

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

Reference Number: CP.PHAR.214

Effective Date: 05.01.16

Last Review Date: 11.18

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[®], Noctiva[™]) is a synthetic vasopressin analog.

**For Health Insurance Marketplace (HIM), Noctiva is non-formulary and cannot be approved using these criteria; refer to the formulary exception policy, HIM.PA.103.*

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.

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 health plans affiliated with Centene Corporation[®] that DDAVP injection, Stimate, and Noctiva 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 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 \geq 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:

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 (factor VIII deficiency);
2. Prescribed by or in consultation with a hematologist;
3. Age \geq 3 months;
4. Factor VIII coagulant activity levels are $>$ 5%;
5. Request is for DDAVP injection or Stimate for one of the following (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;
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:

Medicaid/HIM – 6 months

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 \geq 3 months;
4. Factor VIII coagulant activity levels are $>$ 5%;
5. Request is for DDAVP injection or Stimate for one of the following (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;
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:

Medicaid/HIM – 6 months

Commercial – DDAVP injection: 6 months or to member’s renewal date, whichever is longer; Stimite: 12 months

D. Nocturia (must meet all):

1. Diagnosis of nocturia due to nocturnal polyuria;
2. Age \geq 18 years;
3. Request is for Noctiva;
4. Dose does not exceed 1.66 mcg per day (1 bottle per 30 days).

Approval duration:

Medicaid/Commercial – 12 months

HIM – Refer to HIM.PA.103

E. Other diagnoses/indications

1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial, HIM.PHAR.21 for health insurance marketplace and CP.PMN.53 for Medicaid.

II. Continued Therapy

A. All Indications in Section I (must meet all):

1. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
2. Member is responding positively to therapy;
3. 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. Stimite: 300 mcg per day;
 - c. Noctiva: 1.66 mcg per day (1 bottle per 30 days).

Approval duration:

Medicaid – 12 months

HIM – 12 months for DDAVP injection or Stimite (*refer to HIM.PA.103 for Noctiva*)

Commercial – DDAVP injection: 6 months or to member’s renewal date, whichever is longer; Stimite/Noctiva: 12 months

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

1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy.

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

2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial, HIM.PHAR.21 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.PHAR.21 for health insurance marketplace and CP.PMN.53 for Medicaid or evidence of coverage documents;

B. Noctiva for primary nocturnal enuresis.

IV. 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

DDAVP injection:

- Contraindication(s): moderate to severe renal impairment (creatinine clearance < 50 mL/min), hyponatremia or a history of hyponatremia
- Boxed warning(s): none reported

Stimate:

- Contraindication(s): none reported
- Boxed warning(s): none reported

Noctiva:

- Contraindication(s): 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 m²; 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
- Boxed warning(s): 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.

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, 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 nasal spray (Noctiva)	Nocturnal polyuria	One spray in either nostril approximately 30 minutes before bedtime; dose varies by age and hyponatremia risk: <ul style="list-style-type: none"> • 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

VI. 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)

VII. References

1. DDAVP Injection Prescribing Information. Parsippany, NJ: Ferring Pharmaceuticals; April 2018. Available at: <https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=651f6fee-a2c7-431b-8d5d-58b156c72244>. Accessed July 3, 2018.
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 July 3, 2018.
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 November 29, 2017.
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 November 29, 2017.
6. Noctiva Prescribing Information. Chesterfield, MO: Avadel Specialty Pharmaceuticals, LLC; December 2017. Available at: www.noctiva.com. Accessed July 2, 2018.
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.

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
Policy split from CP.PHAR.12.Blood Factors and converted to new template. Specific approval periods are added: 6 months initial/renewal. Added type 2 vWD indication. Age restrictions added per PI. Stimate removed as it is no longer on PA. Specialist reviewed.	04.01.16	05.16
Trauma/surgery is separated from diabetes insipidus (DI). The nephrogenic DI restriction is removed. Age restriction is removed. The designation “mild to moderate” is removed from VWD. Safety information is removed with the exception of CrCl; current hyponatremia as a contraindication is added.	04.01.17	05.17

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Wording for uses and approval periods for all blood factor products made consistent across all policies. Efficacy statement added to renewal criteria. Hemophilias are specified as “congenital” versus “acquired” across blood factor policies where indicated. Reviewed by specialist-hematology/internal medicine		
1Q18 Annual Review - Policies combined for Centene Medicaid and Marketplace lines of business. Marketplace policy included Stimote. - Added age limit for diabetes insipidus.	11.29.17	01.18
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.	01.23.18	
4Q annual review: added commercial line of business; added Noctiva; modified Medicaid/HIM approval durations to 6 months for initial and 12 months for continued for all indications except nocturia; references reviewed and updated.	07.03.18	11.18

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.

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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.

For Health Insurance Marketplace members, when applicable, this policy applies only when the prescribed agent is on your health plan approved formulary. Request for non-formulary drugs must be reviewed using the formulary exception policy.

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