™: 1.66 mcg per day (1 bottle per 30 days).

Approval Duration
Commercial: DDAVP® Injection: 6 months; Stimate®/Nocdurna®/Noctiva™: 12 months
Medicaid: DDAVP® Injection: 6 months; Stimate®/Nocdurna®/Noctiva™: 12 months

III. Appendices

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
Below are suggested therapeutic alternatives based on clinical guidance. Please check drug formulary for preferred agents and utilization management requirements.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
desmopressin acetate oral tablets	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;
  - Known hypersensitivity to desmopressin acetate or to any of the components of DDAVP®;
  - 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 night-time 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.

References

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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 February 12, 2021.
6. Noctiva Prescribing Information. Chesterfield, MO: Avadel Specialty Pharmaceuticals, LLC; December 2017. Available at: www.noctiva.com. Accessed February 12, 2021.
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Review/Revision History	Review/Revision Date	P&T Approval Date
Policy established.	01/2020	02/07/2020
Policy was reviewed: 1. Clinical policy title was updated. 2. Line of business policy applies to was updated to all lines of business. 3. Initial and continued approval criteria was updated to include “Member	02/12/2021	03/09/2021

has normal serum sodium concentration prior to initiation of therapy". 4. Continued therapy criteria II.A.1 was rephrased to "Member is currently receiving medication..". 5. Updated Appendix C: added Known hypersensitivity to desmopressin acetate or to any of the components of DDAVP®. 6. References were reviewed and updated.		